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Research article

Histopathologic prevalence of benign and malignant canine neoplasms in small animal hospital, Rajamangala University of Technology Tawan-Ok, Chonburi, Thailand: A retrospective study

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Abstract

This retrospective study surveyed the histological prevalence of 180 canine neoplasms registered during 2016-2020 in the small animal hospital, the Rajamangala University of Technology Tawan-Ok, Chonburi, Thailand. Histopathologic diagnosis of each neoplasia was performed using its published diagnosis criteria. The neoplasms were categorized into epithelial, mesenchymal and round-cell neoplasms. Their parameters were related to sex, breed, and neoplastic location. The study consequence revealed that benign neoplasms occurred in the same frequency as malignant neoplasia. Some neoplasms were sex-dependent, particularly mammary adenocarcinoma in females and perianal (hepatoid) gland adenoma in males. The purebred dogs were prone to the malignant mammary gland and benign mesenchymal neoplasia; meanwhile, the crossbred dogs had more frequencies of benign epithelial, benign round cell and malignant mesenchymal neoplasms than the purebreds. The buttock and head were the primary locations of benign epithelial neoplasms. The mammary gland was common for mammary cancers, while the hindlimb was the predilection site of the malignant mesenchymal neoplasia. These results are similar to those described in the previous studies from other regions of Thailand and the rest of the world with a few different points. Therefore, regional veterinarians, particularly in Chonburi province, can confidently use our study findings to set up their preliminary diagnoses for their neoplastic patients.

Keywords: Benign, Canine, Histopathology, Malignant, Prevalence

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INTRODUCTION

Neoplasms are a group of uncontrollably proliferative diseases in which the neoplastic cells always accumulate the mutant genes that regulate cell division, differentiation, and proliferation. Fundamentally, neoplasms are merely classified as benign and malignant, depending on their intrinsic biology. Benign neoplasms (tumours) are usually encapsulated, well-demarcated, slowly expansile to the adjacent tissues, and rarely metastasize to distant tissues. On the contrary, malignant neoplasms (cancers) are aggressive, infiltrative, and prone to metastasis.

Because dogs share the same environment as humans; therefore, they are exposed to various oncogenic factors as humans do (Neo and Tan, 2017). Rungsipipat et al. and Gray et al. have estimated that the prevalence of natural neoplasms in dogs may be higher than in humans twice or more (Rungsipipat et al., 2003; Gray et al., 2020) and may be high as approximately 1: 100 dogs a year (Baioni et al., 2017).

Principally, the final diagnosis of neoplasms is based on histopathology. This gold-standard method can provide more accurate data on neoplasia in all aspects, including cell orientation, intralesional microarchitecture, neoplastic cell morphology and behaviour, clinical staging, grading, and metastasis (Martins et al., 2022). Many retrospective studies of neoplastic prevalence based on histopathology have been done worldwide, as in Australia, Portugal, the West Indies, the USA, the UK, and Thailand (Rungsipipat et al., 2003, Mamom, 2009). The overview results have been in the same direction, with a few different results observed amongst the studies. The difference may be due to the genetic makeup of the breeds, sex, neoplastic location, immunological influence, solar exposure, and geographic difference (Mamom, 2009). Therefore, histopathology is still the best tool for a retrospective study of neoplastic prevalence in a given animal species.

This study aimed to retrospectively evaluate the prevalence of neoplasms registered during 2016- 2020 in the diagnostic centre of the Faculty of Veterinary Science, the Rajamangala University of Technology Tawan-ok, Chonburi, Thailand, using histopathology. All the neoplasms were classified as benign and malignant based on their respective histopathologic criteria. Their malignancies were then related to many biological parameters, such as breed, sex, and neoplastic location.

MATERIALS AND METHODS

Case selection

Hundreds of canine cases with the histories of tissue masses in the small animal teaching hospital, the Rajamangala University of Technology Tawan-Ok during 2016-2020 were retrospectively reviewed. Finally, one hundred and eighty neoplastic dogs were selected to participate this study. The clinical data of each patient, including mass locations, mass features, and the patient signalments (breed and sex), were retrieved from the computerized database for further analysis with histopathology diagnosis.

Preparation of Histopathologic Section

The histopathology section of each case was prepared with the routine protocol. Briefly, a formalin-fixed paraffin-embedded (FFPE) neoplastic tissue was sectioned at 5µm thick. Then, it was deparaffinized with xylene and rehydrated with a graded ethanol series. The section was stained with haematoxylin and eosin and dehydrated by a reversely-graded series of ethyl alcohols. The tissue section was then cleaned with xylene and mounted to a coverslip.

Histopathologic Diagnosis and Malignancy Identification

Histopathologic diagnosis of each neoplasia was performed under light microscopy using its published diagnostic criteria, for example, the 2-tier histologic grading system for mast cell tumour (Kiupel et al., 2011) or the 2011 classification of canine mammary neoplasms and dysplasia for mammary gland neoplasms (Goldschmidt et al., 2011). Further, all neoplasms were grouped into epithelial neoplasms, mesenchymal neoplasms, and round cell tumours after histopathologic diagnosis.

Regardless of neoplastic grading except for mast cell tumour (MCT), the malignancy of each neoplasm was determined based on general pathology and its histopathologic criteria. These included anaplasia, poor differentiation, anisocytosis, pleomorphism, anisokaryosis, bizarre nucleoli, infiltrative growth, and metastasis for malignant neoplasms. The neoplasms with encapsulation, well-differentiation, expansive outgrowth, and no metastasis were defined as benign neoplasms.

Signalment Parameter Setup

In this study, the malignancy of neoplasia was related to several signalment parameters. These included sex, breed, and neoplastic location. The age of the dogs was excluded from the study because it was unknown in many cases. The sex of the dogs was classified as male and female, whereas the breed of the dogs was roughly categorized as purebred and crossbred (mixed). In addition, the neoplastic location was determined as the head, neck, forearm, back, thorax, abdomen, mammary gland, hindlimb, buttock, and visceral organs (Figure 1). Finally, the malignancy was linked to the selected signalment parameters.

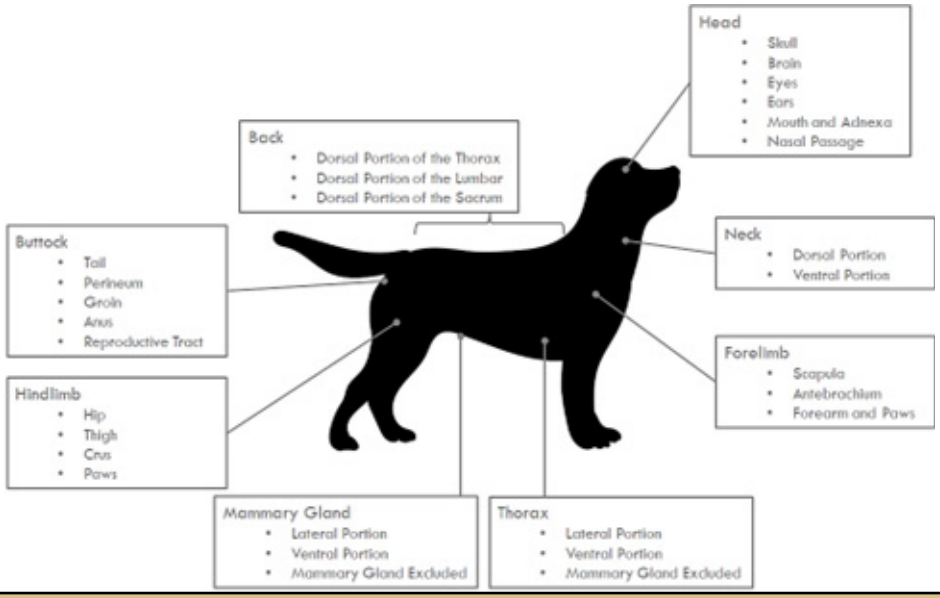

Figure 1 Body regionalization of neoplastic distribution, including the head, neck, forelimb, thorax, mammary gland, hindlimb, buttock, and back. Notably, visceral organs are not shown.

RESULTS

Histopathology prevalence and malignancy distribution

The distribution and malignancy of neoplasms in this study is summarized in Table 1. The occurrence of epithelial neoplasms was significantly different from mesenchymal neoplasms and round cell tumours, 56.66%, 31.67%, and 11.67% respectively. The prevalence of benign epithelial neoplasms was insignificantly different from the malignant neoplasms, as well as in the case of benign mesenchymal neoplasms. The major subtype of the epithelial neoplasms was the glandular neoplasms. Of these, perianal gland tumours and mammary adenocarcinomas were the most frequent benign and malignant neoplasms, respectively. For the mesenchymal neoplasms, the most benign neoplasms were haemangiomas, whereas the malignant neoplasm was fibrosarcoma. Among the round cell tumours, both benign and malignant neoplasms were mast cell tumour (MCT).

Table 1 Histopathological diagnosis and malignancy distribution of canine neoplasms

Type of neoplasm	Malignancy	
	Benign (%)	Malignant (%)
Epithelial neoplasms		
Papilloma	2 (1.11%)	-
Squamous cell carcinoma	-	8 (4.44%)
Basal cell neoplasm	-	4 (2.22%)
Perianal gland tumour	19 (10.55 %)	-
Meibomian gland tumour	6 (3.33 %)	-
Sebaceous gland tumour	3 (1.67%)	-
Mammary gland tumour	4 (2.22 %)	43 (23.88%)
Hair follicle tumour	11 (6.11%)	-
Apocrine sweat gland tumour	2 (1.11%)	-
Subtotal	47 (26.11%)	55 (30.56%)
Mesenchymal neoplasms		
Fibroma	1 (0.55%)	-
Fibrosarcoma	-	13 (7.22%)
Lipoma	6 (3.33%)	-
Liposarcoma	-	1 (0.55%)
Haemangioma	14 (7.77%)	-
Hemangiosarcoma	-	5 (2.77%)
Osteosarcoma	-	2 (1.11)
Chondroma	1 (0.55%)	-
Peripheral nerve sheath tumour	1 (0.55%)	-
Gingival tumour	4 (2.22%)	-
Subtotal	27 (15%)	21 (11.67%)
Round cell tumours		
Mast cell tumour	13 (7.22%)	4 (2.22%)
Histiocytoma	3 (1.67%)	
Lymphoma	1 (0.55%)	
Melanoma		9 (5.00%)
Subtotal	17 (9.44%)	13 (7.22%)
Total	91	89

The histopathology of common neoplasms is shown in Figure 2. Notably, most malignant neoplasms were anaplastic and poorly differentiated. The neoplastic cells were pleomorphic and usually contained bizarre nucleoli. On the contrary, benign neoplasms were encapsulated and well-demarcated. Their cells were usually well-differentiated.

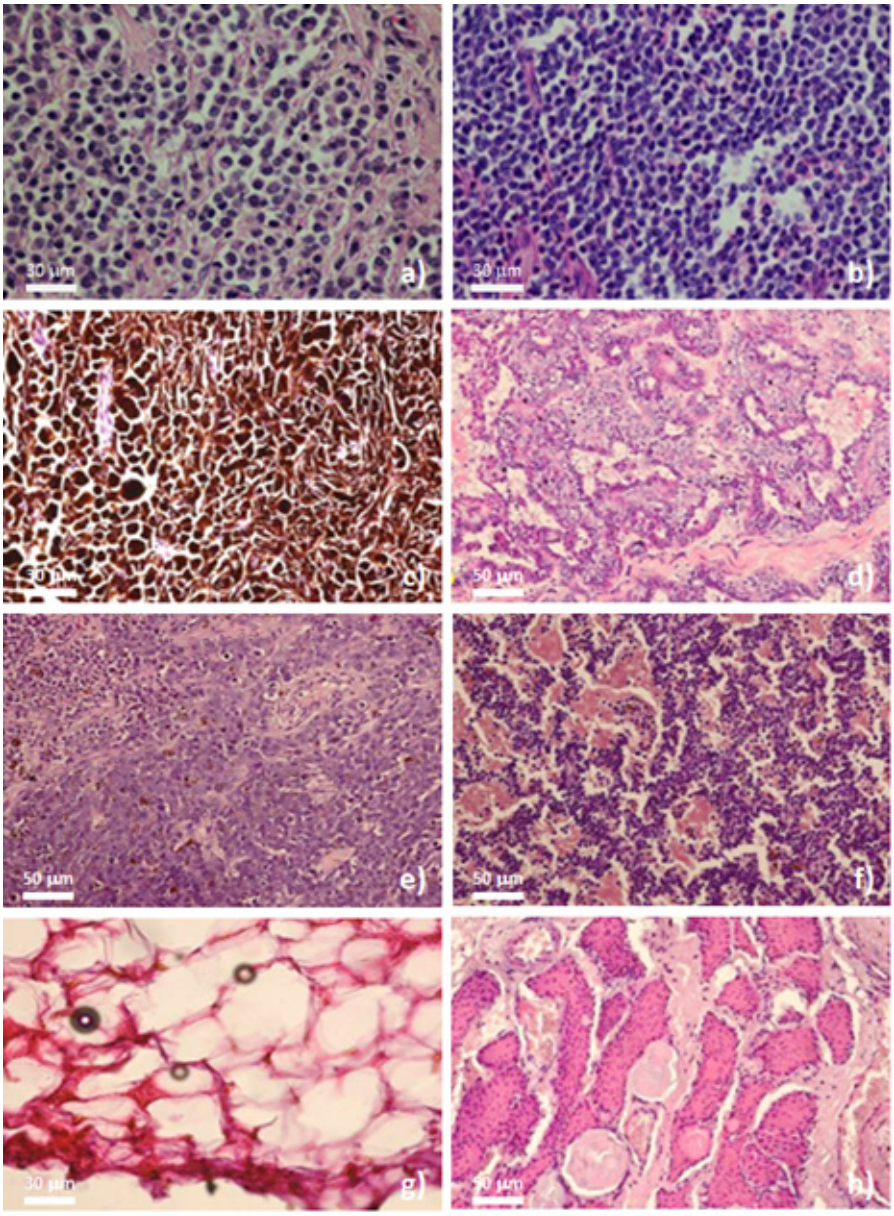

Figure 2 Microscopic features of common canine neoplasia; a) low-grade mast cell tumour, b) high-grade mast cell tumour, c) melanoma, d) mammary gland adenocarcinoma, e) histiocytoma, f) hemangiosarcoma, g) lipoma, h) perianal gland adenoma, H&E

Sex-related Malignancy

As shown in Table 2, the total prevalence of benign neoplasms in male and female were not different from each other. The frequency of benign epithelial neoplasms in the female dogs was lower than the male dogs, while the round cell tumours occurred more frequently in the male dogs. On the contrary, the malignancies in the females were significantly higher when compared to the males. The rate of malignant epithelial neoplasms was highest in the female dogs, mainly from mammary adenocarcinoma, whereas male dogs were prone to malignant round cell tumours. However, benign, and malignant mesenchymal neoplasms in both genders were present at the same rate.

Table 2 Relevance of sex and malignancy, * mammary adenocarcinoma, ** non-mammary adenocarcinoma neoplasia

Malignancy		Female	Male
Benign			
	Epithelial	3*/22**	32
	Mesenchymal	6	5
	Round cell	14	9
	Subtotal	45 (25%)	46 (25.56%)
Malignant			
	Epithelial	44*/5**	11
	Mesenchymal	9	7
	Round cell	4	9
	Subtotal	62 (34.44%)	27 (15%)
	Total	107	73

Relation of Breed Predisposition to Malignancy

In comparison, the numbers of benign epithelial neoplasms were slightly lower than the malignant epithelial neoplasms both in the purebred and crossbred dogs. The occurrence of benign neoplasms in the purebreds was also indifferent to the crossbreds, whereas there was a slight difference in the numbers of malignant epithelial neoplasia between the purebred and crossbred dogs. These similar trends were found in mesenchymal neoplasms, as well. However, the significant differences were in the round cell tumours, particularly mast cell tumour (see supplement A). The purebred dogs were subject to benign tumours, and the mixed-breed dogs were at risk of malignant round cell tumours. Moreover, the frequency of benign round cell neoplasms was greater in the purebreds compared to the crossbreds. In contrast, the malignant round cell neoplasms tended to occur in the crossbreds.

Table 3 Frequency of neoplasms by breed and malignancy

Breed Type		Benign (%)	Malignant (%)
Purebred			
	Epithelial	30 (16.67%)	33 (18.33%)
	Mesenchymal	5 (2.77%)	3 (1.67%)
	Round Cell	12 (6.67%)	1(0.56%)
	Subtotal	47 (26.11%)	37 (20.56%)
Crossbred			
	Epithelial	30 (16.67%)	31 (17.22%)
	Mesenchymal	7 (3.89%)	9 (5%)
	Round Cell	4 (2.22%)	15 (8.33%)
	Subtotal	41 (22.78%)	55 (30.55%)
Total		91	99

Malignancy distribution by body locations

The distribution of several benign and malignant neoplasms was related to the locations on the body. According to the consequence in Table 4, the buttock and head were the predilected sites of benign epithelial neoplasms, especially perianal gland tumours (see the additional information in supplement A). Interestingly, the malignant epithelial neoplasms were lesser presented in those body regions. Nevertheless, mammary adenocarcinoma was the most often diagnosed malignant neoplasm in female mammae. Visceral hemangiosarcoma was also reported in the liver, kidney, and spleen.

Table 4 Distribution of benign and malignant neoplasms by locations

Anatomic Region	Neoplastic category	Benign (n)	Malignant (n)
Head			
	Epithelial	10	6
	Mesenchymal	7	-
	Round Cell	3	6
	Subtotal	20	12
Neck			
	Epithelial	4	-
	Mesenchymal	1	-
	Round Cell	-	-
	Subtotal	5	-
Forelimb			
	Epithelial	1	1
	Mesenchymal	1	3
	Round Cell	2	1
	Subtotal	4	5
Back			
	Epithelial	-	1
	Mesenchymal	1	-
	Round Cell	2	1
	Subtotal	3	2
Thorax			
	Epithelial	3	-
	Mesenchymal	1	-
	Round Cell	-	-
	Subtotal	4	-
Abdomen			
	Epithelial	1	3
	Mesenchymal	4	1
	Round Cell	3	1
	Subtotal	8	5
Mammary land			
	Epithelial	2	1
	Mammary gland	2	44
	Mesenchymal	-	-
	Round Cell	4	2
	Subtotal	8	47
Hindlimb			
	Epithelial	1	2
	Mesenchymal	4	5
	Round Cell	3	4
	Subtotal	8	11
Buttock			
	Epithelial	22	3
	Mesenchymal	6	2
	Round Cell	2	1
	Subtotal	30	6
Visceral organs			
	Epithelial	-	-
	Mesenchymal (Haemangiosarcoma)	-	2
	Round Cell	-	-
	Sub total	-	2
	Total	90	90

DISCUSSION

In the overview, the most frequent neoplasia in this study were cutaneous neoplasms. On the contrary, visceral, and hard-tissue neoplasms were less seen. The primary reason is that skin neoplasms are easily visible; therefore, they usually come to the owner's and veterinarian's attention. (Martins et al., 2022). The results of this study have also suggested that benign and malignant neoplasms had a similar prevalence. This observation resembled the other surveys previously performed in Bangkok, Thailand, and Croatia (Rungsipipat et al., 2003; Šoštarić-Zuckermann et al., 2013) but has distinctly differed from the study in Northern Portugal in which the benign tumours were 2-fold higher than the malignant neoplasms (Martins et al., 2022).

Gender may affect the neoplastic malignancy in a few neoplasms. Perianal gland tumour was the most frequent benign epithelial neoplasm observed in this study, while malignant epithelial neoplasm was mammary adenocarcinoma. The prevalence of perianal gland tumours was predominantly higher in males because of testosterone influence (Devi et al., 2012). On the other hand, all mammary adenocarcinoma took place only in females due to the effect of estrogen. Its prevalence was higher than perianal gland tumours in males. These clues might indicate sex predisposition for these two neoplastic species. Interestingly, the other epithelial neoplasms did not show any sex predilection. This agreement was similar to the studies from many research groups (Rungsipipat et al., 2003; Mamom et al., 2009; Šoštarić-Zuckermann et al., 2013).

The epithelial neoplasms in this study were breed-independent because the distributions of benign and malignant neoplasia in purebred and crossbred dogs occurred at the same frequency. This observation was slightly different from several previous studies that the purebred dogs were prone to some epithelial neoplasia, for example, hair follicle neoplasia in Briards, Giant Schnauzers, and Gordon Setters, and papillomatosis in French Bulldog, Whippet, Vizsla, Rhodesian Ridgeback (Machado et al., 2018), and Bull Mastiff (Hassan et al., 2021).

In this recent study, fibrosarcoma and haemangioma were the most prevalent malignant and benign mesenchymal cells. Moreover, two cases of visceral hemangiosarcoma were identified. In both cases, the neoplasia tended to take place in the vascular-rich organs, including the liver, spleen, and kidney. This incidence might suggest organ predilection for this neoplasm. Although the overall prevalence of mesenchymal neoplasms was lower than the epithelial neoplasms; howbeit, their prevalence seemed to be independent of sex and breed according to the study results (see supplement A). This finding also differed from one study in which hemangiosarcoma was overtly seen in mixed-breed dogs (Chikweto et al., 2011).

Amongst the round cell neoplasms, mast cell tumours had the highest prevalence in this study (see supplement A). This tendency was also reported in most previous studies (Rungsipipat et al., 2003; Pakhrin et al., 2007; Mamom et al., 2009; Villamil et al., 2011; Šoštarić-Zuckermann et al., 2013; Martins et al., 2022). Our data has shown that low-grade mast cell tumours in the crossbreds occurred 3-times in the purebreds, and all high-grade mast cell tumours were present in the mixed-breed dogs only. This result was similar to all former studies in Thailand (Rungsipipat et al., 2003; Mamom et al., 2009).

The different matter was seen in the other studies in the USA, West Indies, and Northern Portugal (Chikweto et al., 2011; Villamil et al., 2011; Martins et al., 2022). Probably, the discrepancy may be due to the genetic makeup of the studied dogs or even the number of mixed-breed dogs in the study areas (Rungsipipat et al., 2003). However, sex and breed predilections for other round-cell tumours were not evident in the current study.

Benign neoplasms were dominantly observed at the buttock, particularly perianal gland tumours and the head regions for other neoplasia. The mammary region was another location at which many neoplasms were present. Of these, mammary adenocarcinoma was the primary malignant neoplasia. Low-grade mast cell tumours, melanoma, histiocytoma, and fibrosarcoma also tended to distribute in this area in a square manner. This observation resembled the study from Rungsipipat et al., 2003 with a slight deviation. Therefore, the distribution of the above neoplasms may depend on the specific locations. However, the other neoplasms were not related to the body parts in this study.

As shown in this study and other research worldwide, mammary gland adenocarcinoma, mast cell tumours, and perianal gland tumours were frequently diagnosed in dogs (Rungsipipat et al., 2003; Mamom et al., 2009; Choi, 2019). Thus, having the prevalence of neoplasia in dogs is essential since the surveyed data can help veterinarians to diagnose and determine an appropriate strategy to cope with various neoplasms easily (Pakhrin et al., 2007). Even though the overall prevalence of neoplasia in this study was reasonably related to the previous studies in other parts of Thailand (Rungsipipat et al., 2003; Mamom et al., 2009); however, some studied parameters slightly deviated from the documented data obtained in the rest of the world. Maybe, the variation resulted from the geographic location, breed preference, environmental influence, dog lifestyle, the number of studied dogs, studied parameter setup, and sample selection criteria (Rungsipipat et al., 2003; Chikweto et al., 2011; Villamil et al., 2011; Ribeiro et al., 2020). For instance, Thailand and other tropical countries always have long daylight. Thus, dogs in these countries are usually prone to squamous cell carcinoma, haemangioma and hemangiosarcoma because of prolonged exposure to the UV compared with their counterparts in the temperate countries (Hargis et al., 1992; Nikula et al., 1992; Chikweto et al., 2011). The lifestyle of the dogs and owners also influences the study result discrepancy (Mamom et al., 2009). Dogs in a suburban area may live outdoors longer than urban dogs. Therefore, they may be at risk of chronic exposure to allergens, toxic chemicals, and oncogenic viruses that can induce neoplastic formation.

CONCLUSIONS

The histopathologic prevalence of benign and malignant canine neoplasms in the small animal hospital, the Rajamangala University of Technology Tawan-Ok, was successfully established. The study consequence is beneficial for veterinarians to diagnose common neoplasms in dogs from this geographic zone and to plan an appropriate therapy rapidly. However, the information may be outdated quickly since the new neoplastic cases in dogs seems to increase annually. Therefore, we recommend that the survey should be reviewed as much as possible to keep all data updated.

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AUTHOR CONTRIBUTIONS

SM, DR and RU designed the experiment protocols and performed the experiments. SM, DR, and DK interpreted the data. SM and DK wrote the manuscript. DK finalized the manuscript. All authors allowed this manuscript to be published.

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