UNIVERSITI PUTRA MALAYSIA

ANALYSIS OF 10 YEARS (2007 – 2016) OF EPIDEMIOLOGICAL DATA OF URINARY STONES IN DOGS AND CATS FROM A REFERRAL CENTRE IN MALAYSIA

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ANALYSIS OF 10 YEARS (2007 – 2016) OF EPIDEMIOLOGICAL DATA OF URINARY STONES IN DOGS AND CATS FROM A REFERRAL CENTRE IN MALAYSIA

HAMEEDUNISHA TAJUDEEN

A project paper submitted to the

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CERTIFICATION

It is hereby certified that we have read this project paper entitled, Analysis of 10 years (2007 – 2016) of epidemiological data of urinary stones in dogs and cats from a referral centre in Malaysia, by Hameedunisha Tajudeen and in our opinion it is satisfactory in terms of scope, quality, and presentation as partial fulfillment of the requirement for the course VPD 4999 – Project.

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DEDICATIONS

In the name of Allah, The Most Benevolent, The Most Merciful

Faculty of Veterinary Medicine, Universiti Putra Malaysia

Animal Medical Center, Sdn. Bhd.

Dr. Sivagurunathan

Dr. Amilan Sivagurunathan

Mr. Shree Sivagurunathan

Mr. Abdul Rahman

Mrs. Yasmin Tajudeen

And to all my teachers who have committed themselves towards the noble cause of education.

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CONTENTS

LIST OF TABLES

Page

LIST OF FIGURES

Page

ABSTRAK

Abstrak daripada kertas projek yang dikemukakan kepada Fakulti Perubatan Veterinar untuk memenuhi sebahagian daripada keperluan kursus VPD 4999 – Projek.

ANALISA 10 TAHUN (2007 – 2016) DATA EPIDEMIOLOGI PENYAKIT BATU KARANG DALAM ANJING DAN KUCING DARIPADA PUSAT RUJUKAN DI MALAYSIA

Oleh:

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2017

Penyelia: Dr. Lim Sue Yee

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Batu karang adalah penyakit biasa dalam anjing dan kucing. Kajian ini bertujuan untuk menganalisa data epidemiologi batu karang yang diperolehi daripada pusat rujukan di Malaysia sepanjang 10 tahun (2007 - 2016). Rekod analisa batu karang telah dianalisa dan dibandingkan dengan baka, umur, jantina, status pemandulan, skor berat badan, pH kencing dan lokasi anatomi.

Driapada 1086 penyakit batu karang yang dianalisa, 90.4% merangkumi anjing manakala 9.6% merangkumi kucing. Kebanyakan kes batu karang pada anjing (89.8%) dan kucing (92.2%) melibatkan saluran kencing bawah. Batu karang struvite (61.1%) banyak ditemui pada anjing manakala calcium oxalate (CaOx) (51.9%) banyak ditemui pada kucing. Purata umur anjing adalah 5.8 tahun manakala umur kucing adalah 7.6 tahun. Anjing didapati 2.7 kali lebih berisiko mendapat struvite manakala kucing adalah 2.4 kali lebih berisiko mendapat CaOx. Selain itu, kucing jantan lebih berisiko mendapat CaOx berbanding kucing betina. Baka anjing dan kucing yang sering terlibat adalah baka anjing Shih Tzu, Miniature Schnauzer, kucing tempatan berbulu pendek, kucing Parsi, dan anjing serta kucing kacukan. Ini merupakan kajian epidemiologi pertama mengenai batu karang di Malaysia, dan terdapat perbezaan ketara antara kes anjing dan kucing. Data dalam kajian ini boleh digunakan untuk kajian lanjutan berkaitan pengurusan kes batu karang mengikut spesis haiwan.

Kata kunci: *Penyakit Batu karang, Struvite, Calcium oxalate, baka haiwan*

ABSTRACT

An abstract of the project paper presented to the Faculty of Veterinary Medicine in partial fulfilment of the course VPD 4999 – Project.

ANALYSIS OF 10 YEARS (2007 – 2016) OF EPIDEMIOLOGICAL DATA OF URINARY STONES IN DOGS AND CATS FROM A REFERRAL CENTRE IN MALAYSIA

By

Hameedunisha Tajudeen

2017

Supervisor: Dr. Lim Sue Yee

Co-Supervisor: Assoc. Prof. Dr. Gurmeet Kaur Dhaliwal

Urolithiasis a common urinary problem in dogs and cats. The objective of this study was to evaluate epidemiological data derived from a referral center in Malaysia over 10 years (2007 – 2016). Urolith analysis results of dogs and cats pertaining to their respective urolith type and composition, were evaluated and compared with breed, age, sex, neuter status, body condition score, urine pH and anatomical location.

Out of 1086 uroliths analyzed, 90.4% were from dogs and 9.6% from cats. Majority of uroliths from dogs and cats (89.8% and 92.2%, respectively) were from the lower urinary tract. Struvite (61.1%) was most commonly found in dogs and calcium oxalate (CaOx) (51.9%) in cats. The average age of dogs and cats were 5.8 years for struvite and 7.6 years for CaOx. Dogs were 2.7x more likely to develop struvite than cats and cats were 2.4x more likely to develop CaOx than dogs. Bitches were 11.9x more likely to develop struvite than males. Meanwhile, toms were 1.5x more likely to develop CaOx than queens. Most common dog and cat breeds associated with struvite and CaOx were Shih Tzu, mixed-breed dogs, Miniature Schnauzers, Domestic Shorthair, Persians and mixed-breed cats. This is the first epidemiological study of uroliths in Malaysia, with significant differences in urolith occurrence between dogs and cats. This baseline data can be useful for further investigative studies towards species specific management of urolithiasis.

Keywords: *Urolithiasis, Urolith, Struvite, Calcium oxalate, Breed*

1.0. INTRODUCTION

Urolithiasis can be defined as a general term that refers to the causes and effects of uroliths anywhere within the urinary tract (Osborne et al., 2008). Urolithiasis is a common urological problem found in dogs and cats that were presented to small animal practices all over the world (Tion et al., 2015). This has urged countries to conduct frequent quantitative analysis of uroliths and evaluate occurrences of various uroliths in relation to species, breed, age, sex, neuter status, anatomical location, body condition score (BCS) and urine pH. There were also observations of trends of uroliths by countries in order to ultimately determine successful treatment and prevention plans (Bartges & Callens, 2015). The intention is to conduct a similar study in Malaysia, because there have been no published studies on the uroliths of dogs and cats in Malaysia. Conducting a study such as this would provide a baseline towards investigative studies in the future. The objective of this study was to determine if there is a significant difference between the occurrence of uroliths in dogs and cats over a 10 year period. Furthermore, the objective of this study was to also evaluate the potential risk factors associated with uroliths such as age, breed, sex, neuter status, BCS, anatomical location and urine pH. The hypothesis of this study was that there is a significant difference between the occurrence of uroliths in dogs and cats. There are also significant associations between uroliths and descriptive data of dogs and cats.

2.0 LITERATURE REVIEW

2.1.Urolithiasis

Urolithiasis is a common urological problem in dogs and cats. 3% of dogs and 7% of cats presented to veterinary hospitals are due to urolithiasis and urological diseases respectively (Osborne et al., 1995a; Osborne et al., 1995b). In a study on obstructed cats, 59% of them were diagnosed with urolith plugs, 12% for uroliths and 29% for non specific causes (Osborne et al., 1989). In another study on non-obstructed cats, 13% of them were diagnosed with urolithiasis (Buffington et al., 1997). In dogs presented with urinary tract infection (UTI), 35.5% of them were diagnosed with urolithiasis (Waki, et al., 2009). The prevalance of urolithiasis in dogs has been reported to be 0.5% - 1% in Germany, 0.24% in Sweden and 0.1%– 0.3% in Czech Republic (Hesse et al., 2008; Wallerstrom &Wagberg, 1992; Kucera, 1999).

Uroliths are formed due to familial, congenital or acquired pathophysiological factors that has led to an increased risk of precipitation of excretory metabolites in urine which eventually leads to urolith formation (Osborne et al., 2008). The exact mechanism of how uroliths form is incompletely understood in both dogs and cats; however, there are 3 contributing factors towards uroliths formation. They are 1) The matrix, which is an inorganic core protein that helps initiate the urolith formation. 2) Organic or inorganic crystallization inhibitors, which may be deficient or dysfunctional in certain animals that have uroliths and 3) Precipitation crystallization factors, which play a complex role amongst urine solutes and other chemical factors in the urine that can lead to conditions that favor crystallization (Brown, 2013).

In most studies, uroliths are classified as that type if it consists of more than 70% of that particular mineral, provided there is no nidus or shell (Hesse et al, 2012; Houston & Moore, 2009; Westropp e.t al., 2005). Compound uroliths are those that have a nuclei with different layers of mineral types. Mixed uroliths are those that have less than 70% of a single mineral component (without a nucleus or shell) (Vrabelova et al., 2011). Uroliths have also been classified based on location (nephroliths if uroliths are found in kidneys, ureteroliths if in the ureters, cystoliths if in the bladder etc.) (Brown, 2013). These uroliths have been analyzed based on associations/differences amongst age, breed, sex, body condition score (BCS) and location. Furthermore, there seems to be a call for routine analysis of uroliths because studies also showed variation in trends over time. These variations occur due to change in maintenance and therapeutic diets. For example, Minnesota Urolith Center analyzed 350,803 uroliths of dogs and cats from 1981 to 2007. They found that during the 1980s, struvite was the most common stone detected in dogs (78%). However, in 2007, 41% of uroliths were calcium oxalate (CaOx) and 40% were struvite. Likewise, CaOx were more prevalent in cats during the 1980s, but in 2007, 78% of uroliths were struvite (Osborne et al., 2008). There have been similar findings in other literatures as well (Bartges & Callens, 2015; Cannon et al., 2007; Hesse et al., 2012; Low et al., 2010; Houston and Moore, 2009).

2.2. Types of uroliths

Common uroliths found in dogs are struvite, CaOx, and urate. Less commonly found are cystine, silica, calcium phosphate, and xanthine material (Brown, 2013). Likewise, in cats, struvite, CaOx, and urate are more common while uric acid, calcium phosphate, and cystine uroliths are less common (Brown, 2013).

2.2.1. Struvite

Struvites are the most common uroliths found in dogs and cats. They represented nearly half of total uroliths submitted for analysis, from countries around the world to Minnesota Urolith Center (Osborne et al., 2008). The increase in the trend of struvite uroliths at that time was attributed to a possibility of diets that reduce urine acidity (alkaline urine) and has adequate quantities of magnesium, both of which are risk factors associated with struvite formation (Osborne et al., 2008). Struvite are mainly composed of magnesium ammonium phosphate with minimal amounts of matrix. They are formed sterile in cats due to dietary and metabolic factors (Grauer, 2015; Syme, 2012). However, in dogs (for males and females), most struvite uroliths are induced due to infection from urea-splitting bacteria such as *Staphylococcus* spp., *Proteus* spp. and *Ureaplasma* spp. (Erickson & Rubin, 2007). Struvite form when the urine pH is alkaline, as the solubility of magnesium ammonium phosphate reduces in an alkaline pH. Struvite can form within 2 weeks of a dog acquiring a UTI (caused by *Staphylococcus* spp.). Foreign bodies (e.g. suture material) can act as a nidus for infection-induced struvite formation (Erickson & Rubin, 2007). Risk factors associated with struvite formation are diets high in magnesium, phosphorous, sodium chloride and calcium, UTI (in dogs and cats), renal tubular disorders and drug therapy that causes alkaline pH (Grauer, 2015).

2.2.2. Calcium Oxalate

CaOx is the second most common urolith found in both dogs and cats comprising of 41.3% and 40.8% respectively, of uroliths submitted for analysis to Minnesota Urolith Center from countries around the world (Osborne et al., 2008). The increase in the trend of CaOx uroliths are unknown, however a hypothesis suggests that diets that have been known to lower the risk of struvite formation has led to an increased risk of CaOx formation (Osborne et al., 2008). This is because these diets contain dietary acids and precursors that may induce hypercalciuria and hypocitraturia (citrate is an inhibitor of calcium oxalate crystal formation) and is also associated with aciduria and acidemia (Osborne et al., 2008). CaOx uroliths are a result of an altered balance of calcium and oxalate in the urine and inhibitors of crystallization. In dogs, infection does not seem to cause oxalate stone formation and their urine pH is mostly < 6.5 at the time of diagnosis (Grauer, 2012). Risk factors associated with CaOx formation are low magnesium diets that lead to an acidic urine, hypercalciuria due to excess gastrointestinal absorption of calcium, hypercalcemia and urine acidifying medications (Erickson & Rubin, 2007). CaOx are mostly radio dense and are mostly rough and oval or round in shape (Gough & Thomas, 2004).

2.2.3. Ammonium Urate

In dogs, these are the third most common uroliths which is commonly located in the bladder (Tion et al., 2015). These uroliths form when there is improper conversion of uric acid to allantoin within the hepatocytes, which in turn leads to high serum and urine concentrations of uric acid. In cats, ammonium urate comprises of 3% to 10% of feline uroliths, however, the formation of urate uroliths is incompletely understood (Grauer, 2014). The contributing factors associated with urate stone formation are porto vascular anomalies and deficits in renal tubular absorption. Risk factors are diets high in purine precursors, increased renal production, prolonged urine retention or ammonium production due to microbial urease (Erickson & Rubin, 2007). These uroliths are relatively radiolucent (Grauer, 2014).

2.2.4. Cystine

These uroliths are a result of a congenital disorder which is due to defective proximal tubular reabsorption of cystine and other amino acids such as ornithine, lysine and arginine, resulting in cystinuria and the eventual formation of cystine uroliths (Treacher, 1964). They are relatively uncommon in cats compared to dogs (Gough & Thomas, 2004). These uroliths are likely to form in an acidic urine. Cystine uroliths are smooth, oval in shape and are often radiolucent on radiograph (Gough & Thomas, 2004).

2.2.5. Calcium Phosphate

Hydroxyapatite and carbonate apatite uroliths are more common while brushite uroliths are relatively uncommon (Tion et al., 2015). These uroliths are uncommon in cats (Tion et al, 2015). These uroliths often occur in minor components along with struvite and CaOx uroliths and the risk factors associated with calcium phosphate uroliths are similar to that of CaOx formation (Tion et al., 2015).

2.2.6. Silica

There is not much knowledge in regard to this urolith formation and the pathogenesis. However, silica uroliths are often found in an acidic urine, occur frequently in dogs than cats and are often jack shaped (Grauer, 2015). The risk factors associated with silica formation are diets that are high in plant derived ingredients such as corn gluten feed and soybean hulls (Grauer, 2015).

2.3.Urolith composition

Uroliths may be composed of layers that consist of same or different mineral types. These layers are representative of the different phases involved in mineral deposition (Ulrich, 1996). The nidus is an area that initiates the growth of uroliths and is not necessarily located at the center of uroliths (Ulrich, 1996). The stone makes up the major part of entire urolith and when it is homogenous, it may not necessarily consist of a nidus or other mineral layers (Ulrich, 1996). The shell consists of one or more complete outer layers of the urolith, while the surface crystals are located on the outer most surface and are incomplete layers of the urolith (Ulrich, 1996).

2.4.Location

Uroliths affect the lower and the upper portion of the urinary system. It can cause lower urinary tract obstruction, ureteral obstruction, acute renal failure, chronic kidney disease (due to compressive injury), pyelonephritis and tubular damage (Adams, 2015: Cannon et al., 2007; Osborne at al., 2008).

2.4.1. Upper urinary tract

Uroliths located here (such as nephroliths and ureteroliths) are less common in both dogs and cats (Adams, 2015). However, this could also be due to marked underdiagnoses of upper tract uroliths and the difficulty associated with upper tract uroliths removal for analysis (Stevenson, 2002; Adams, 2015). The most common composition of nephroliths and ureteroliths in dogs and cats are CaOx (Cannon et al., 2007; Low et al., 2010; Osborne et al. 2008), followed by the second most common composition which is dried solidified blood calculi in cats and struvite in dogs (Westropp et al., 2006).

2.4.2. Lower urinary tract

The lower urinary tract is the most common location of uroliths. Furthermore, the vast majority of uroliths submitted for analysis from North America were retrieved from the lower urinary tract (Cannon et al., 2007). Lower urinary tract uroliths are common mainly due to the quadruped stance that dogs and cats have, compared to humans (that are biped) (Syme, 2012). The most common site for uroliths formation in cats is the bladder and/or urethra (Hesse et al., 2012) and mainly consists of struvite and CaOx uroliths (Cannon et al., 2007). In dogs, infection induced struvite are the most common uroliths located in the bladder (Syme, 2012), followed by CaOx being the second most common (Houston et al., 2004). Urates (in dogs and cats) and cystine (in dogs) are also found in the lower urinary tract (Syme, 2012).

2.5. Sex

A study conducted by the Canadian Veterinary Urolith Center from 1998 to 2003, revealed that struvite were most common amongst bitches as they are more likely to develop a UTI (Houston & Moore, 2009; Syme, 2012) and CaOx were most common amongst male dogs (Houston & Moore, 2009). One exception to this is that the schnauzer bitch tends to develop CaOx uroliths more frequently than struvite uroliths (Houston & Moore, 2009). In cats, the occurrence of struvite uroliths is equally distributed amongst males and females (Syme, 2012). Tom cats are 1.5 times more likely to develop CaOx uroliths than queens (Westropp et al., 2005). Tom cats are also 2.5 times more likely to have urate uroliths compared to queens (Cannon et al., 2007). There were similar findings in other studies (Appel et al., 2010; Houston & Moore, 2009). However, in dogs, urate uroliths were found to be more common in bitches (Low et al., 2010) and dried solidified blood calculi more common in tom cats than dogs (Cannon et, al., 2007). Xanthine uroliths are evenly distributed amongst male and female cats (Bartges & Callens, 2015). Cystine uroliths and silica uroliths are the most common in male dogs (Osborne et al., 1999; Grauer, 2015).

2.6.Neuter status

Spayed female dogs and cats have increased risk for urolithiasis than intact females (Syme, 2012). Neutered male dogs have a higher risk of developing CaOx uroliths and spayed female dogs have an increased risk of developing struvite uroliths (Lekcharoensuk et al., 2000; Okafor, 2013). This is because spayed bitches have an increased risk of developing a recessed vulva (Wang et al., 2006). Anatomical defects such as a recessed vulva increases the chances of spayed bitches acquiring a UTI, as the vulva opening is narrower and closer to the rectum (Bjorling, 2011; Chew & Westropp, 2012). Neutered cats are 7 times at risk of developing CaOx and 3.5 times at risk of developing struvite uroliths than intact cats (Westropp et al., 2005). Neutered cats are also 12 times as likely to develop urate uroliths than sexually intact cats (Albasan et al., 2012).

2.7. Breed

Certain uroliths have been found to occur more frequently in certain breeds of dogs and cats due to their genetic predisposition. Table 1 is a brief summary of the various breeds of dogs and cats that are either predisposed or frequently associated with their respective uroliths.

	Dogs	Cats
Struvite	Bichon Frise, Cocker Spaniel, Lapland, Miniature Poodle, Miniature Schnauzer, Shih Tzu, Yorkshire Terrier (Gough & Thomas, 2004)	Manx, Siamese, Domestic Longhair (Cannon et al., 2007)
CaOx	Bichon Frise, Lapland, Miniature Poodle, Miniature Schnauzer, Shih Tzu, Yorkshire Terrier (Gough & Thomas, 2004)	Burmese, Himalayan, Persian (Gough & Thomas, 2004), Domestic Longhair (Cannon et al., 2007), Domestic Shorthair (Houston & Moore, 2009)
Urates	Bulldog, Dalmatian, Miniature Schnauzer, Shih Tzu, Yorkshire Terrier (Gough & Thomas, 2004) In Dalmatians, English Bulldog, Russian Terriers, there is a defect of the uric acid transporter (SLC2A9). This alters the transport of uric acid through the hepatic and renal system leading to high serum concentrations of uric acid (Grauer, 2014).	Siamese, Egyptian Mau, Birman (Grauer, 2014)

Cystine	American Water Spaniel, Australian Shepherd, Basenji, Basset Hound, Bichon Frise, Bulldog, Bullmastiff, Chihuahua Daschund, French Bulldog, Manchester Terrier, Miniature Pinscher, New Foundland, Scottish Deerhound, Silky Terrier, Staffordshire Bull Terrier, Welch Corgi (Gough & Thomas, 2004)	Uncommon in cats (Gough & Thomas, 2004)
Calcium Phosphate	Bichon Frise, Cocker Spaniel, Miniature Poodle, Miniature Schnauzer, Shih Tzu, Springer Spaniel, Yorkshire Terrier (Gough & Thomas, 2004)	Uncommon in cats (Tion et al., 2015)
Silica	German Shepherd, Golden Retriever, Labrador Retriever, Lapland, Miniature Schnauzers, Shih Tzu, Yorkshire Terrier (Gough & Thomas, 2004)	No breed predispositions (Grauer, 2015)

Table 1: *Breeds of dogs and cats commonly presented/ predisposed to their respective uroliths*

2.8. Body condition score

Studies have shown that dogs that are obese or with a greater body condition score are at an increased risk of developing CaOx uroliths. (Kennedy et al., 2016; Lekcharoensuk et al., 2000). Obese cats have also been associated with urolithiasis (Loftus & Washalag, 2015). However, the exact composition occurrence of uroliths amongst obese cats is not widely studied. Studies also state that the change in trends of struvite and CaOx uroliths in dogs and cats could be associated with changes in health trends (Obesity, activity etc.) (Syme, 2012).

2.9. Age

Geriatric cats and dogs are at an increased risk of developing CaOx uroliths (Syme, 2012). Urate uroliths are common in younger cats and dogs with an average age of 6 years and 4.5 respectively (Appel et al., 2010; Bartges & Callens, 2015). This is due to contributing factors associated with urate stone formation such as porto vascular anomalies and deficits in renal tubular reabsorption that occurs in young animals (Grauer, 2014). Struvite uroliths are common in younger dogs and cats, aged between 2 to 7 years (Cannon et al., 2007). Cystine uroliths mostly occur in middle aged dogs and cats (Syme, 2012). Xanthine uroliths occur in cats less than 5 years of age (Bartges & Callens, 2015).

3.0 MATERIALS AND METHODS

Urolith samples (that were surgically removed or voided) from various veterinary clinics in Malaysia (peninsular and East Malaysia) were sent to Minnesota Urolith Centre for analysis via a single referral center in Malaysia (Animal Medical Center, AMC). Urolith analysis was performed utilizing quantitative methods such as optical crystallography using a polarizing microscope, infrared spectroscopy, x-ray diffraction, energy dispersive techniques, and others (Ulrich, 1996). Sample submission forms (Appendix A) with respective urolith results were compiled at AMC. These documents were accessed for details such as patient identification, species, breed, age, sex, neuter status, BCS, anatomical location from where the uroliths were retrieved, urine pH, along with their respective uroliths analysis result. These data were compiled into a worksheet[1] and further analyzed using a commercial statistical program[2]. The data records collected and recorded were from 2007 to 2016 (10 years). Uroliths that were more than 70% of a mineral type were included in this study. Uncommon uroliths identified in this study (silica, brushite, newberyite, calcium phosphate apatite, calcium phosphate carbonate, sodium acid urate and miscellaneous uroliths) were classified under others to increase the strength of statistical analysis. Differences between means of interval variables (age and urine pH) in dogs and cats were compared to the most common uroliths (struvite and CaOx) using independent samples T-test provided all assumptions to run this test was

[1] Microsoft Word Excel, 2016

[2] Statistical Program for Social Sciences (SPSS)- 24

fulfilled. Relationships between categorical variables such as stone type, BCS, breed, sex and anatomical location of the uroliths, were evaluated with Chi-square test of homogeneity. The prevalence was expressed as 95% of Confidence Interval (CI). The level of significance for all comparisons was determined at $P < 0.05$.

The null and alternative hypothesis for this study suggests that:

1. Null hypothesis:
    a. There is no significant difference between occurrence of uroliths in dogs and cats.
    b. There are no significant associations between uroliths with breed, age, sex, neuter status, anatomical location, BCS, and urine pH of dogs and cats.
2. Alternative hypothesis
    a. There is a significant difference between occurrence of uroliths in dogs and cats.
    b. There are significant associations between uroliths with breed, age, sex, neuter status, anatomical location, BCS and urine pH of dogs and cats.

If $P < 0.05$, the null hypothesis is rejected or the alternative hypothesis is accepted. If $P > 0.05$, the null hypothesis fails to be rejected.

4.0 RESULTS

4.1.Urolith occurrence in dogs and cats

Out of 1,165 uroliths that were analyzed, 1,086 uroliths were included in this study as they comprised of more than 70% of their respective mineral type. Majority of uroliths came from dogs (90.4%) (Table 2). The most common uroliths recognized in dogs and cats were struvite and CaOx (Table 3). Struvite comprised of the majority of uroliths from dogs (61.2%) and CaOx from cats (51.9%). It was found that there was a significant difference between species (dogs and cats) and their common uroliths (*P* = 0.001). Dogs were 2.7 times more likely to get struvite uroliths and cats were 2.4 times more likely to get CaOx uroliths.

	Frequency	**Percent**	**Valid Percent**
Canine	982	90.4	90.4
Feline	104	9.6	9.6
Total	1086	100.0	100.0

Table 2: *Frequency distribution of uroliths in dogs and cats*

	Frequency	Percent	Valid Percent
Struvite	639	58.8	58.8
CaOx	359	33.1	33.1
Ammonium Urate	59	5.4	5.4
Calcium Phosphate Carbonate	8	0.7	0.7
Silica	1	0.1	0.1
Brushite	3	0.3	0.3
Newberyite	1	0.1	0.1
Cystine	11	1.0	1.0
Sodium Acid Urate	1	0.1	0.1
Calcium Phosphate Apatite	1	0.1	0.1
Uric acid	1	0.1	0.1
Miscellaneous	2	0.2	0.2
Total	1086	100.0	100.0

***Table 3**: Urolith types found in dogs and cats combined*

4.2. Trend of struvite and CaOx in dogs and cats over a 10-year period

In dogs (Fig. 1), the trend of struvite has been decreasing while CaOx has been increasing over the past 10 years. In cats (Fig. 2), there was not much change with regard to the trend of struvite but there has been an increase in CaOx trends over the past 10 years.

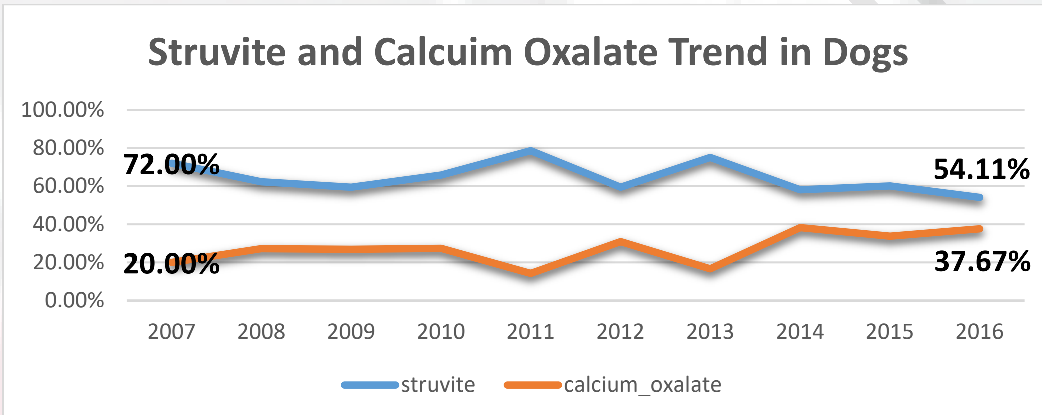

Figure 1*- Struvite and CaOx trends in dogs from 2007 – 2016*

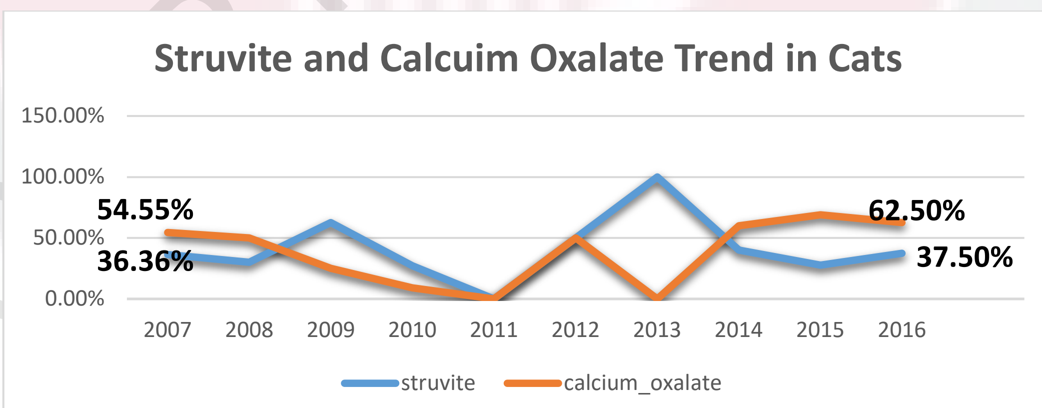

Figure 2*- Struvite and CaOx trends in cats from 2007 – 2016*

4.3. Occurrence of uroliths based on the sex of dogs and cats

In both dogs and cats, it was found that majority of the uroliths came from males (52.6% and 54.8%, respectively) (Table 4). In dogs, majority of females had a significant association (P = 0.001) with struvite, whereby female dogs were 11.9 times more likely to get struvite compared to male dogs. Male dogs had a significant association (P = 0.001) with CaOx and ammonium urate, whereby male dogs were 9.9 times and 6.9 times more likely to get CaOx and ammonium urate respectively compared to female dogs. In cats, it was found that both males and females had more of CaOx uroliths (56.1% and 46.8%, respectively). However, there were no significant associations with both sex and any of the common uroliths in cats.

	Dogs		**Cats**		**Total**
	Male	**Female**	**Male**	**Female**	
Struvite	196	401 (P = 0.001)	20	18	635
CaOx	159 (P = 0.001)	42	32	22	255
Ammonium Urate	44 (P = 0.001)	6	4	4	112

Calcium Phosphate Carbonate	0	7	1	0	8
Cystine	11	0	0	0	11
Others	7	0	0	3	10
Total	517	456	57	47	1077

Table 4: *Urolith occurrence amongst males and females in cats and dogs*

4.4.Occurrence of uroliths based on the neuter status of dogs and cats

Out of 976 dogs and 104 cats that had uroliths (with neuter/intact status recorded), majority of dogs (81.6%) and cats (65.1%) were not neutered. However, there were no significant associations between neuter status and any of the uroliths in both dogs and cats.

4.5. Average age of dogs and cats with uroliths

The age of dogs at which uroliths were retrieved were significantly different (*P*= 0.001) between struvite and CaOx. However, no such differences were noted in cats. It was observed that dogs and cats developed CaOx at an older age (7.6 years ± 3 years) and struvite at a younger age (5.8 years ± 4.8 years). Cystine was found to develop in middle aged dogs (4.5 years ± 1.8 years). Other uroliths (silica, brushite, newberyite, apatite) were found to develop in middle aged dogs and cats (5.1 years ± 2.8 years) (Table 5).

	Dogs		Cats		Total	
	Mean ± S.D	**Median**	**Mean ± S.D**	**Median**	**Mean ± S.D**	**Median**
Struvite	5.8 ± 4.9 (*P* = 0.001)	5.2	5.9 ± 3.5	5	5.8 ± 4.8	5.2
CaOx	7.6 ± 2.9 (*P*= 0.001)	7.5	7.4 ± 3.7	7	7.6 ± 3.0	7.5
Ammonium Urate	5.7 ± 3.0	5.5	6.2 ± 1.5	6	5.8 ± 2.9	6.0
Calcium Phosphate Carbonate	5.6 ± 3.6	5.5	10.7 ± 0.1	10.7	6.3 ± 3.8	6.0
Cystine	4.5 ± 1.8	4.0	nil	nil	4.5 ± 1.8	4.0
Others	4.8 ± 2.9	5.0	5.6 ± 3.2	6.9	5.1 ± 2.8	5.5
Total	6.3 ± 4.3	6.0	6.8 ± 3.6	6.8	6.4 ± 4.2	6.0

Table 5: *Average age of dogs and cats with uroliths*

4.6. Anatomical location of uroliths from dogs and cats

Majority of the uroliths were retrieved from the lower urinary tract (bladder, urethra and/or voided) out of which 939 uroliths (89.8%) were from dogs and 99 (92%) from cats. The most common uroliths found in the lower urinary tract from dogs and cats combined were struvite (98.6%), CaOx (97.4%) and ammonium urate (100%). CaOx was a common urolith found in the upper urinary tract of dogs and struvite was a common urolith found in the upper urinary tract of cats. There was a significant association ($P = 0.001$) between the common uroliths and the anatomical location of dogs, but there were no such associations found in cats.

4.7. Occurrence of uroliths based on the BCS of dogs and cats

Out of 917 dogs and 97 cats that had uroliths (with BCS data recorded), majority of dogs (75.4%) and cats (67%) were within the normal BCS. However, there were no significant associations between BCS and any of the uroliths in both dogs and cats.

4.8. Average urine pH of dogs and cats with uroliths

In this study, it was found that dogs that had struvite did have alkaline urine, however cats did not (Table 6). Both dogs and cats had an acidic urine for CaOx, cystine and other minor uroliths. Urine pH in dogs was found to have a significant difference ($P = 0.001$) between struvite and CaOx. Cats did not have any significant differences between urine pH and any of the uroliths.

	Dogs		Cats		Total	
Urolith	**Mean ± S.D**	**Median**	**Mean ± S.D**	**Median**	**Mean ± S.D**	**Median**
Struvite	7.1 ± 1.0 (*P* = 0.001)	7.0	6.4 ± 0.9	6.0	7.1 ± 1.0	7.0
CaOx	6.6 ± 1.1 (*P* = 0.001)	6.5	6.2 ± 0.8	6.0	6.5 ± 1.1	6.5
Ammonium Urate	6.8 ± 1.0	7.0	6.6 ± 0.6	7.0	6.8 ± 0.9	7.0
Calcium Phosphate Carbonate	7.0 ± 1.0	7.0	8 ± 1.0	8.0	7.3 ± 1.0	7.5
Cystine	6.8 ± 0.3	7.0	nil	nil	6.8 ± 0.3	7.0
Others	6.2 ± 0.3	6.0	7.0 ± 1.0	7.0	6.5 ± 0.8	6.2
Total	6.9 ± 1.0	7.0	6.8 ± 0.8	6.0	6.9 ± 1.0	7.0

Table 6: *Average urine pH of dogs and cats with uroliths*

4.9. Common breeds of dogs and cats with uroliths

Forty-nine breeds in dogs and ten breeds in cats were recognized of having uroliths in this study. The most common breeds (top 5) in dogs that had majority of uroliths were Shih Tzu (32.9%), mixed breeds (16.4%), Miniature Schnauzers (10.5%), Miniature Pinschers (3.4%) and Pugs (3%). Dalmatians (81.3 %) mainly had ammonium urate uroliths compared to other breeds. Making Dalmatians 79.1 times more likely to get ammonium urate compared to other breeds. There were significant associations (P = 0.001) between the top 5 breeds and struvite and CaOx uroliths in dogs, whereby Shih Tzu were 1.2 times more likely to have struvite uroliths and 1.1 times likely to have CaOx compared to other breeds. The common breeds of cats recognized of having uroliths were Domestic Shorthairs (DSH) (65.4%), Persians (14.4%) and mixed breeds (6%). There was a significant association (P = 0.001) between CaOx urolith and the common breeds in cats, whereby the DSH cat was 1.8 times more likely to have CaOx compared to other breeds.

5.0 DISCUSSION

Struvite and CaOx comprised of the majority of uroliths in this study and this is consistent with the current literature. In this study, it has been observed that in dogs, the trend of struvite has been decreasing while CaOx has been increasing over 10 years. In cats, there were not much changes with regard to the trend of struvite but there has been an increase in CaOx trends over the past 10 years. This finding of increased CaOx trends in dogs and cats was consistent with many other studies (Cannon et al; 2007; Hesse et al, 2012; Low et al., 2010; Osborne et al, 2008; Vrabelova et al., 2011). This change in trend of struvite and CaOx is multifactorial. However, the most probable explanation could be due to dietary alterations (in dogs and cats) and urinary tract infections (in dogs). Diets used to reduce the risk of struvite create an acidic urine and contains low magnesium and phosphorus levels which can lead to an increased risk for CaOx formation (Erickson & Rubin, 2007; Osborne et al, 2008).

Struvite in dogs are infection induced due to urease producing bacteria and bitches are at an increased risk of developing UTIs (Erickson & Rubin, 2007; Syme, 2012). The anatomical conformation of the female urethra (short and wide) makes bitches more likely to get UTI (Weichselbaum et al., 1998). This may explain why majority of bitches in this study had struvite. Whilst this finding does not dispute other similar research, the status of UTI in each case was not established in this study as submission forms lacked substantial amount of data regarding bitches being diagnosed with UTIs.

Majority of queens and toms had CaOx uroliths. The possible reasoning behind this would be due to acidifying diets that serve as a potential risk factor towards CaOx urolith formation (Osborne et al, 2008). It was observed that all cystine uroliths (n=11) formed in male dogs. This is because of a congenital disorder (defective proximal tubular reabsorption of cystine) that is more likely to occur in male dogs (Treacher, 1964). Similarly, the presence or absence of a congenital disorder could not be established in this study.

Other research demonstrated that struvite is commonly found in younger dogs and cats aged between 2 to 7 years (Cannon et al., 2007), which was consistent in this study, whereby the average age of dogs and cats that developed struvite were 5.8 ± 4.8 years old. According to Syme (2012), geriatric cats and dogs were at an increased risk of CaOx uroliths. Dogs and cats in this study that had CaOx uroliths did fall under the geriatric category at an average age of 7.6 ± 3.0 years. It was found that in this study urate and cystine uroliths developed at a younger age in dogs (5.8 ± 2.9 years and 4.5 ± 1.8 years respectively), which was consistent with other research findings (Appel et al., 2010; Syme, 2012).

The lower urinary tract was the most common site where majority of uroliths were found in dogs and cats. The possible explanation for this would be due to the quadruped stance of dogs and cats. The ventral positioning of the bladder makes it convenient for crystal aggregates and small uroliths to be retained and eventually develop into clinically evident uroliths (Syme, 2012). Whilst nephroliths and ureteroliths are a growing concern in companion animals, not much can be concluded regarding this in this study as very few uroliths (19 uroliths from dogs and 4 from cats) were retrieved from the upper urinary tract and to infer this data would be unreasonable. However, the small number of uroliths from the upper urinary tract can be explained due to marked underdiagnoses of upper tract uroliths and the difficulty associated with upper tract uroliths removal for analysis (Stevenson, 2002; Adams, 2015).

Several reports state that neutered and obese dogs and cats are at an increased risk for urolithiasis (Kennedy et al., 2016; Lekcharoensuk et al., 2000; Loftus & Washalag, 2015; Okafor, 2013; Syme, 2012; Westropp et al., 2005). This finding was not consistent in this study, which revealed majority of dogs (81.6%) and cats (65.1%) that had uroliths to be intact and majority of dogs (75.4%) and cats (67%) to be within the normal BCS. This could be because of the Malaysian demographic of owners not neutering majority of their dogs and cats and maintaining them under a normal BCS. Furthermore, the lifestyle of dogs and cats in Malaysia might not be as sedentary as those from developed countries which explains the normal BCS of dogs and cats from Malaysia.

CaOx crystal formation is most favourable when the urine pH is < 6.5 (Grauer, 2012). This is consistent with our study whereby dogs and cats with CaOx had a urine pH of 6.5 ± 1.1. On the other hand, struvite in dogs and cats mainly form in an alkaline urine (Syme, 2012), which was consistent with the urine pH of dogs in this study ($pH = 7.1 \pm 1.0$) but was not consistent with cats ($pH = 6.4 \pm 0.9$). The inconsistency of our study with previous findings, whereby the urine pH in cats with struvite was acidic, could be due to the intake of therapeutic/calculolytic diets against struvite uroliths in 33.4% of cats in this study.

Whilst Shih Tzu and Miniature Schnauzers have been reported to have an increased risk for struvite and CaOx (Gough & Thomas, 2004), which is also consistent in this study, these breeds are over represented in our study due to their popularity in Malaysia. Similarly, DSH and Persians did have majority of struvite and CaOx compared to other breeds, but they were overrepresented in Malaysia as well. Dalmations were found be 79 times more likely to have ammonium urate compared to other breeds. This is because Dalmatians have a genetic predisposition towards ammonium urate formation. Research has shown that a defect in uric acid transporter (SLC2A9) alters the transport of uric acid through the hepatic and renal system and subsequently leads to high serum concentrations of uric acid (Grauer, 2014).

6.0 CONCLUSION

This was the first study that comprised of a large scale evaluation of uroliths in dogs and cats in Malaysia. In this study, there was a significant difference between the occurrence of uroliths in dogs and cats. Struvite was most likely to occur in dogs while CaOx was more likely to occur in cats. In dogs, struvite and CaOx were significantly associated with age, breed, sex, anatomical location and urine pH. In cats, only CaOx was significantly associated with the common breeds (DSH and Persians). This difference in the occurrence of uroliths calls for a species specific approach towards the management of urolithiasis in dogs and cats in Malaysia. The changes in the trend of uroliths in dogs and cats also calls for routine analysis of uroliths for proper management in the future. Diets play a crucial role towards urolith formation in dogs and cats, prospective evaluation of diets along with respective urolith findings will add value towards determining the most effective preventive and therapeutic approach towards urolithiasis. However, certain limitations of this project was the inability to determine the cause- effect relationship towards urolithiasis in Malaysian dogs and cats. Furthermore, disease frequency of urolithiasis could not be determined as well. Such limitations further calls for investigative studies towards urolithiasis in dogs and cats of Malaysia.

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8.0 APPENDICES

A. Appendix

UNIVERSITY OF MINNESOTA COLLEGE OF VETERINARY MEDICINE

Submission form for quantitative urolith analysis

Please send stones DRY (not in formalin), and in an UNBREAKABLE container. Please do not send urine samples or sediment.
Please label the sample with the **ANIMAL'S NAME**, and the **OWNER'S SURNAME**

SUBMITTED BY VETERINARY SURGEON:

☐Mr ☐Mrs ☐Miss ☐Ms ☐Dr Date ______

Surname ______

Practice Name ______

Address ______

______

Postcode ______

Telephone Number ______

Facsimile Number ______

Owner's Name ______

Owner's Address ______

______

______

Animal's Name ______

Species ______

Breed (specific) ______

Birth Date ______

Gender M MC F FS UNK

Source: ☐Renal pelvis
☐Ureter
☐Bladder
☐Urethra
☐Voided
☐Other ______

Date voided or removed ______

What food was fed prior to urolith diagnosis?

______

Approximately how long was the patient fed this food?

______

Was a Hill's* Prescription Diet* product fed? ☐ Yes ☐ No

If yes, which one?

	Dry	Canned		Dry	Canned
Canine c/d	☐	☐	Feline c/d	☐	☐
Canine s/d		☐	Feline k/d	☐	☐
Canine u/d	☐	☐	Feline s/d	☐	☐
			Feline x/d		☐

☐ Other ______

If yes, how long was the Prescription Diet* product fed?

From ______ To ______

Urinary pH at, or just prior to, urolith removal ______

Previous uroliths? ☐ Yes ☐ No

If yes, date of detection ______

If yes, what was the composition? ______

Was the urine cultured prior to stone retrieval? ☐ Yes ☐ No

Bacterial growth? ______

If yes, isolates ______

______

Were antibiotics given prior to stone retrieval? ☐ Yes ☐ No

If yes, type ______

Dosage ______

Were urinary acidifiers or alkalinizers given prior to stone retrieval?
☐ Yes ☐ No

If yes, type ______

Dosage ______

Was allopurinol given prior to stone retrieval? ☐ Yes ☐ No

If yes, dosage and duration ______

Previous illness or injury

Diagnosis ______ Date ______

Diagnosis ______ Date ______

Patient's current body weight

☐ Underweight ☐ Normal ☐ Overweight

FOR URETHRAL PLUGS ONLY

HOW IS THE PLUG PRESERVED?

1. No preservative
2. 10% buffered formalin
3. Other

Preferred method for plug submission: ½ dry, ½ in formalin

FOR ANALYSE SEND SKJEMAET TIL DENNE ADRESSEN

Hill's*

Kruuse Norge AS
Postboks 150
1441 Drøbak

*Varemerker tilhører Hill's Pet Nutrition, Inc. ©2002 Hill's Pet Nutrition, Inc.

flutdup0205(NO)213996

SEND WHITE COPY WITH SAMPLE. KEEP YELLOW COPY FOR YOUR RECORDS PLEASE TICK HERE IF YOU REQUIRE MORE FORMS: ☐