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Epidemiology of tumors in dogs in the capital of the state of Mexico from 2002-2016

[*Epidemiologia de tumores em cães da capital do Estado do México durante o período de 2002-2016*]

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ABSTRACT

A retrospective and cross-sectional study of canine tumors was performed in the capital of State of Mexico from 2002-2016. Since then, 393 tumors were remitted. Descriptive epidemiology was made from all data: breed, age, sex, and tumor features. Then the risk association between cutaneous and non-cutaneous tumors with variables such as sex, breed, and age were analyzed through an exact Fisher test and Odds ratio. In addition, some characteristics of the canine population were studied under a survey. Of all tumors, skin tumors were the most frequent (59.0%). The group of tumors related to ultraviolet radiation was the most common (15.1%). The frequency of tumors in females was 53%, nevertheless, males had more risk to develop cutaneous tumors (OR=1.88, 1.24-2.84) (0.003). The Pure breeds were the most common (82.5%) and the most frequent age range was > 7 years (54.7%). The survey showed that males (53%) and the age range 1-7 years (62.1%) were the most frequent. Conclusions, age, breed, and sex were identified as the major risk factors for tumorigenesis. Likewise, skin tumors were associated with exposure to ultraviolet radiation, probably to the height of the locality (2667mamls).

Keywords: dog, tumors, epidemiology, skin tumors, ultraviolet radiation

RESUMO

Um estudo retrospectivo e transversal dos tumores caninos foi realizado na capital do Estado do México durante o período de 2002-2016. Desde esse período, 393 tumores foram remetidos. Epidemiologia descritiva foi feita com base em todos os dados: raça, idade, sexo e características do tumor. Em seguida, a associação de risco entre tumores cutâneos e não cutâneos com variáveis como sexo, raça e idade foi analisada por meio do teste exato de Fisher e odds ratio. *Além disso, algumas características da população canina foram estudadas em uma pesquisa. De todos os tumores, os de pele foram os mais frequentes (59,0%). O grupo de tumores relacionados à radiação ultravioleta foi o mais comum (15,1%). A frequência de tumores no sexo feminino foi de 53%, no entanto os machos apresentaram maior risco de desenvolver tumores cutâneos (OR = 1,88; 1,24-2,84) (0,003). As raças puras foram as mais comuns (82,5%), e a faixa etária mais frequente foi >7 anos (54,7%). A pesquisa mostrou que os machos (53%) e a faixa etária de um a sete anos (62,1%) foram os mais frequentes. Conclusões: idade, raça e sexo foram identificados como os principais fatores de risco para a tumorigênese. Da mesma forma, os tumores cutâneos foram associados à exposição à radiação ultravioleta, provavelmente até a altura da localidade (2667m ANM).*

Palavras-chave: cão, tumores, epidemiologia, tumores cutâneos, radiação ultravioleta

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INTRODUCTION

Currently, tumors are one of the main causes of death in the veterinary practice of small species, this is because the survival time has increased in these species as in humans (Fleming *et al.*, 2011; Choi *et al.*, 2016). Epidemiological studies have shown that the most frequent neoplasms in these species are those of the skin, followed by mammary gland, hematopoietic system, and soft tissues (Brønden *et al.*, 2010; Grüntzig *et al.*, 2016). Another important aspect that has generated epidemiology is the knowledge of risk factors that affect the individual, both, genetically and environmentally (Fleming *et al.*, 2011). It is known that animal characteristics such as age, breed, and sex play an essential role in triggering the growth of a neoplasm in the individual. Certain breeds such as Labrador, Boxer, Golden Retriever, Rottweiler, among and others, have a genetic predisposition to cancer (Dobson, 2013). It is also considered that at any age, the individual is susceptible to develop tumors, however, there is a marked predisposition in long-lived animals and this is associated with a progressive accumulation of genetic mutations that lead to cancer (Reif, 2007). About the environmental factors involved in the development of neoplasms, chemical contaminants present in the environment as pyrethroids have been associated with the presence of mammary gland carcinomas (Reif, 2007). Ultraviolet light rays mainly UBVs have also been studied as a cause of squamous cell carcinoma (SCC) in animals with poor skin pigmentation (Reif, 2007). However, in spite of having this information that allows us to have an overview of some risk factors and distribution of the disease, in Mexico the epidemiological information in this species is very limited restricted, being limited to conferences and databases of private veterinary hospitals and universities. A second issue is the lack of knowledge on the essential characteristics of the canine population, for instance, gender, age and breed, as well as aspects that involve pet holding (housing, feeding and health) that can guide us to understand the causes to develop cancer. In Mexico, there are few studies on the canine population characteristics; however, they are guided to the investigation of local zoonotic diseases (Ortega *et al.*, 2007; Kisiel *et al.*, 2016). In Mexico, there are few epidemiological analyses on veterinary oncology published in scientific journals (Fajardo *et al.*, 2013; Salas *et al.*, 2015). In a first article, we published the prevalence of tumors in the dogs of the municipality of Toluca. In this second work, the following eight years were collected to increase the sample size and a survey was carried out to explore some characteristics of the canine population and the possible risk factors involved with tumorigenesis in dogs, all this to be able to enlarge the perspective of oncological behavior in veterinary medicine.

MATERIALS AND METHODS

A retrospective and cross-sectional epidemiological study of tumors in dogs diagnosed by histopathology was performed in the *Centro de Investigación y Estudios Avanzados en Salud Animal* (CIESA-FMVZ-UAEM) through the database compiled in the period 2002-2016. Data on age, breed, sex, and final diagnosis (histogenesis, biological behavior, and tumor type) were analyzed with descriptive statistics using the STATA 7.0 program. Likewise, in order to associate the characteristics of the individual (race, age, and sex) with the localization of the tumors (cutaneous and non-cutaneous), an exact Fisher test was carried out, and to determine the risk of development with these variables, an odds ratio test was used by means of the STATA 7.0 program. Data without identification were discriminated for the tests. All samples received during the period were processed by conventional histochemistry methods and for the diagnosis of specific tumors, special stains such as Fontana, Giemsa, and Periodic Acid Stain (PAS) were made. The diagnosis was made according to the International Histological Classification of Tumors of the Domestic Animals of the World Health Organization and of the Institute of Pathology of the Armed Forces with the cooperation of the American Registry of Pathology (AFIP/OMS, 2004).

Some of the characteristics of the canine population and the possible risk factors involved with tumorigenesis in dogs were evaluated through personal interview surveys conducted with the population from Toluca city. The total number of people to be surveyed was calculated using the finite population sample size formula (Jaramillo and Martinez, 2009). The selection criterion for the people surveyed was that they be

residents of Toluca, regardless the age or gender, and the survey was applied to people without dogs in order to know the number of people who do not have dogs at home. The places where the surveys were carried out were in parks, schools, and private homes. Fifty pilot surveys were applied in a period of 15 days for validation of final survey. The survey consisted of three sections with closed questions, multiple choice or dichotomous response depending on the nature of the question (Jaramillo and Martinez, 2009). The first section of the survey collected information regarding the characteristics of the individual as race breed, age, and sex; the second section was focused on the type of the dogs feeding dogs have; the third, in the type of habitat where they live and if they attended to periodic medical consultations with the veterinary doctor.

RESULTS

A total of 393 tumors were remitted and diagnosed by histopathology in the laboratory during the study period. Skin tumors were the most frequent (59.0%), followed by reproductive tract (16.3%), mammary gland (12.5%) digestive tract (4.6%), lymphatic (3.6%), skeletal-muscle (2.5%), respiratory (1.3%) and endocrine tumors (0.2). Fibroma, mast cell tumor and histiocytoma where the most frequent skin tumors followed by tumors that were associated with exposure to solar radiation (Figure 1).

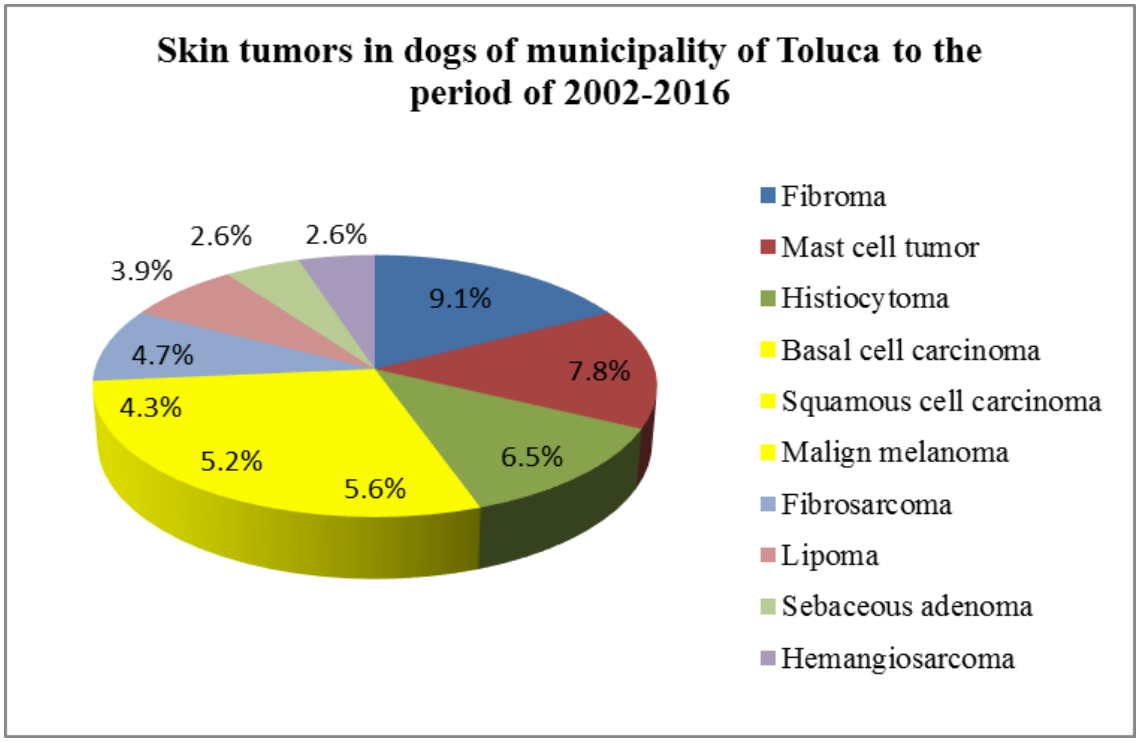

Figure 1. Frequency of the ten most frequent skin tumors of dogs from the municipality of Toluca. The tumors associated with exposure to ultraviolet radiation are shown in yellow.

The results of tumor frequencies by age considering the individual's biological characteristics and histopathological characteristics of the neoplasms are summarized in Table 1. The group of age that had the highest frequency of tumors was: dogs older than 7 years (54.7%) followed by the group from 1 to 7 years (34.6%). In relation to sex, the frequency of tumors was higher in females (52.9%) than males (47.1%). Pure breeds 82.5% were more frequent than mixed breeds 17.5%. The most common pure breed was Labrador (11.4%) followed by Poodle (7.8%) and Schnauzer (6.1%).

The benign neoplasms were more frequent than malignant and were mostly found in females (Table 1), the mixed breeds had the higher frequency 23% (52/224).

Table 1. Frequency of tumors by age considering the biological characteristics of the individual, histopathological and tumor location in dogs from the municipality of Toluca

		AGE n (%)				Total cases n (%)
		< 1 year	1 to 7 years	> 7 years	N/D	
		24 (6.1)	136 (34.6)	215 (54.7)	18 (4.6)	393 (100)
Biological characteristics of the individual						
Sex	Male	13 (3.3)	73 (18.6)	88 (22.4)	5 (1.3)	179 (45.5)
	Female	11 (2.8)	63 (16)	125 (31.8)	9 (2.3)	208 (52.9)
	N/D			2 (0.5)	4 (1)	6 (1.6)
Most common breed		Schnauzer 3 (0.7)	Mixed breed 35 (8.9)	Labrador 30 (7.6)	Mixed breed 6 (1.5)	
Anatomopathological tumoral characteristics						
Biological behavior	Malign	4 (1)	53 (13.5)	91 (23.2)	8 (2)	156 (39.7)
	Benign	20 (5.1)	83 (21.1)	124 (31.6)	10 (2.5)	237 (60.3)
Histogenesis	Epithelial	12 (3.1)	47 (12)	115 (29.3)	7 (1.8)	181 (46)
	Mesenchymal	12 (3.1)	89 (22.6)	100 (25.4)	11 (2.8)	212 (54)
Common localization by tumor site		Skin	Skin	Skin	Skin	Skin
		22 (5.6)	80 (20.4)	115 (29.2)	15 (3.8)	232 (59)

N: number of cases
N/D: no data

Regarding to histogenesis, there were more tumors of mesenchymal than epithelial origin (Table 1). Of the mesenchymal tumors, the majority was benign (148/212) and was more presented in females than in males (106 vs 102). The mixed breed dogs were the ones that presented the most type of tumor (24%). Of the tumors of epithelial origin, 54.1% were benign, presented more in females (102/181) (56.3%) and the most affected breed was Poodle (13.2%).

The results demonstrated that pure breeds had more risk of development cutaneous tumors than those in other organs (OR=3.7, 2.13 – 6.43). In contrast, the mixed breed dogs presented more risk of developing tumors in another organ mainly in the reproductive system (56.2%) and mammary gland (4.3 %) (Table 2).

Significant differences were found (P 0.002) among the age groups; the group under 1-year-old *vs* the groups of 1 to 7 years and > 7 years, where more than 64% of the tumors were cutaneous. In puppies, histiocytomas (16.6%), pilomatricomas (16.6%), fibromas (12.5%) and squamous cell carcinomas (4.1%) were the most frequent cutaneous tumors.

As in race and age, the sex variable also revealed significant differences (P 0.003). In females, homogeneous numbers of tumors were observed. However, males showed more risk to develop cutaneous tumors compared to non-cutaneous tumors (OR=1.88, 1.24 – 2.84).

The 1500 surveys applied to inhabitants from the municipality of Toluca revealed that: 1,012 (67.5%) people responded positively to having one or more dogs at home, while 488 (32.5%) reported having no dog at home. The male dogs were more numerous than females (Table 3). Most people had adult dogs of 1 to 7 years (62.1%). The majority of dogs were pure breed (62.7%), but a large percentage was mixed breed (37.3%). Chihuahua was the most frequent pure breed (6.7%) followed by Schnauzer (6.6%), Poodle (4.8%) and German shepherd (4.3%). More than 50% of dogs were fed with commercial diets (Tab 3) and lived outside the home, exposing them to certain solar radiation a day, despite having some type of roof provided by the owners (Table 3). Only 47.4% of people took their dogs to veterinary medical visits twice a year and 32.3% to surgical neutering.

Table 2. Risk of development cutaneous tumors in relation to the breed, age and sex of dogs in the municipality of Toluca

Variable	Cutaneous (%)	Non-cutaneous (%)	OR	IC
Breed				
Pure breed	204 (64.96)	110 (35.04)	3.7*	(2.13 – 6.43)
Mixed breed	23 (33.3)	46 (66.7)	1.0	
AGE				
< 1 year	22 (91.67)	2 (8.33)	7.7*	(1.71 – 34.07)
1 – 7 years	80 (58.82)	56 (41.18)	1.0	
> 7 years	115 (53.49)	100 (46.51)	0.80	(0.80 - 1.91)
Sex				
Females	108 (51.92)	100 (48.08)	1.88*	(1.24 – 2.84)
Males	120 (67.04)	59 (32.96)	1.0	

OD: odds ratio
CI: confidence interval
*Development risk

Table 3. Percentage of characteristics of the canine population according to the sex of the municipality of Toluca obtained through the survey

	Sex (%)		Total of survey (%)
	Male	Female	
	53.4	46.6	100.0
AGE			
< 1 year	11.4	7.7	19.1
1 to 7 years	32.7	29.4	62.1
> 7 years	9.3	9.4	18.7
N/D	0	0.1	0.1
Breed	Mixed Breed	Mixed Breed	
	18.2	19.1	
Feeding			
Commercial dog food	25.6	25.0	50.6
Homemade food	7.1	4.6	11.7
Combination feeding	20.7	17.0	37.7
N/D	0	0.1	0.1
Habitat			
Inside home	19.7	18.4	38.1
Outside home with shade	30.1	24.1	54.2
Outside home without shade	2.6	3.0	5.6
Inside and outside	0.9	1.1	2.0
N/D	0.1	0.0	0.1
Medical visits			
Two per year	24.4	23.0	47.4
Once per year	24.8	19.8	44.6
Per disease	4.2	3.8	8.0
Neutering			
Yes	15.4	16.9	32.3
No	37.9	29.7	67.6
N/D	0	0.1	0.1

N/D: no data

DISCUSION

The cutaneous tumors were the most frequent in this article. The high frequency could be explained because cutaneous tumors are more visible and clinically explorable, this agrees with other reports (Santos *et al*., 2013; Choi *et al.*, 2016; Grüntzig *et al.,* 2016). Into the group of the cutaneous tumor; the tumors associated with exposure to solar radiation were the most frequent. This may be due to the housing conditions of the dogs from this locality since more than 50% of the dogs live outside the home, exposing them to certain solar radiation a day despite having some type of roof provided by the owners. In human medicine, the main risk factor for these tumors is the exposure to B ultraviolet rays. Some studies in dogs support a possible association between these risk factors and these tumors (Reif, 2007; Santos *et al*., 2012; Tomoko *et al*., 2016).

According to the Atmospheric Monitoring System in Toluca, at certain hours of the day, it can reach 11 points of UV index, this is largely associated with being the highest capital of Mexico and North America with an altitude of 2667 meters above sea level (mamsl). A long exposure (10-25 minutes) could trigger skin cancer associated with the altitude which put these animals to a higher risk to develop cutaneous tumors associated to the direct and high exposure of UV-ray.

The highest frequencies of tumors observed in dogs older than 7 years are comparable to those published in Mexico and other countries (Fajardo *et al*., 2013; Brønden *et al*., 2010; Santos *et al*., 2013), which have been associated with more prolonged exposure to risk factors and thus to mutations accumulated in cell cycle regulatory genes and other cell genes (Reif, 2007). Further, the survey showed most people had adult dogs. This reflects the exponential increase of tumors in adult dogs from this municipality.

By the other hand, puppies were more at risk to developing benign cutaneous tumors of young dogs as histiocytomas (16.6%) and pilomatricomas (16.6%) (AFIP/OMS, 2004). Other tumors observed in puppies were fibromas (12.5%) and squamous cell carcinomas (4.1%) that increase with age (Grüntzig *et al*., 2016). However, in this study, the SCC could be associated with the sun exposure that the dogs from this municipality have and by chronic inflammations in the case of fibroma.

The frequency of tumors was higher in females (52.9%), these results were influenced by the presence of mammary gland tumors, which were third most frequent tumors and were not occur in males. It is worth noting that mammary gland tumors were more frequent in Poodle (24.4%), followed by Cocker (12.2%). Similar results had shown an association between Poodles and breast tumors (Salas *et al*., 2015; Choi *et al*., 2016).

Males had more risk to develop cutaneous compared to non-cutaneous tumors (OR=1.88, 1.24 – 2.84) contrary to that found by Grüntzig *et al*. (2016) and Brønden *et al*. (2010). Our data may be influenced by the higher frequency of males in Toluca in agreement with another study conducted in another locality of the country (Kisiel *et al*., 2016). In general, there was not a real sex predisposition for cutaneous tumors. However, Mohamed (2006) reported a greater frequency of histiocytomas and melanomas in males, equivalent to our results (8/15 histiocytomas, 6/11 melanomas).

The most popular dogs in the retrospective study were pure breeds (82.5%) analogous to reported in other articles (Fajardo *et al*., 2013; Santos *et al*., 2013). Nevertheless, in the survey mixed breeds were the most popular breeds, however, there is no information about predisposition of dogs with a lot of genetic variability to a specific tumor; therefore, further research should be done. In the same way, the pure breeds had more risk of development cutaneous tumors than in other organs (OR=3.7, 2.13 – 6.43). These results agree with studies reporting a higher predisposition of pure breeds, such as Labrador, being the most affected in this study (8.7%). This race has a predisposition for fibrosarcomas and mastocytomas (Dobson, 2013). In contrast, the mixed breed dogs presented more risk of development tumors of another organ mainly in the reproductive system (56.2%) and mammary gland (4.3 %) (0.000). In relation to non-cutaneous tumors, TVT was the most frequent tumor (13.74%), and similarly, the most frequent mesenchymal tumor (26%) occurring in the majority of cases in the reproductive system (85.1%). Due to the transmissible characteristics of TVT, this tumor occurs mainly in dogs

without reproductive control such as mixed breed dogs that generally have a wandering behavior that causes its spread (Ganguly *et al*., 2013). The majority of owners from this municipality reported having non-neutered dogs (67.6%), this could reflect that the veterinary services are not economically accessible and the low cost or free spay-neuter governmental programs are insufficient for the entire population. Therefore, the high prevalence of non-neutered dogs in this municipality can be reflected in the high presence of TVT in both street dogs and owned dogs, in addition to the high frequency the mammary gland tumors favored by the presence of hormones (estrogens) (Reif, 2007; Rivera *et al*., 2009).

As reported in the same locality, benign neoplasms were more frequent than malignant and may be associated with the age population of dogs (Fajardo *et al*., 2013). Regarding histogenesis, mesenchymal tumors were more numerous than epithelial tumors; these results differ from other countries (Grüntzig *et al*., 2016; Choi *et al*., 2016), who described a greater number of epithelial tumors. In our case, the increase of mesenchymal origin tumors was due to the high frequency of CTVT.

Finally, regarding eating habits, most people responded to feed their dogs with commercial croquettes diets. In another Mexican city, they (77%) also reported a high frequency of diets based on dry food (Ortega *et al*., 2007). This could be one of the risk or trigger factors associated with increased cancer in pets, due to the growing use of commercial foods as the single base of their nutrition. Commercial dog food contains several carcinogens, mainly free radicals, heterocyclic amines, and polycyclic aromatic hydrocarbons (PAHs) formed during any stage of the food manufacturing and have been related to the development of colon-rectal cancer, lymphoma and mammary gland in rodents (Dan *et al*., 2012).

CONCLUSIONS

Most of our results on the frequencies of tumors are comparable to those reported in other countries; however, population characteristics vary from place to place. Therefore, performing endemic studies allows a deeper understanding of the factors involved in tumorigenesis. Proof of this was the close association found in the breed, age and sex of the canine population and the diagnosed tumor variants in dogs. The close association of these studied variables in the presentation of skin tumors was confirmed by the found high incidence of tumors associated with this risk factor, and the housing conditions that dogs in this zone suffer. Our results provide an overview of the possible risk factors for tumorigenesis in this city and the effect they are causing in companion animals. This work generated invaluable data that opens a gap for future research; in particular, on the effects of ultraviolet rays emitted in this municipality.

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