UNIVERSITI PUTRA MALAYSIA

RETROSPECTIVE STUDY ON THE PREVALENCE OF DIABETES MELLITUS IN CATS PRESENTED TO UNIVERSITY VETERINARY HOSPITAL, UNIVERSITI PUTRA MALAYSIA FROM 2010 TO 2015

SHAM PEI NI

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SHAM PEI NI

A project paper submitted to the
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It is hereby certified that we have read this project paper entitled "Retrospective Study on the Prevalence of Diabetes Mellitus in Cats Presented to University Veterinary Hospital, Universiti Putra Malaysia from 2010 to 2015" by Sham Pei Ni and in our opinion it is satisfactory in terms of scope, quality and presentation as partial fulfilment of the requirement for the course VPD 4999 – Project.

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DEDICATION

This thesis is dedicated to my family, my best friends and the one I love, who had accompanied me in my journey of becoming a veterinarian.

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I would like to express my deepest appreciation to all these who provided me the possibility to complete my final year project.

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CONTENTS

LIST OF ABBREVIATIONS

%	Percent
ALT	Alanine amino transferase
DM	Diabetes Mellitus
g	Gram
Hpf	High Power Field
L	Liter
mmol	Millimole
n	Number
U	Unit
UPM	Universiti Putra Malaysia
UVH	University Veterinary Hospital
µmol	Micromole

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ABSTRAK

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

KAJIAN RETROSPEKTIF TERHADAP PREVALENS DIABETES MELITUS PADA KUCING YANG DIBAWA KE HOSPITAL VETERINAR, UNIVERSITI PUTRA MALAYSIA DARI TAHUN 2010 HINGGA 2015

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2016

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Diabetes melitus (DM) merupakan satu daripada endocrinopati yang paling biasa berlaku di kalangan kucing dan prevalensnya lebih kurang 1% di Amerika Syarikat dan Australia. Di Malaysia tiada pendokumenan telah dibuat terhadap prevalens DM felin ini. Justeru, satu kajan retrospektif telah dijalankan di Hospital Veterinar Universiti (UVH), Universiti Putra Malaysia (UPM) terhadap kes yang dibawa pada tempoh tahun 2010 hingga 2015. Objektif kajian

ini ialah untuk menentukan prevalens DM felin berasaskan kes yang dibawa kepada UVH, menghuraikan petanda klinikal, dan untuk menentukan sama ada prognosis kucing mengidap DM boleh dilakukan melalui penemuan klinikopatologi. Dalam kajian ini 25 ekor kucing dilapor mengidap DM dalam tempoh pensampelan ini. Enam belas ekor kucing yang menerima rawatan insulin dikategorikan mengikut kucing yang mandiri dan yang kemudiannya mati. Hasil kajian menunjukkan yang prevalens DM pada kucing yang dibawa ke UVH ialah di antara 0.03 % hingga 0.17 %. Kucing diabetes menunjukkan leukogram keradangan, hiperglisemia, azotemia, kepekatan alanine aminotransferase serum meningkat, hiperproteinemia, glucosuria, dan hematuria. Prognosis kucing diabetes yang menerima rawatan insulin adalah lebih baik secara ketara (P=0.036) daripada yang tidak menerima rawatan insulin. Bagaimanapun, hanya kepekatan serum yang lebih rendah ketara (P=0.05) dalam kucing diabetes yang mandiri daripada yang kemudiannya mati.

Katakunci: felin, diabetes melitus, glucosuria, hyperglisemia, insulin.

ABSTRACT

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

RETROSPECTIVE STUDY ON THE PREVALENCE OF DIABETES MELLITUS IN CATS PRESENTED TO UNIVERSITY VETERINARY HOSPITAL, UNIVERSITI PUTRA MALAYSIA FROM 2010 TO 2015

By

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Diabetes mellitus (DM) is one of the most common endocrinopathies in cats and the prevalence is about 1% in the United States of America and Australia. In Malaysia, there is lack of documentation on the prevalence of feline DM. Therefore, a retrospective study was carried out at the University Veterinary Hospital (UVH), Universiti Putra Malaysia (UPM) on cases presented from year 2010 to 2015. The objectives of the study were to determine the prevalence of feline DM based on cases presented to UVH, to describe clinical signs, and to determine whether the prognosis of cats with DM can be determined from

clinicopathological findings. In the study, 25 cats were reported to be diabetic during the sampling period. Sixteen of these cats that received insulin treatment were categorised as either survived or dead cats. The results showed that the prevalence of DM in cats presented to UVH was between 0.03 and 0.17%. Diabetic cats showed polyuria and polydipsia. From clinicopathological findings, diabetic cats showed inflammatory leukogram, hyperglycaemia, azotemia, increased serum alanine aminotransferase concentration, hyperproteinaemia, glucosuria, and hematuria. Urinalysis showed that diabetic cats commonly showed glucosuria, proteinuria, and high urine specific gravity. The prognosis of diabetic cats with insulin treatment was significantly (P=0.036) better than those that did not receive insulin treatment. However, only serum creatinine concentration was significantly (P=0.05) lower in diabetic cats that survived from those that eventually died.

Keywords: feline, diabetes mellitus, glucosuria, hyperglycaemia, insulin

1.0 INTRODUCTION

Diabetes mellitus (DM) in cats was first discovered over 75 years ago and is one of the most common endocrinopathies (Rand and Marshall; 2004; Little, 2014). The disease is characterised by chronic hyperglycaemia resulting from defect in insulin secretion and/or action in cats. Generally, DM is divided into insulin-dependent diabetes mellitus (Type 1 DM) and non-insulin-dependent diabetes mellitus (Type 2 DM).

Type 1 DM is characterised by immunologic destruction of β-cell and minimal secretory response to β-cell secretagogues, such as glucose, glucagon, and arginine (Scott-Moncrief, 2010). Type 1 DM cats is characterized by decreased insulin secretion. On the other hand, in Type 2 DM there is abnormal insulin secretion in conjunction with peripheral insulin resistance. In cats with Type 2 DM, the total insulin secretion may be normal or increased. According to Rand and Marshall (2004), about 80 to 95 % of feline DM is analogous to human Type 2 DM. Approximately one-half to three-quarters of cats with diabetes mellitus require insulin injection especially in insulin-dependent DM. The non-insulin dependent DM in cats may or may not need insulin administration to control hyperglycaemia. However, most cats with DM ultimately need insulin treatment to control the disease.

Insulin, a hormone secreted by the pancreas, is needed by the body to transport glucose out of the bloodstream into energy producing cells. In cats with DM, secretion of insulin from the pancreas is impaired or the body's cells are resistant to the insulin action. Consequently, this compromise body ability to regulate blood glucose resulting in alteration in body functions and disturbance in

metabolism of carbohydrates, proteins, and fats. Glucose that cannot adequately enter most body cells accumulates in the bloodstream and secreted into urine. Lack of tissue glucose uptake causes fat and muscle tissues breakdown in a futile attempt to supply the desired energy as alternative energy sources for metabolism (Little, 2014).

In the United States of America and Australia, about 1 % of cats are with DM (Huang, 2012). According to Baral *et al.*, (2003), the prevalence of feline DM is approximately one in 200 cats in a primary accession of feline only practice. However in Malaysia, there is lack of documentation on feline DM. Therefore, a retrospective study on feline DM at University Veterinary Hospital (UVH), Universiti Putra Malaysia (UPM) from year 2010 to 2015 was carried out to fulfil the following objectives:

i. To determine prevalence of feline DM in UVH, UPM.
ii. To describe patient signalment, clinical findings, clinicopathological findings and treatment outcomes in diabetic cats.
iii. To identify the prognosis of diabetic cats based on clinicopathological findings.

The following hypothesis are proposed:

i. The prevalence of feline DM in UVH, UPM is low.
ii. Diabetic cats with insulin treatment has better prognosis compare to diabetic cats without insulin treatment.
iii. Prognosis of feline DM can be made based on clinicopathological findings.

2.0 LITERATURE REVIEW

2.1 Risk Factors

Diabetes mellitus can affect all cats. The disease often occurs in older (> 7 years old) and obese cats (Prahl *et al.*, 2007; Huang, 2012). Male cats are more commonly afflicted with DM than female cats. Burmese cat breed is commonly related with DM (Rand and Marshall, 2004; Huang, 2012). According to Lederer *et al.,* (2003), DM in Burmese cat is more likely a multifactorial disease. Obesity and physical inactivity can be predisposing factors to DM in cats (Rand and Marshall, 2004). In one study, cats that gained 44 % of their body weight had a 50 % decrease in their insulin sensitivity and some even had values in the diabetic range (Appleton *et al.*, 2001). Physical inactivity and indoor confinement was shown to predispose Burmese cats to DM (Lederer *et al.*, 2003). Chronic pancreatitis and hormonal diseases (such as hyperthyroidism, Cushing's disease and acromegaly) are potential environmental causes of impaired insulin secretion. For example, pancreatitis leads to a variable loss of β-cells. This was supported by a study where 50 % of diabetic cats had histological evidence of pancreatitis (Rand and Marshall, 2004). However, whether or not obesity contributes to subclinical pancreatitis and the subsequent loss of β-cells in cats remains to be determined (Rand and Marshall, 2004).

Certain medications such as megastrol acetate and corticosteroids like prednisolone have all been link to the risk factors of DM in cats. For example, prolonged use of glucocorticoids and progestogen can cause insulin resistance in cats (Rand and Marshall, 2004). Repeated administration of these drugs is associated with an increased risk of DM in cats (Lederer *et al.*, 2003).

2.2 Clinical Signs

Diabetic cats may present a variety of symptoms. Classical clinical signs in diabetic cats are polyuria, polydipsia, polyphagia, and weight loss (Bagchi and Sreejayan, 2012). However, these symptoms are dependent on the time interval between onset of hyperglycaemia in the cats and the owner seeking veterinary advices. The symptoms are also influenced by the severity of hyperglycaemia or concurrent disease such as pancreatitis. For example, clinical signs of polyuria and polydipsia only developed once the blood glucose concentration exceeds the renal tubular threshold, approximately 200 to 250 mg/dL (Rucinsky *et al.*, 2010). At this stage, glucosuria can occur. Excess glucose in urine leads to excess urination and thirst in cats. If insulin is deficient or ineffective, there will be spontaneously breakdown fat and protein stores as alternative energy sources, resulting in loss in body weight. Often cats with DM exhibit unexplained polyphagia. However, it was suggested by the murine model that decreased circulating level of insulin and leptin can lead to increase release of ghrelin as trigger for diabetic polyphagia (Rios and Ward, 2008).

Other symptoms such as inactive, lethargy, weakness, poor body condition, unkempt hair coat and plantigrade stance can be also be observed in diabetic cats. Plantigrade stance is a form of diabetic neuropathy. It occurs approximately in 10 % of diabetic cats. Alteration in the sorbitol metabolic pathway is believed to be the aetiology of plantigrade stance (Rios and Ward, 2008). However, the clinical signs often improved or disappear when hyperglycaemia is controlled with insulin and dietary treatments (Reusch, 2010).

2.3 Diagnostic Tools

In initial assessment of DM in cats, investigation should always include history, physical examination, complete blood count, serum biochemistry test, urinalysis, serum thyroxine test and serum fructosamine test (Rucinsky *et al.*, 2010). History and physical examination can aid veterinarian in identification of abnormality such as dehydration, plantigrade stance, or ketotic breath in the cats.

From laboratory assessment, typical findings in blood profile include stress leukogram and persistent fasting hyperglycaemia (Rand and Marshall, 2004; Rios and Ward, 2008). Due to the tendency of cats to develop stress hyperglycaemia, persistent hyperglycaemia can be challenging to ascertain. As an alternative test, serum fructosamine test can used (Rios and Ward, 2008). Fructosamine is a glycosylated protein that binds glucose to amino acid residues (albumin) in circulation. The concentration of serum fructosamine is a reflection of mean blood glucose level over the preceding one to three weeks. Values above the reference range would confirm the diagnosis of DM in cats (Rios and Ward, 2008). In addition, cats with diabetic ketoacidosis may reveal elevated liver enzymes, azotemia, and alteration in electrolyte concentration in blood profile.

From the urinalysis result, glucose, protein, ketone, bacteria, and/or cast may be shown in the samples (Rucinsky *et al.*, 2010). Cats aged >7 years old with clinical signs of weight loss and polyphagia; serum thyroxine test is strongly suggested to rule out or rule in hyperthyroidism. Abdominal ultrasonography and feline pancreatic lipase immunoreactivity concentration test may also be useful in evaluating diabetic cats concurrent with pancreatitis.

2.4 Treatments and Management

Diabetes mellitus is treatable but requires long-term commitment from the veterinarian and owner. In clinical DM management, insulin treatment is required in addition to diet therapy. The purposes of insulin treatment are to avoid or improve complication such as diabetic ketoacidosis and peripheral neuropathy, prevent symptomatic hypoglycaemia and promote good quality life (Rios and Ward, 2008).

In diet therapy, feeding multiple meals such as four times daily is ideal to manage weight together with control od calories intake (Rucinsky *et al.*, 2010). For diabetic cats with poor body condition, free choice feeding is acceptable. For obese diabetic cats, environment enrichment is highly encouraged (Rucinsky *et al.*, 2010).

Glargine (U-100) or the veterinary-approved human protamine zinc insulin (PZI U-40) is the common insulin preparation with long duration of action for diabetic cats (Rucinsky *et al.*, 2010). Judicious dosing is recommended and early and sudden increase in insulin dose should be avoided. This is because diet change may alter food intake and affect response to insulin. So, it is recommended that the insulin dose is adjusted to food intake and if there is no improvement of clinical signs after a week of insulin therapy.

In initial approach of insulin treatment, starting dose of 1U per cat for every 12 hours is suggested based on estimation of the cat lean body weight (Rucinsky *et al.*, 2010). Starting dose of insulin should not exceed 2U per cat for every 12 hours even for large size cat. The blood glucose should be measured every two to three hours for cats on PZI and every four hours for cats on insulin Glargine; for

duration of 10 to 12 hours following insulin administration (Rucinsky *et al.*, 2010). Reevaluation have to be done immediately if cat show any sign of hypoglycaemia, to include include weakness, lethargy, lack of coordination, convulsion and coma. Left untreated hypoglycemia can be fatal to cats (Rucinsky *et al.*, 2010).

According to Rucinsky *et al.*, (2010), after establishing the appropriate insulin dose, monitoring of insulin treatment in the cats should begin and this requires a long term commitment from the owner. Owner should be advised to monitor and record food and water intake daily and insulin dosage and clinical signs presented by their cats. The body weight should be monitored weekly and blood glucose spot checks done twice a month to assess the condition of the cat.

Veterinarian on the other hand should maintain good communication with owner concerning the insulin treatments, follow-up appointments, associated costs and home care for their diabetic cats.

Prognosis of DM in cats vary since age and concurrent disease can affect the survival rate. For example, diabetic ketoacidosis, concurrent disease and poor hyperglycaemia control may reduce cat's survival. In addition, many cats do not live beyond 12 months after diagnosis (Rand and Marshall, 2004). Nevertheless, some cats may lose the need for insulin, months or years after diagnosis. For example, if DM in cats is the result of obesity, the prognosis is likely to be good prognosis if the weight of the cat is under control. However, if the cause of DM is unknown, the disease most probably will persist; however, it can be managed with success with proper treatment and home-care.

3.0 MATERIALS AND METHODS

3.1 Source of Data

A retrospective study was performed based on the records available at the Haematology and Clinical Biochemistry Laboratory, Department of Veterinary Laboratory Diagnosis, Faculty of Veterinary Medicine, UPM, for a period of 6 years from January 2010 to December 2015. The reports were screened for blood and urinalysis profiles of cats that are suggestive of diabetes mellitus. Then, the case numbers of the representative cases were obtained and patient medical records were reviews from Achieves of UVH, UPM. From the patient medical records, patient signalment inclusive of age, breed, gender and neuter status, clinical findings, diagnostic investigations (blood and urinalysis profiles), therapeutic plan and clinical outcomes were recorded for the diabetic cats.

Sixteen cats that had received insulin treatment, were categorised into 2 group, which survived and dead diabetic cats. The clinicopathological findings of the two groups were analysed and compared. Data that were missing and not applicable were recorded as not available (NA).

3.2 Data Tabulation and Statistical Analysis

All data recorded were tabulated in Microsoft Excel spreadsheet and transferred to IBM Statistical Package for the Social Sciences software version 23.0 to further statistical analysis to include Shapiro-Wilk test, Mann-Whitney test, independent t-test and Chi-square analysis. Statistical significance at value of $p < 0.05$ was used. Data collected in this study was analysed using descriptive method.

4.0 RESULTS

4.1 Prevalence of Diabetes Mellitus in Cats

From January 2010 to December 2015, a total of 25 cats were diagnosed with DM at UVH, UPM. The occurrence of cases was from 1 to 8 cases per year. The prevalence of feline DM in UVH are as in Table 1.

Table 1: Prevalence of DM in cats presented to UVH, UPM from 2010 to 2015

Year	Number of cats		Prevalence (%)
	diagnosed with diabetes mellitus	Total cats presented to UVH, UPM	
2010	3	2418	0.12
2011	1	3258	0.04
2012	8	4835	0.17
2013	7	5260	0.13
2014	3	5527	0.05
2015	3	6526	0.05

4.2 Age, Gender, Neuter status, Breed of Cats

Age group of diabetic cats in this study are categorised following a convenient life-stage classification developed by the Feline Advisory Bureau (Amy *et al.*, 2010). The majority of cat diagnosed with DM were adult cats (n=9, 36 %). This followed by senior cats (n=6, 24 %), mature cats (n=5, 20 %) and geriatric cats (n=3, 12 %). The least fall in the categories of junior cats (n=2, 8 %), as reviewed in the Figure 1.

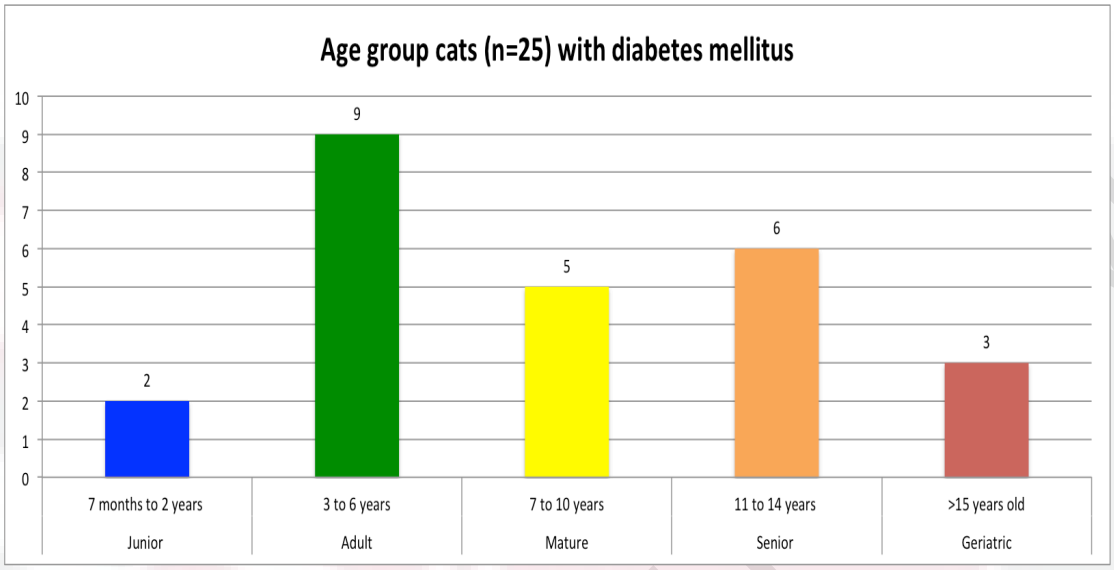

Figure 1:Age group cats (n=25) with DM.

Among the 25 cats diagnosed with DM, there are 19 male cats (76 %) and 6 female cats (24 %). In addition, 10 of the male cats and 5 of the female cats were neutered (Figure 2).

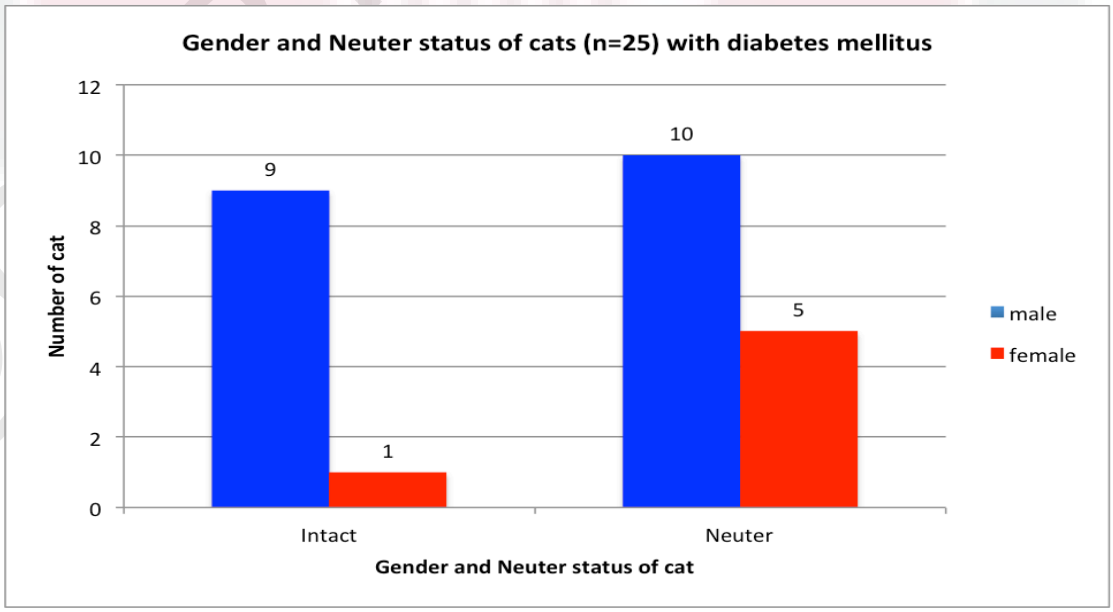

Figure 2: Gender and neuter status of cats (n=25) with DM.

Furthermore, 84% of cats diagnosed with DM were Domestic Short Hair cat breed. The rest were breed of Domestic Short Hair cross, Siamese, Siberian cross and Persian cats, which contribute only 3.85 % each (Figure 3).

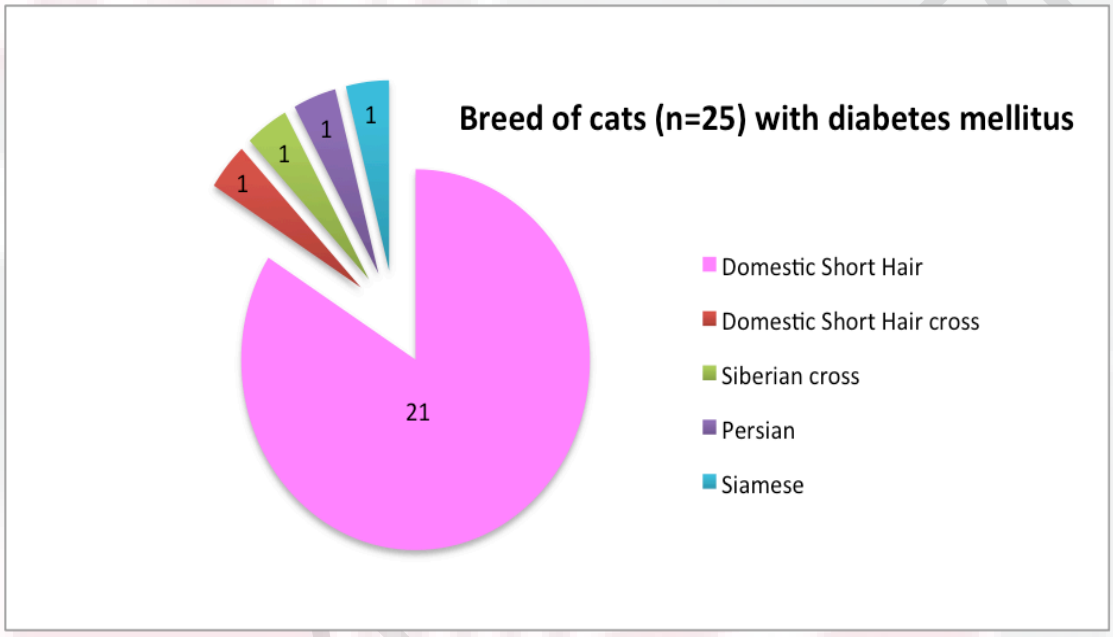

Figure 3: Breed of cats (n=25) with DM.

4.3 Physical Examination Findings

For cat diagnosed with DM, clinical signs associated with the disease include polyuria and polydipsia, dullness and depressed, lose weight (Table 2). For instance, 72 % of the diabetic cats showed polyuria and polydipsia; and 44 % of diabetic cats are dull and depressed upon presentation and 36 % of cats lost weight and had reduced appetite after onset of diabetes mellitus.

Table 2: Clinical signs presented by cats (n=25) with diabetes mellitus

Physical examination Findings	Number	Percentage*
Polyuria and Polydipsia	18	72%
Dull and Depressed	11	44%
Lose weight	9	36%
Reduce appetite	9	36%
Dehydration	7	28%
Polyphagia	4	16%
Pale	4	16%
Distended abdomen	4	16%
Unkempt hair coat	3	12%
Plantigrade stance	3	12%
Hypothermia	2	8%
Vomiting	2	8%

*based on each clinical signs presented by cat.

4.4 Clinicopathological Findings

A blood profile and urinalysis was available for majority of the diabetic cats in this study (Table 4). Based on the haemogram, it showed that 55 % of diabetic cats had neutrophilia with left shift; 40 % had monocytosis; while 45 % had thrombocytopenia. The serum biochemistry profiles showed that all diabetic cats had hyperglycaemia. Sixty percent of diabetic cats had increased serum urea concentration and 55 % of had increased serum ALT concentration. In addition, 82 % of the diabetic cats showed hyperproteinaemia and 55 % had hyperglobulinaemia while 20 % had increased serum creatinine. The urinalysis results showed that 92 % of the urine samples from diabetic cats were turbid due to presence of fat droplets, 91 % revealed glucosuria and 64 % showed proteinuria. All diabetic cats had hematuria while 18 % of cats had bilirubinuria. Two cats (18 %) have pH value above normal range. Lastly, 36 % of diabetic cats had urine specific gravity of < 1.035.

Table 3: Clinicopathological findings in cat with DM.

Variable	N	Median	Mean	Range	Reference Range (RR)	Compared to Reference Range		
						Higher n(%)	Within n(%)	Lower n(%)
Complete Blood Count								
Band neutrophil ($\times 10^9$/L)	11	0.25	0.69	0.06-2.50	<0.3	6 (55%)	5 (45%)	0
Seg. Neutrophil ($\times 10^9$/L)	11	7.60	11.90	3.57-27.10	2.5-12.5	4 (40%)	6 (55%)	1 (5%)
Monocyte ($\times 10^9$/L)	11	0.63	1.078	0.14-3.26	0.2-0.8	4 (40%)	6 (55%)	1 (5%)
Thrombocyte ($\times 10^9$/L)	11	331.00	337.10	71.80-584.00	300-700	0	6 (55%)	5 (45%)
Serum Biochemistry test								
Urea (mmol/L)	12	13.00	15.078	6.40-34.70	3-10	7 (60%)	5 (40%)	0
Creatinine (µmol/L)	12	155.00	172.42	59.00-461.00	60-193	2 (20%)	10 (80%)	0
Glucose (mmol/L)	12	22.25	26.01	13.20-48.80	3.1-7.2	12 (100%)	0	0
Total Protein (g/L)	11	88.30	86.82	66.80-105.50	55-75	9 (82%)	2 (18%)	0
Globulin (g/L)	11	45.70	54.45	26.00-79.20	25-4	6 (55%)	5 (45%)	0
Sodium (mmol/L)	10	142.50	142.19	128.90-156.00	146-156	0	4 (40%)	6 (60%)
Potassium (mmol/L)	10	4.00	3.88	2.20-5.30	3.9-5.5	0	5 (50%)	5 (50%)
Alanine aminotransferase (U/L)	11	92.40	172.13	33.9-609.70	10-90	6 (55%)	5 (45%)	0
Bilirubin (Total) (µmol/L)	2	22.90	22.90	7.00-38.80	1.7-17	1 (50%)	1 (50%)	0
Urinalysis								
Turbidity	12	1+	1+	Clear to 2+	Normal	11 (92%)	1 (8%)	0
Glucosuria	11	4+	4+	Negative to 4+	Negative	10 (91%)	1 (9%)	0
Proteinuria	11	1+	2+	Negative to 3+	Negative	7 (64%)	4 (36%)	0
Ketonuria	11	Negative	1+	Negative to 3+	Negative	4 (36%)	7 (64%)	0
Hematuria (Hpf)	11	5	15	0-60	Negative	11 (100%)	0	0
Bilirubinuria	11	Negative	Negative	Negative to 2+	Negative	2 (18%)	9 (82%)	0
pH value	11	6.00	6.36	6.00-8.00	6.0-6.5	2 (18%)	9 (82%)	0
Specific Gravity	11	1.037	1.040	1.018-1.060	1.035-1.060	0	7 (64%)	4 (36%)

4.5 Survivability of Diabetic Cats Receiving Insulin Treatment

Among 25 cats, only 16 cats (64 %) received insulin treatment while 3 cats (12 %) did not. Six cases did not have data on the treatment record. Out of 16 cats that have received insulin treatment, 12 cats (75 %) survived, but 4 cats (25 %) died (2 were euthanised and 2 died in natural cause). Three cats (100 %) without insulin treatment died (Figure 4).

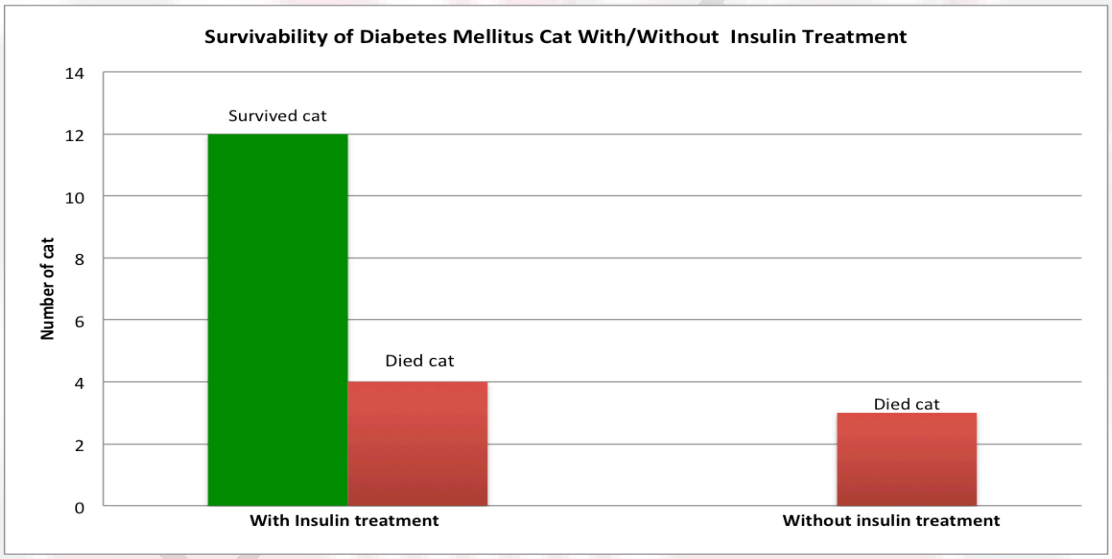

Figure 4: Survivability of diabetic cats with or without insulin treatment.

4.5 Prognosis of Diabetic Cats Based on Clinicopathological Findings

From the Table 5, there is no significant ($p>0.05$) association between the clinicopathological findings and survivability of diabetic cats. Therefore, the hypothesis that states the prognosis diabetic cats can be made based on clinicopathological findings is rejected. However, the results may be influenced by small sample size and missing data.

Table 4: Comparison of clinicopathological findings between diabetic cats that survived versus those that died.

Variable	Survived Mean ± SE	Dead Mean±SE	P value	Reference Range (RR)
Complete Blood Count				
Band neutrophil ($\times 10^9$/L)	0.63±0.25	1.30*	0.82	0.06-2.50
Seg. Neutrophil ($\times 10^9$/L)	12.96±2.95	1.30*	1.00	3.57-27.10
Monocyte ($\times 10^9$/L)	0.85±0.28	3.26*	1.00	0.14-3.26
Thrombocyte ($\times 10^9$/L)	321.18±51.55	496*	0.33	71.80-584.00
Serum Biochemistry test				
Urea (mmol/L)	13.98±1.92	20.55±14.15	0.35	6.40-34.70
Creatinine (µmol/L)	147.90±14.25	295.00±16.60	0.05	59.00-461.00
Glucose (mmol/L)	27.05±2.62	24.10±8.31	1.00	13.20-48.80
Total Protein (g/L)	85.36±3.79	71.10*	0.20	66.80-105.50
Globulin (g/L)	48.12±5.19	37.70*	0.40	26.00-79.20
Sodium (mmol/L)	144.12±2.95	134.45±5.55	0.18	128.90-156.00
Potassium (mmol/L)	4.24±0.36	2.45±0.25	0.38	2.20-5.30
Alanine aminotransferase (U/L)	172.12±41.84	609.70*	1.00	33.9-609.70
Bilirubin (Total) (µmol/L)	22.90±15.90	*	*	7.00-38.80
Urinalysis				
Turbidity	1+±0.19	1+*	1.00	Clear to 2+
Glucosuria	4+±0.40	4+*	1.00	Negative to 4+
Proteinuria	1+±0.45	3+*	1.00	Negative to 3+
Ketonuria	1+±0.40	3+*	0.36	Negative to 3+
Hematuria (Hpf)	16.50±7.45	*	0.55	0-60
Bilirubinuria	Negative±0.20	*	1.00	Negative to 2+
pH value	6.40±0.26	6.00*	1.00	6.00-8.00
Specific Gravity	1.039±0.0034	1.042*	0.83	1.018-1.060

* mean is constant when animal is dead. The value have been omitted.

5.0 DISCUSSION

In this study of feline DM, for the years 2010 to 2015, the lowest prevalence was 0.03 % and the highest was 0.17 %, a range that was lower than that reported in the United States of America and Australia (Huang, 2012). However, since the study was conducted in cases presented to UVH, UPM, these prevalence values are not representative of the total incidence in the cat population of Malaysia.

In this study, the mean age of cats at the time diagnosed with DM was 8.6 years old. According to Prahl *et al.*, (2007), cats aged more than 7 years old were at highest risk of acquiring DM compared to cats less than 1 year. That study also suggested that the risk of DM increased with age of the cat. Older cats are more likely to develop DM because they cannot adequately respond to increased insulin requirement and maintain a healthy glucose homeostasis.

Among the cats in the present study, 76 % of diabetic cats were male while 24 % were female cats. Male cats were at higher risk of getting DM compared to female cats. Male cats were more likely to gain weight faster than female cats. Thus the gender differences in incidence of DM may be associated with rate of body weight gain and development of insulin sensitivity (Prahl *el al.*, 2007). In addition, male cats regardless of any weight had higher basal insulin concentration and lower insulin sensitivity compared with female cats making the males more prone to become resistant to insulin than female cats (Appleton *et al.*, 2001).

Sixty percent of the diabetic animals were neutered. It seems that glucose tolerance test results did not change after cats were neutered (Hoenig and Ferguson, 2002; Thiess *et al.*, 2004).

According to breed, 84 % of diabetic cats in this study are Domestic Short Hair cat breed. However, this finding may be biased as this breed is an indigenous cat breed found in large numbers in Malaysia.

According to Rand and Marshall, (2004), a diagnosis of DM in cats is made based on the presence of appropriate clinical signs, persistent fasting hyperglycaemia (blood glucose >16 mmol/L) and glucosuria. In addition, clinical signs of DM become more apparent when blood glucose concentration exceeds the renal threshold (>14 mmol/L). Glucose that leaks with the urine is not fully reabsorbed in the proximal tubules and cause osmotic diuresis.

In this study, 72 % of diabetic cats were shown to had history of polyuria and polydipsia. These symptoms are due to excessive glucose in the blood and urine that lead to excessive urination and increased water consumption by the cats (Reusch, 2010). Diabetic cats often have good appetite but tend to lose weight due to diabetic polyphagia. Weight loss is also a result of calories lost in glucose-laden urine (Greco, 2007). In this study, 36 % of diabetic cats had weight loss while 16% had polyphagia.

Polyuria associated unkempt skin coat had shown in three diabetic cats in this study, while three diabetic cats had plantigrade stance that is the result of cats becoming progressively weaker especially of their hind limbs. Subsequently, the condition impairs their ability to jump and causing them to walk with their hocks touching the ground. Although the hind limbs were affected first, signs can progress to the fore limbs weakness (Rand and Marshall, 2004).

Besides classical clinical signs of DM, 44 % of diabetic cats were dull and depressed upon presentation. This may be an early sign of diabetic ketoacidosis

(Reusch, 2010). If these signs go unnoticed, untreated cats will be at higher risk of developing diabetic ketoacidosis and hyperosmolar nonketotic syndrome. As metabolic condition continues to deteriorate, clinical signs of anorexia, vomiting and dehydration may develop (Reusch, 2010). For example in this study, 36 % of diabetic cats were anorexia; 28 % of them were dehydrated; and 8 % of diabetic cats had history of vomiting. These clinical signs were perhaps a result of an autonomic neuropathy. As DM progress, ketosis and hyperosmolality can lead to vomiting and severe dehydration (Greco, 2002). In this study, four cats also had distended abdomen and were suspected to suffer from concurrent pancreatitis. However, laboratory analyses did not show significant finding.

Concurrent disease may worsen insulin resistance and hinder treatment success. Therefore, a complete blood count, serum biochemical panel, urinalysis and urine culture should be performed routinely (Reusch, 2010). Typical haematological abnormalities in diabetic cats include a stress leukogram. However, in this study, 55 % of the diabetic cats showed inflammatory instead of stress leukogram, as evidence of neutrophilia with left shift. Among the diabetic cats, 40 % showed monocytosis and 55 % showed hyperglobulinaemia. The haematological findings are suggestive of concurrent infection or inflammation (Rios and Ward, 2008). 45 % of diabetic cat showed thrombocytopenia, suggested to be false thrombocytopenia, which is a common occurrence in cats.

All diabetic cats show hyperglycaemia with mean blood glucose concentration of 26 mmol/L. However, diabetes hyperglyceamia need to be differentiated from stress-induced hyperglycaemia by alternative use of serum fructosamine test (Rand and Marshall, 2004).

The study also showed that 55 % of diabetic cats had increased serum ALT concentration with a mean value at 172 U/L. This finding is similar to those of Reusch (2010). The increase in serum ALT activity is suggested to be the result of reactive hepatopathy and hepatic lipidosis in diabetic cats (Greco, 2007).

Moreover, 60 % of diabetic cats showed increased urea. Elevation of tissue polypol concentration resulting from hyperglycaemia can contribute to renal dysfunction. This may be accompanied by thickening of glomerular basement membranes and glomerular hypertension (Greco, 2007). Thus, azotemia can be presented as a late consequence of diabetic nephropathy.

In this study, 82 % of diabetic cat had hyperproteinaemia. This may probably a manifestation of haemoconcentration that is often seen in DM. In DM, persistent hyperglycaemia causes increased binding of plasma protein to glomerular basement membrane (Greco, 2007). Therefore, diet therapy of low-carbohydrate and high protein diet combined with insulin treatment may help to prevent progression of diabetic nephropathy in cats (Deborah, 2006).

Urinalysis showed that 91 % of urine samples of diabetic cats had glucosuria, while 64 % had proteinuria. The proteinuria may be indicative of bacterial infection or damage to glomerular membrane secondary because of DM (Rios and Ward, 2008). According to Reusch (2010), hematuria correlated strongly with a positive urine bacterial culture. However, since urine cultures was not done in these cats, the cause of proteinuria cannot be positively associated with infection in the diabetic cats in this study.

Reusch, (2010) also showed that urine specific gravity in diabetic cat is more than 1.020 and sporadic ketone bodies may be found. In this study, 91 % of

diabetic cats revealed urine specific gravity of >1.020, which could possibly cause glucosuria (Rios and Ward, 2008). Ketonuria found in four diabetic cats in this study is due to fat mobilization that is often seen in DM.

In term of survivability, diabetic cats received insulin treatment had better prognosis compared to those without insulin treatment (P=0.036). Furthermore, the only significant difference was found in creatinine, where insulin-treated diabetic cats that survived had lower creatinine concentration than those that died.

In summary, the haemogram of diabetic cat that eventually died showed higher number of band neutrophils and monocytes compare to that survived. From the serum biochemistry panels, diabetic cats that eventually died show higher serum urea, creatinine, and ALT concentrations compared cats that survived, while the sodium and potassium were lower. This serum changes can be life-threatening to diabetic cat with ketoacidosis. Diabetic cats that died had moderate proteinuria and ketonuria compare to mild proteinuria and ketonuria in those that survived. These changes may complicate the DM, resulting in poor prognosis in diabetic cats.

6.0 CONCLUSION

In conclusion, this retrospective study had showed low prevalence of DM in cats presented to UVH, UPM from January 2010 to December 2015. Feline DM is a multifactorial disease where both genetic and environmental factors are involved in the pathogenesis. Diabetic cats showed polyuria and polydipsia. From clinicopathological findings, diabetic cats showed inflammatory leukogram, hyperglycaemia, azotemia, increased serum alanine aminotransferase concentration, hyperproteinaemia, glucosuria, and hematuria. On the other hand,

prognosis of diabetic cat with insulin treatment is significant better compared to diabetic cat without insulin treatment. With good blood glucose control, it may facilitate diabetic cats to undergo clinical remission.

7.0 RECOMMENDATION

One of the limitation of this study was incomplete data. Manual data retrieval was time-consuming. In addition, there is lack of consistency in blood and urinalysis findings among cats with DM. Therefore, it would be favourably for future similar studies for a computerized recording system to be placed in UVH and diagnostic laboratories. Furthermore, it is suggested that the sample size need to be bigger to allow for better conclusion to be made from the study.

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8.0 APPENDICES

Table 8.0: Case number and laboratory number of 25 diabetic cats.

Cat	Case No.	Lab No.	Age	Gender and Neuter Status	Breed
1	037095	2010/105 2010/165 2010/332	11	Intact Male	Domestic Short Hair
2	032734	2010/1311	6	Spayed Female	Domestic Short Hair
3	039072	2010/2531	3	Intact Male	Domestic Short Hair
4	036772	2011/1508	12	Castrated Male	Domestic Short Hair
5	043937	2012/80 2012/360	1.5	Intact Male	Domestic Short Hair
6	418743	2012/1059	12	Castrated Male	Domestic Short Hair
7	044759	2012/899	5	Intact Female	Domestic Short Hair

8	048401	2012/4207	6	Intact Male	Domestic Short Hair
9	045066	2012/1245	3	Intact Male	Domestic Short Hair
10	046040	2012/2209	6	Castrated Male	Domestic Short Hair
11	046974	2013/1283 2013/2929	7	Spayed Female	Domestic Short Hair
12	032914	2012/3369	4	Castrated Male	Domestic Short Hair
13	047336	2013/334 2013/3230 2013/3253	6	Intact Male	Domestic Short Hair
14	049289	2013/427 2013/283	9	Castrated Male	Domestic Short Hair cross
15	007489	2013/440	21	Castrated Male	Domestic Short Hair
16	011791	2013/594 2013/596 2013/649	16	Spayed Female	Domestic Short Hair
17	052616	2013/3100	9	Castrated Male	Domestic Short Hair
18	052109	2013/2603 2013/2622	8	Intact Male	Domestic Short Hair
19	054191	2013/4313	1	Intact Male	Siamese
20	039783	2014/751 2014/130	9	Intact Male	Domestic Short Hair
21	055442	2014/572	6	Castrated Male	Domestic Short Hair
22	059100	2014/3380	11	Castrated Male	Domestic Short Hair
23	021126	2015/1625	14	Castrated Male	Siberian cross
24	066130	2015/3418	13	Spayed Female	Persian
25	068198	2015/4451	16	Spayed Female	Domestic Short Hair