PATHOMORPHOLOGICAL ANALYSIS OF THE MOST COMMON CANINE SKIN AND MAMMARY TUMOURS

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Abstract. Canine skin and mammary tumours are one of the fastest progressive causes of canine morbidity. Macroscopic and histological analyses of the skin biopsies were performed on 116 canines. The most common tumours were: histiocytoma (11.1%) in young dogs (2.97 years of age), mast cell tumour (9.5%) in middle-aged dogs (7.68 years) and simple mammary carcinoma (14.7%) in older dogs (9.72 years). Females were more affected by simple mammary carcinoma (100%) and by lipoma (66.7%) while males were more affected by hepatoid gland adenoma (83.3%) and by histiocytoma (61.5%). The prevalence of tumours in purebred dogs accounted for 73.3% and in mongrels 26.7%. The skin tumours were most frequently located in the limb regions (28.5%). Among these, 50.8% were benign and 49.2% were malignant. The multiple tumours identified in 27.6% of the examined dogs were comprised of skin melanomas (75.0%), hepatoid gland adenomas (66.7%) and sebaceous gland adenomas (50.0%).

Keywords: dog, tumour, skin, mammary gland, pathomorphology

Introduction. Skin tumours are the most common tumours in dogs (Murphy, 2006; Chikweto et al., 2011) accounting for approximately 30% of all diagnosed tumours (MacDonald et al., 2008).

Mammary glands are the second most common site for tumour development subsequent to dermal sites in dogs (Sontas et al., 2009) and account for approximately 82% of all tumours in reproductive organs (Gobello, Corrada, 2001; Kovacevic et al., 2005).

The international histological classification of tumours in the skin, melanocytic and soft tissues of domestic animals was modified by the World Health Organisation (WHO) in 1998 (Goldschmidt et al., 1998; Hendrick et al., 1998; Sharif, 2006).

The incidence of benign skin tumours in dogs is found 10 times more frequently than in cats. Malignant tumours in dogs are considerably less frequent (from 25 to 35%) than in cats (approximately 75%) (MacDonald et al., 2008; Warland, Dobson, 2011).

In canines, the highest predisposition to tumours occurs in the sixth year of age and with every subsequent year the risk increases (Morris, Dobson, 2001). The incidence of cutaneous histiocytoma, papiloma, follicular and dermoidal cyst in dogs is considerably higher until the age of two years (Goldschmidt et al., 2000; Bomhard, 2001; Fulmer, Mauldin, 2007). Squamous cell carcinomas are more common in older dogs (Lakatos et al., 2000).

The mammary gland is a modified sweat gland (Krstic et al., 2004). The critical age for mammary tumours in females is the eighth year of life and the risk increases with each subsequent year. The incidence of malignant mammary tumours is higher in middle and older age females. At 9 to 11 years of age, dogs have maximum risk of developing mammary tumours (Gobello, Corrada, 2001; Sontas et al., 2009; Gerry, 2009).

Sexual differentiation is an important factor for dogs in diagnosing perianal gland tumours which are considerably more common in males (89%) than in females (11%) (Goldschmidt et al., 2000; Pakhrin et al., 2007). Cutaneous histiocytoma and melanoma are also more common in males (52–69%) than in females (31–48%) (Bomhard, 2001). Lipomas are more common in females (68%) than in males (32%) (Sharif, 2006). In females, malignant mammary tumours account for approximately 50% of all tumours. No significant sex-linked relationship was found in diagnosed skin tumours (Goldschmidt, Shofer, 1992; Bomhard, 2001; Pakhrin et al., 2007).

It is notable that some breeds of pedigree dogs appear to be at increased risk of certain types of cancer suggesting underlying genetic predisposition to cancer susceptibility (Dobson, 2013). The malignant cutaneous histiocytoma was initially diagnosed in Miniature Schnauzers yet today it is diagnosed in various breeds of dogs (Sharif, 2006). Mast cell tumours are more often diagnosed in Boxers, pugs and Boston Terriers (Sharif, 2006). The incidence of squamous cell carcinoma is higher in bloodhounds, Giant Schnauzers and poodles (Aiello, 1998; Dobson, 2013). Mammary gland tumours can be diagnosed in females of all breeds yet it is assumed that mongrel females are less affected (Gobello, Corrada, 2001). The predisposition to mammary gland tumours is higher in female Poodles, English Setters, Pointers, Fox Terriers, Boston Terriers, Cocker Spaniels, Afghan Hounds, German Shepherds, Miniature Poodles, Toy Poodles, Maltese Bichons, Chihuahuas, Beagles, Dachshunds, West Highland White Terriers, and Yorkshire Terriers (Perez et al., 1998; Gobello, Corrada, 2001; Sontas et al., 2009).

Skin tumours are classified into two categories: tumours depending on anatomical location (head, neck, limb, back, abdominal, perianal, and tail areas) and tumours indifferent to anatomical location (Bomhard, 2001; Sharif, 2006). Sharif M. (2006 m.) in his PhD thesis supplemented this classification and included the mammary gland area (Sharif, 2006). The anatomical location means that the prime cells of a certain type of tumour occur namely in that location. For example, the

anal sack tumours occur only in the perianal area. Perianal tumours may develop around the anus, on the upper and lower parts of the tail, in the preputium area or in the caudal region of hind legs (Williams et al., 2003). Ceruminous gland tumours are common only in the area of ear canal (Goldschmidt et al., 2000; Sharif, 2006). The tumours of eccrine glands develop in the footpad areas. Sebaceous gland adenoma is common in head area (49.5%). Trichoblastomas are often diagnosed in the head and neck areas (Sharif, 2006).

Usually tumours are single yet there are many tumours occurring simultaneously in a few locations. The number of tumours on the skin surface is a very important factor identifying and diagnosing malignancy according to TNM classification (MacDonald et al., 2008). Multiple skin tumours often are indications of metastases in other tissues (Warland, Dobson, 2011).

Many researchers have reported the following as the most commonly identified skin tumours in dogs: mast cell tumour (mastocytoma) (7–21%) (Webster et al., 2006; Sharif, 2006; Romansik et al., 2007; Warland, Dobson, 2011); hepatoid gland adenoma (approximately 18% – Goldschmidt, Shofer, 1992); (5.4% – Sharif, 2006); lipoma – 6–8% (Bomhard, 2001; Sharif, 2006); sebaceous cells hyperplasia and gland adenoma (4–7% – Bomhard, 2001); (2.8% - Sharif, 2006); histiocytoma (>10% - Gorman, 1996); (16.4% – Sharif, 2006); melanocytic tumours (6% – Bomhard, 2001); (2.7% – Sharif, 2006); squamous cell carcinoma (4–18% - Gorman, 1996); fibrosarcoma (9–14% – Gorman, 1996); (3.9% – Sharif, 2006); basal cell tumours (4–6 % – Bomhard, 2001).

The objective of the presented study was to conduct a pathomorphological analysis of skin and mammary tumours in dogs and to evaluate the incidence of tumours in relationship to the age, sex and breed of dogs, anatomical location and number of tumours.

Material and methods. The specimens of skin tumours in dogs were selected randomly. 116 specimens of mammary and skin tumours were collected after surgical treatment of dogs from veterinary clinics. Formalin buffer solution 10% was used as a fixative. A record was filled in with the data about the age, sex and breed of dogs, number and location of tumours and growth characteristics. The tumour specimens were prepared for histopathological examination using the automated tissue processor (Shandon Pathcentre, UK, 2004). Paraffin blocks were made using paraffin block shaper (CD 1000, Italy, 2004). The paraffin blocks were cut into 4 µm thick sections using a semi-automated microtome (Shandon Finesse ME, JK, 2004). The paraffin sections were straightened in a 39 C° water bath and dried in a thermostat for 12 hours at 37 C° (Jouan Innovens, France, 2004). The paraffin sections were then stained using the standard hematoxylin-eosin staining method (Kiernan, 2008).

Microscopic analysis was performed using a light microscope. The view was described in detail and photographed (Olympus DP12-2). The final histological diagnosis was made according to the origin and differentiation of tumour cells.

Statistical analysis was performed using statistical programs „Microsoft Office Excel 2007" and „IBM SPSS Statistics 19". The parameters chosen for tumour characteristics were as follows: mean, standard deviation, mode, median, and maximum. The comparison between groups was performed using "crosstab" and "comparing means" functions of "IBM SPSS Statistics 19" program.

Results. A total of 116 specimens of skin and mammary tumours in dogs (56 males and 60 females) were examined. Benign tumours accounted for 50.8% and malignant tumours for 49.2% of the total.

The age of dogs at detection of mammary and skin tumours ranged from 6 months to 19 years. The dogs were classified into eight age groups (every two years till 14 years of age and older). The determined highest incidence (20.7%) of mammary and skin tumours was in the fourth age group (6 to 8 years of age) (Fig. 1).

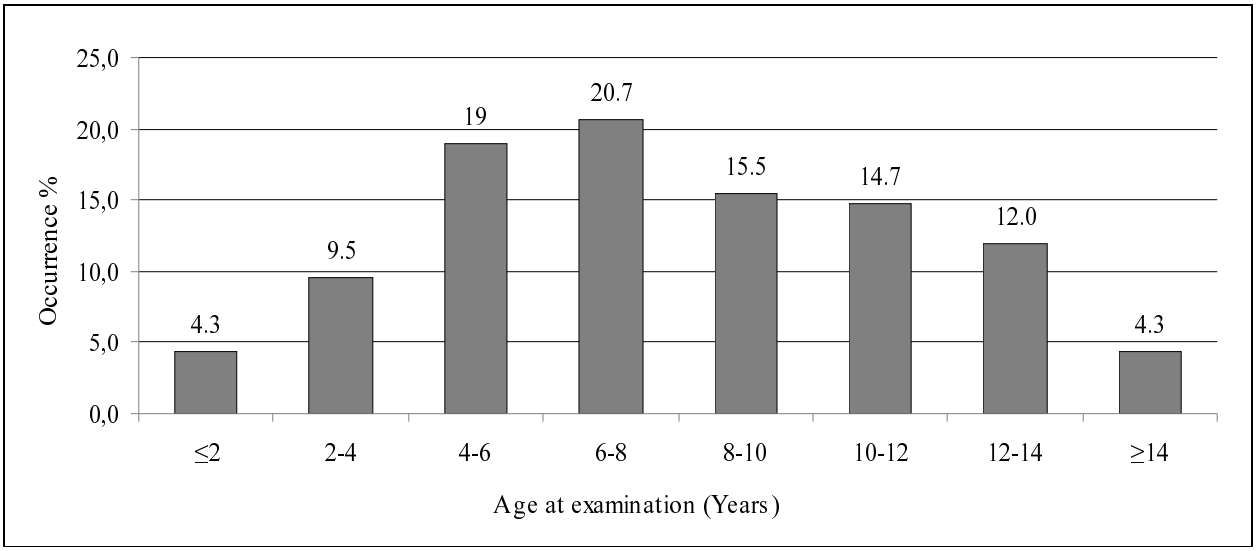

Fig. 1. **Occurrence of skin and mammary tumours (%) in dogs by age groups** (n-116)

Based on statistical analysis, the determined mean age was 7.59 years, standard deviation ± 3.69 years, median 7.0 years, mode 6 years, age of the youngest dog 0.5 years and the age of the oldest dog 19 years (Table 1).

The young dogs mainly were affected by cutaneous histiocytoma. Mast cell tumour, fibroma, lipoma were most common among the dogs of medium age. Melanoma, squamous cell carcinoma and simple mammary carcinoma were most common among older dogs (Table 2; Fig. 3).

Table 1. **Data on the age of the examined dogs**

Number of dogs	116
Mean age of dogs (years)	7.59
Standard deviation (years)	±3.69
Youngest dog (years)	0.5
Oldest dog (years)	19
Median (years)	7.0
Mode (years)	6

Table 2. **Distribution of skin and mammary tumours by age group**

Type of tumour	Mean age (y)	Standard deviation (y)	Number of cases	%
Histiocytoma	2.97	1.90	13	11.1
Trichoblastoma (basal	5.64	0.9	7	7.5
Keratoacanthoma	7.20	2.61	5	4.2
Mast cell tumours	7.68	3.49	11	9.4
Fibroma	7.80	3.27	5	4.2
Fibrosarcoma	8.20	2.68	5	4.2
Lipoma	8.48	1.99	6	5.2
Melanoma	9.00	3.56	4	3.5
Hepatoid gland adenoma	9.17	2.64	6	5.2
Squamous cell carcinoma	9.50	2.29	3	2.6
Simple mammary	9.72	3.19	17	14.7
Sebaceous gland	14.13	3.97	4	3.5
Other tumours	-	-	30	25.8
Total	7.59	3.69	116	100

Mammary and skin tumours were more common in females (51.7%) than in males (48.3%). The distribution of skin and mammary tumours in relation to sex and according to anatomical location is represented in Fig. 2.

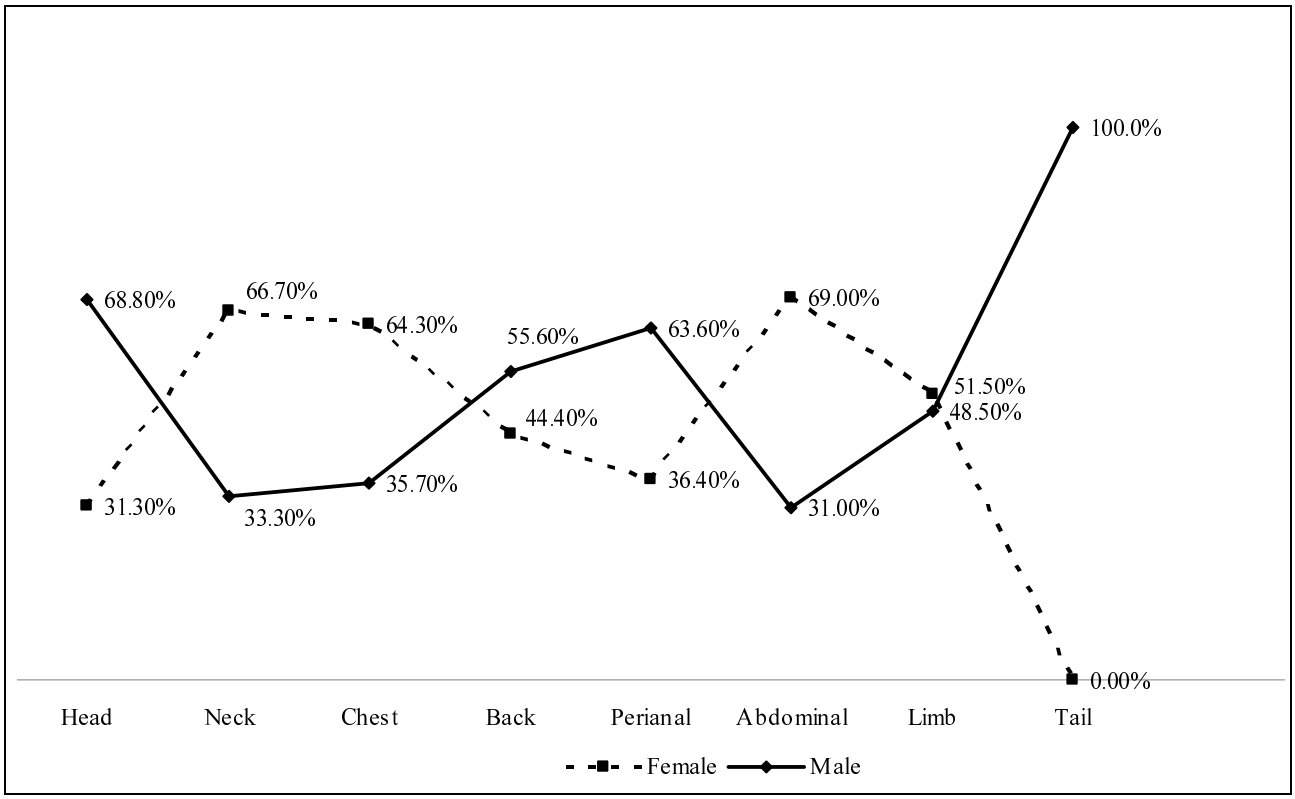

Fig. 2. **Distribution of skin and mammary tumours in relation to sex and according to anatomical location**

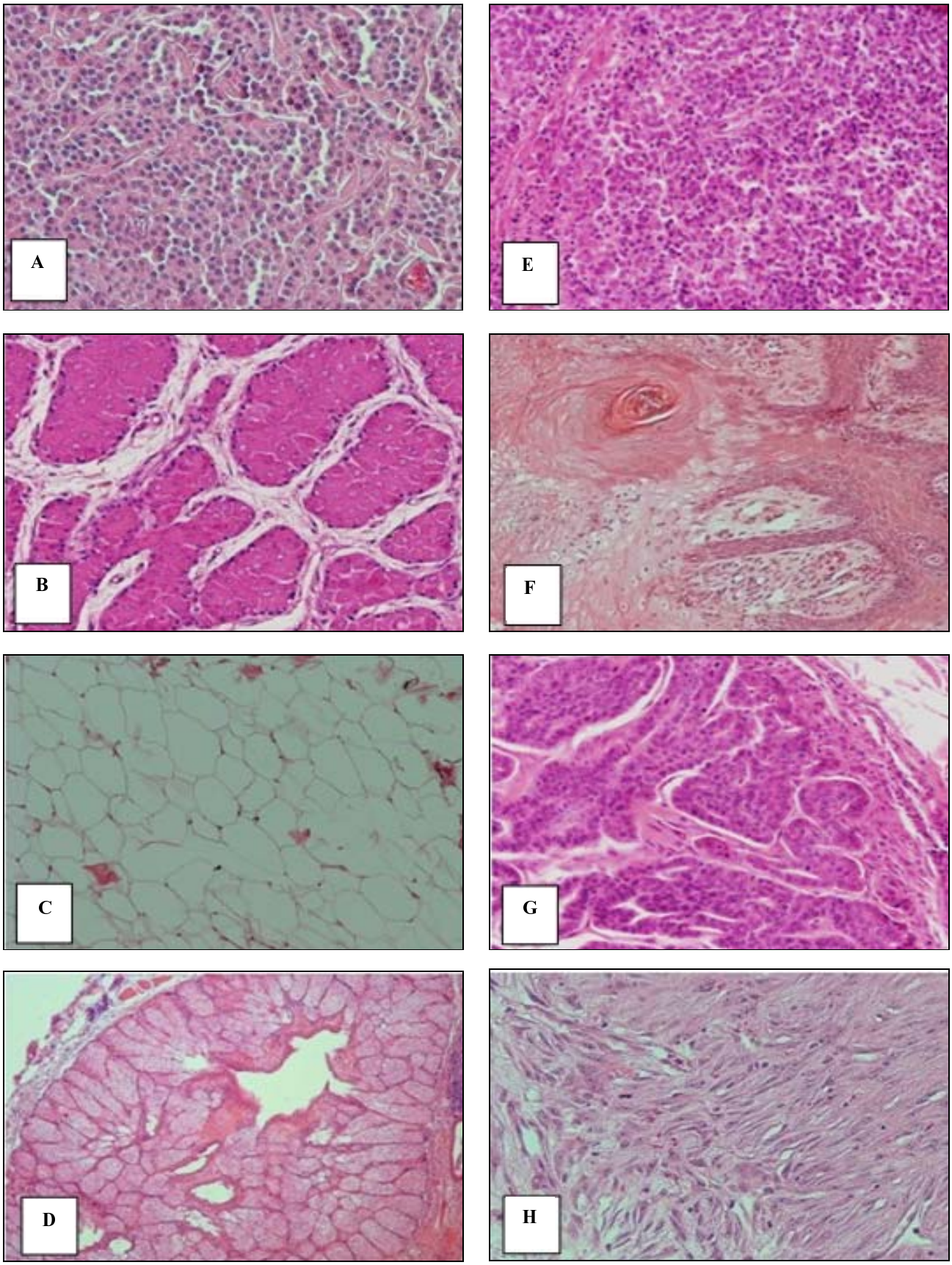

Fig. 3. **Pictures of histological images of the most common skin and mammary tumours in dogs** (H/E):
A – mast cell tumour, (X 200; B – perianal gland adenoma (X 200); C – lipoma (X 100); D – sebaceous gland adenoma (X 50); E – histiocytoma (X 200); F – squamous cell carcinoma (X 100); G – simple mammary carcinoma (X 200); H – fibrosarcoma (X 200).

Males are more frequently affected by cutaneous histiocytoma and hepatoid gland adenoma whereas females are more frequently affected by simple mammary carcinoma and lipoma (Table 3; Fig. 3).

Skin and mammary tumours in purebred dogs accounted for 73.3% whereas in mongrel breeds they accounted for only 26.7%. The distribution of the incidence of skin and mammary tumours in purebred dogs was as follows: in German Shepherds 6.9%, in Yorkshire Terriers and boxers 4.3%, in Labrador Retrievers, poodles, Dachshunds and French Bulldogs 3.5% each, and in other breeds 30.1%.

Distribution of the anatomical location of tumours showed that they most commonly develop in the limb area (28.5%) (Fig. 4).

Incidence of skin and mammary tumours by histological diagnosis according to anatomical location is represented in Table 4.

Table 3. **Distribution of mammary and skin tumours by sex of dogs**

Histologic diagnosis	Incidence of tumours (%)		Incidence of tumours (cases)	
	Female	Male	Female	Male
Simple mammary carcinoma	100.0	0.0	17	0
Histiocytoma	38.5	61.5	5	8
Mast cell tumour	45.5	54.5	5	6
Lipoma	66.7	33.3	4	2
Hepatoid gland adenoma	16.7	83.3	1	5
Fibroma	40.0	60.0	2	3
Fibrosarcoma	0	100.0	0	5
Keratoacanthoma	80.0	20.0	4	1
Melanoma	0	100.0	0	4
Other tumours	48.6	51.4	18	19
Total	51.7	48.3	60	56

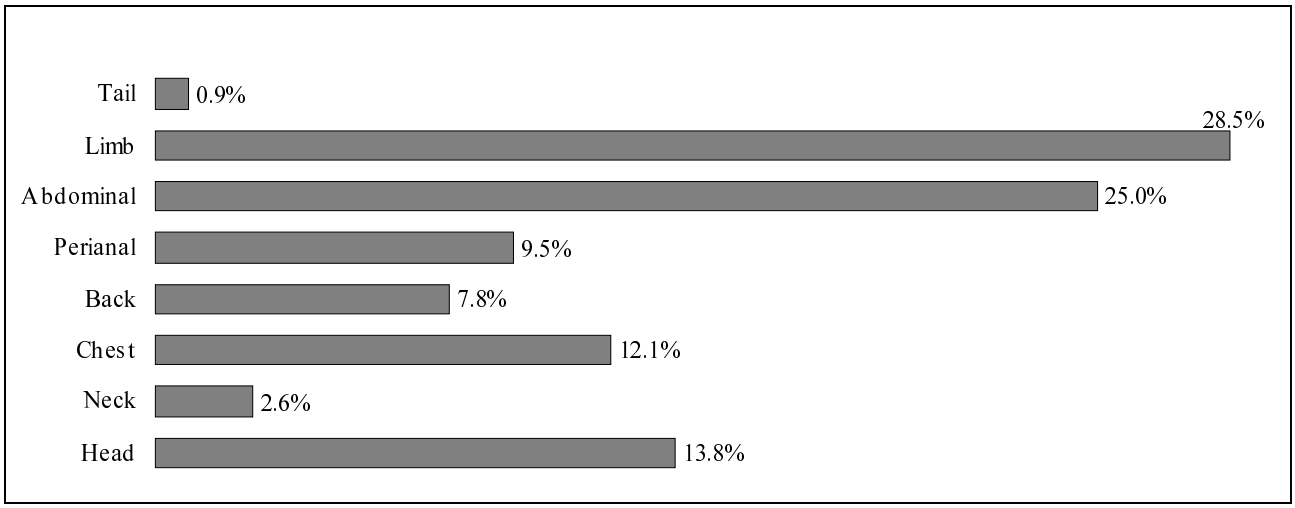

Fig. 4. **Distribution of skin and mammary tumours according to anatomical location (%)**

Table 4. **Incidence of skin and mammary tumours (%) by histological diagnosis according to anatomical location**

	Simple mammary carcinoma	Fibroma	Fibrosar-coma	Histio-cytoma	Lipoma	Mast cell tumours	Hepatoid gland adenoma	Squamous cell carcinoma	Other types of tumour	Total
Head	0	0.9	0	1.6	0	1.6	0	0	9.7	13.8
Chest	3.5	0.9	0	0.9	0.9	0.9	0	0.9	4.1	12.1
Back	0	0	0	0.9	0	0.9	0	0.9	5.1	7.8
Perianal	0	0	0	0	0.9	0	5.2	0	3.4	9.5
Abdominal	11.2	0	0.9	0	1.6	1.6	0	0	9.7	25.0
Limb	0	2.4	3.3	7.7	0.9	4.4	0	0.9	8.9	28.5
Other	0	0	0	0	0.9	0	0	0	2.4	3.3
Total	14.7	4.2	4.2	11.1	5.2	9.4	5.2	2.6	43.3	100

Single tumours were diagnosed in 72.4% of dogs whereas multiple tumours were detected in 27.6% of examined dogs. Multiple tumours accounted for 75.0% in the cases of skin melanoma, 66.7% in the cases of hepatoid gland adenoma, 50.0% in the cases of sebaceous gland adenoma, 47.1% in the cases of simple mammary carcinoma, 42.9% in the cases of squamous cell carcinoma, 40.0% in the cases of keratoacanthoma and 33.3% in the cases of lipoma.

Discussion. Tumours are among the most rapidly progressing causes of death in dogs (Dobson, 2013).

According to the data obtained in the present study, skin and mammary tumours occur in all age groups of dogs. In the groups of dogs aged up to 2 years and more than 14 years skin tumours accounted for 4.3% in each. In Germany, the skin tumours in the group of dogs aged up to 2 years accounted for 15.2% and in the group of dogs aged 14 years and older for 4.6% (Sharif, 2006). According to our data, the mean age of dogs affected by skin tumours is 7.59 years with the possible deviation ±3.69 years. The highest incidence of skin tumours (20.7%) was determined in the group of dogs aged 6–8 years, mode 6 years, and median 7.0 years. In Germany, the mean age of dogs affected by skin tumours is 7.5 years (the highest incidence occurs at the age of 10 years; skin tumours are diagnosed in dogs aged <1 to 18 years) (Sharif, 2006). In Korea, the value is 7.94 (the highest incidence occurs at the age of 8.3 years; skin tumours are diagnosed in dogs aged 3 months to 19 years) (Pakhrin et al., 2007). The increasing age of dogs adds to the risk of skin tumours (Dobson et al., 2002). Among dogs which died being 10 years of age, the tumour induced lesions accounted for 45% (Dobson et al., 2002).

In the present study, cutaneous histiocytoma was more common in young dogs (11.1%). The mean age was 2.97 years. Many authors have reported that in young dogs aged up to 2 years skin histiocytoma accounted for more than 10% (Morris, Dobson, 2001; Bomhard, 2001; Chikweto et al., 2011; Warland, Dobson, 2011). In Germany, the mean age of dogs affected by cutaneous histiocytoma is 2 years (Sharif, 2006), in Australia, 3.9 years (from the age of 5 months to 13 years), in Zimbabve, 5.45 years (from the age of 0.6 years to 12 years) (Mukaratirwa et al., 2005), in West India, 4.7 years (from 3 months to 14 years) (Chkweto et al., 2011). K. Fulmer and E. Mauldin (2007) indicate in his article that cutaneous histiocytoma most frequently occur in dogs aged up to 4 years.

The incidence of mast cell tumours is higher in dogs of middle age (9.4%, 11/116). The mean age of dogs is 7.68 years. The mean age of dogs affected by mast cell tumours in Germany is 7 years (Sharif, 2006), in West India 7.3 years (Chikweto et al., 2011), and in Korea 7.4 years (from the age of 5 months to 16 years) (Pakhrin et al., 2007). Many authors have indicated that the mean age of dogs affected by mast cell tumours is 8 years (Bomhard, 2001; Murphy, 2006; Warland, Dobson, 2011).

Dogs of older age are more predisposed to simple mammary carcinoma; the mean age is 9.72±3.19 years. In Turkey, the mean age of females affected by mammary tumours is 10.3 ±0.2 years (n-150) (from 4 to17 years) (Sontas et al. 2009). Many authors agree that the eighth year of life is the critical age for mammary tumours in females. With every subsequent year, the risk increases (Moulton, 1990; Sontas et al., 2009). The highest incidence of mammary tumours in females is determined in the 9th–11th year of life (Gobello, Corrada, 2001; Sontas et al., 2009). According to our data, among the most frequent skin tumours was sebaceous gland adenoma which accounted for 3.5%; the mean age of affected dogs being 14.13±3.97 years. In Korea, the incidence of sebaceous gland adenoma is 6.68%; the mean age of affected dogs is 10.4 years (diagnosed in dogs aged from 4 months to 16 years) (Pakhrin et al., 2007). The highest incidence of sebaceous gland adenoma was determined in older dogs; the mean age of affected dogs is 9.1 years (Vail, Withrow, 2001).

According to our data, the skin and mammary tumours in females accounted for 51.7% and in males 48.3%. The incidence of mammary tumour (14.7%; 17 cases) in females accounted for 100% and in male not a single case was identified. In males, mammary tumours occur very rarely (MacDonald et al., 2008). The incidence of cutaneous histiocytoma (11.1%) accounted for 61.5% in males and 38.5% in females. In West India, the incidence of cutaneous histiocytoma was determined as equal in females and males (Chikweto et al., 2011). In Germany, the values were 67% in males and only 33% (n-134) in females (Sharif, 2006). Many authors have reported similar results. D. Bomhard (2001) indicated that cutaneous histiocytoma in males accounted for 59.23% and in females for 40.77%. M.H. Goldsmidt (1992) reported that cutaneous histiocytoma in males accounted for 52% and in females 48%. Our study showed that the incidence of hepatoid gland adenoma in dogs (5.2%; 6 cases) accounted for 83.3% in males and 16.7% in females. The incidence of hepatoid gland adenoma in Germany has been reported to account for 88% in males and 16% in females (Sharif, 2006). D. Bomhard (2001) reported the following values: 88.92% in males and 11.8% in females. M.H. Goldsmidt (1992) indicated that the incidence of perianal gland tumours in male dogs was 76% and in females 44%. The occurrence of perianal gland tumours in males is influenced by androgenic hormones (Sanja et al., 2005). According to our data, the incidence of lipoma (5.2%) in females was 66.7% and in males only 33.3%. The findings in Germany showed the incidence to be 63% in females and 37% in males. Females are more predisposed to lipoma than males (Bomhard, 2001).

According to our data, the incidence of skin and mammary tumours in purebred dogs accounted for 73.3% and in mongrels 26.7%. Among the purebreds, German Shepherds accounted for 6.9%. They were affected by mammary tumours, hepatoid gland adenoma and keratoacanthoma accounting for 1.7% each. Toy Terriers, Dachshunds, Yorkshire Terriers, and Boxers were mainly affected by cutaneous histiocytoma and mast cell tumour.

In Germany, the reported incidence of mentioned tumours in German Shepherds was 7.2% and in Boxers 4.4% (Sharif, 2006). Many authors from different geographical regions have indicated that mammary tumours are more common in Poodles, Spaniels, English Setters, German Shepherds and Dachshunds (Euler, 2011; Dobson, 2013). Post mortem examination of Boxers has shown that tumour induced lesions accounted for 41.9% (Walter, Schwegler, 1992). Boxers are highly predisposed to mast cell tumours (Warland, Dobson, 2011; Dobson, 2013). German Shepherds are at a greater risk to be affected by hemangiosarcoma (Dobson, 2013). Large breed dogs are at a greater risk to be affected by subcutaneous tumours. Post mortem examination of Dachshunds showed that tumour induced lesions made up 16.7% (Walter, Schwegler, 1992). The differences of reported data on the incidence of skin tumours in breeds of dogs might have appeared due to different popularity of certain breeds in certain geographical regions.

Our study showed that skin and mammary tumours of dog located in the limb area 28.5%, in the abdominal area 25%, in the perianal area 9.5%, and in the back area 7.7%. In West India, the most common anatomical site of tumour development was determined in the trunk area. The parts of body characterised by lower incidence of tumours was arranged in the following sequence: legs, head, neck, etc. (Chikweto et al., 2011). In Korea, tumours in the trunk area were 30.8%, head and neck areas 20.9%, perianal area 8.59%, tail area 3.91% (Pakhrin et al., 2007). In Germany, tumours in the limb areas were 34.7%, head area 23.8%, perianal area 9.6%, chest area 8.2%, neck area 7.8%, back area 6.7% and abdominal area 5.6%. Tumours in other areas were >5% (Sharif, 2006). The different distribution of tumours in terms of anatomical location may be influenced by different climate of geographical regions and different classifications used by researchers. A. Chikweto (2011) has reported that in West India the greatest number of skin tumours in dogs was determined in the trunk area (the percentage has not been indicated). According to M. Sharif's data (2006; Germany), skin tumours in the back area of dogs comprised only 6.7% (the trunk area is divided into abdominal, chest, back and perianal areas).

Our data showed that benign skin and mammary tumours in dogs comprised 50.8% and malignant 49.2%. In West India, the ratios of benign and malignant tumours were 61.7% vs 38.3% (Chikweto et al., 2011). In Korea, the ratios were 69.25% vs 30.7% (Pakhrin et al., 2007). In Turkey, the ratio of benign and malignant mammary tumours in females was 12.3% vs 78.3% whereas hyperplasia comprised 8.0% (Sontas et al., 2009).

Single tumours were diagnosed in 72.4% of dogs and multiple tumours 27.6%. The multiple tumours affected by melanoma comprised 75.0%, hepatoid gland adenoma 66.7%, simple mammary carcinoma 47.1% and squamous cell carcinoma 42.9%. During a similar investigation conducted in the northern part of Greece single skin tumours were diagnosed in 80.5% of dogs and multiple skin tumours 19.5% of dogs (n-174) (Kadrymidou et al., 2002). Multiple skin tumours tend to be malignant (lymphoma, melanoma, mast cell tumour) (Murphy, 2006). Apocrine sweat gland adenocarcinoma manifested as multiple skin tumours in only 11% of cases (Simko et al., 2003). Among benign skin tumours keratoacanthoma manifested as multiple tumours (MacDonald et al., 2008). Multiple mammary glands tumours are not always malignant (Sontas et al., 2009).

Conclusions

1. The age, sex and breed of dogs and anatomic location and number of tumours are factors which markedly affect the incidence of skin and mammary tumours.
2. The incidence of skin and mammary tumours increases in older dogs.
3. Young dogs are more predisposed to skin histiocytoma, dogs of middle age to mast cell tumours and older dogs to simple mammary carcinoma.
4. The incidence of simple mammary carcinoma and of lipoma is higher among bitches whereas tumours of perianal glands and skin histiocytoma are more frequent in males.
5. The predisposition of purebred dogs to skin and mammary tumours is by 73.3 % higher than that of mixed breeds (mongrels) (26.7 %).
6. Skin tumours tend to localise in the limb areas (28.5 %).
7. The multiple tumours usually occur in the cases of skin melanoma, adenoma of hepatoid glands and adenoma of sebaceous glands.

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