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Clinicopathological Profiling of Chronic Kidney Disease in Cats Presented at University Veterinary Hospital, Universiti Putra Malaysia from 2016-2021

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ABSTRACT

Chronic kidney disease (CKD) is common in cats, typically showing increased prevalence in geriatric patients. This study profiled clinicopathological changes across CKD stages in 136 cats -without concurrent diseases- selected from the Veterinary Laboratory Services Unit database. Cases were classified into stages II, III, and IV based on the International Renal Interest Society (IRIS) creatinine guidelines. Signalment and clinicopathological data including hematology, serum biochemistry and urinalysis were analysed. Domestic Shorthair (77.2%) was the most common breed affected, followed by Persian (5.9%) and mixed breed cats (5.9%). Males (60.1%) were more frequently diagnosed than females (37.5%). Notably, cats aged 5 to 8 years (n=48) were overrepresented with CKD regardless of stage. Erythrocyte counts and haemoglobin levels were significantly higher ($p<0.05$) in stage II than in stage IV. Similarly, packed cell volume, reticulocyte counts, and urine specific gravity were significantly higher ($p<0.05$) in stage II than in stages III and IV. Levels of band and segmented neutrophils, as well as monocytes increased as stages advance, reaching the highest in stage IV cats ($p<0.05$). Phosphate level was significantly higher ($p<0.05$) in stages IV than in stages II and III. Urea and creatinine concentrations in stage IV were approximately four times higher than those in stage II. High-normal sodium and albumin, low-normal chloride and normal potassium were common across all stages. These findings suggest that non-regenerative anaemia and tubular dysfunction characterise later CKD stages. Understanding these patterns is vital for monitoring disease progression and optimising therapeutic interventions.

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INTRODUCTION

Chronic kidney disease (CKD) is a metabolic disease that is frequently seen in cats, in which the prevalence increases with age

(Bartges, 2012; Brown et al., 2016). The prevalence of CKD in geriatric cats has climbed from 35% (Krawiec & Gelberg, 1989) to as high as 80% (Chen et al., 2020). Although geriatric cats have a higher prevalence, all cats of all ages are likely to be affected with CKD (Bartges, 2012; Chen et al., 2020).

Chronic kidney disease occurs due to kidney structure and function damage over a long period, which subsequently become more severe and irreversible (Bartges, 2012). Chronic kidney disease can be contributed by various underlying diseases such as amyloidosis, toxication, chronic pyelonephritis or glomerulonephritis, feline infectious peritonitis, lymphoma, polycystic kidney disease, feline leukaemia and hypoxia (Brown et al., 2016; Sparkes et al., 2016). Progressive damage to the kidney causes a reduction of large amounts of functional nephron units and gradually impairs glomerular filtration rate (GFR) for excretion of metabolites, leading to build up of by-products such as blood urea nitrogen (BUN) and creatinine in the body (McLeland et al., 2015).

Chronic kidney disease can be diagnosed using a combination of thorough physical examination, patients' history, complete blood count (CBC), serum biochemistry, urinalysis, abdominal radiograph or ultrasonography, and renal scintigraphy or renal biopsy. According to the International Renal Interest Society (IRIS) staging system, CKD can be classified into four stages using serum creatinine level in fasted patients as a measure of GFR (IRIS, 2023). Symmetric dimethylarginine (SDMA), an amino acid that is the by-product of intranuclear protein methylation, was introduced as a renal biomarker primarily excreted through renal filtration and is considered to be more sensitive than serum creatinine as the former is less influenced by muscle mass (Hall et al., 2014; Sargent et al., 2021). Serum SDMA detects as little as 25% loss of kidney function, while creatinine typically does not rise until 75% of function is lost. Unlike creatinine, SDMA is not influenced by confounding conditions such as muscle mass, making it more reliable for assessing kidney function (Sargent et al., 2021).

At the terminal stage of oliguric feline CKD patients, the classical clinicopathological findings include azotaemia (elevated serum creatinine and BUN), hyponatremia, hypochloremia, hyperkalemia, hyperphosphatemia, isosthenuria (S.G. 1.008-1.012), non-regenerative anaemia, and proteinuria (Elliott & Barber, 1998; Polzin, 2013; Reynolds & Lefebvre, 2013). Histologically, it was found that kidney lesions are more destructive and irreversible in stage III and IV than stages I and II CKD (McLeland et al., 2015). It is hypothesised that the severity of lesions between CKD stages may also reflect in the clinicopathological parameters. Nevertheless, CKD in feline patients may not usually be presented with the typical clinicopathological findings in clinical practice, as it may be influenced by various risk factors of CKD, such as age, comorbidities and environmental factors (Brown et al., 2016). Given that Malaysia's tropical climate predisposes feline populations to dehydration that may induce hemoconcentration, there is a risk that the

underlying abnormalities may be masked that can compromise the accuracy of assessment of CKD based on clinicopathological parameters. Despite these challenges, comprehensive clinicopathological profile of feline CKD remain sparse within the Malaysian context. Hence, the main objective of this study is to profile clinicopathological parameters (haematology, serum biochemistry and urinalysis) in cats presented with various stages of CKD at University Veterinary Hospital (UVH), Universiti Putra Malaysia (UPM).

MATERIALS AND METHODS

Case Inclusion

In this retrospective study, the digital clinicopathological data of all cases presented at UVH, UPM and submitted to the Clinical Pathology Laboratory, Veterinary Laboratory Services Unit (VLSU), UPM between the year 2016 and 2021 was obtained with permission. Data was screened and narrowed to feline cases that have all three results of CBC, serum biochemistry and urinalysis. Patients' history and disease diagnosis confirmatory from UVH clinicians were not attainable in this study due to limited access during the COVID-19 pandemic.

The clinicopathological data was retrospectively refined to feline cases that were suspected to have CKD based on a few criteria. Firstly, the cases must have serum creatinine ≥ 140 µmol/L. Secondly, the cases have no evidence of feline lower urinary tract disease from the urinalysis results. The evidence includes pale reddish or reddish coloured urine, or presence of numerous erythrocytes or leukocytes per high power field under microscopic examination. Thirdly, cases should not have other concurrent diseases such as cardiovascular, liver disease and diabetes mellitus. A total number of 136 cases fulfilled all three criteria and were selected for this study.

Clinicopathological Data

Complete clinicopathological profiles from each case were compiled, including signalment, haematological, serum biochemistry and urinalysis parameters. Using serum creatinine concentration results, the cases were categorised into stages II (140-250 µmol/L), III (251-440 µmol/L) and IV (>440 µmol/L) following the IRIS staging system of CKD for cats (IRIS, 2023). Stage I serum creatinine value (<140 µmol/L) was excluded from the inclusion criteria. It is acknowledged that the IRIS staging used in this study is based on the serum creatinine concentration only, although creatinine together with SDMA concentrations are preferred. Due to limitations of obtaining other parameters that includes SDMA from UVH database, the staging of CKD in these patients were categorised descriptively using serum creatinine concentration.

Statistical Analysis

Statistical analysis was performed using IBM SPSS statistical software, version 23 with CKD stages (II-IV) as the independent variable, and the categorical variables (breed, age, sex, and urine protein) and clinicopathological parameters as dependent variables. Descriptive analysis was employed for the categorical variables. Chi-square and Fisher's exact analyses were then performed to determine the association between the signalment and CKD stages. Data for clinicopathological parameters that were normally distributed which are the packed cell volume (PCV), mean corpuscular volume (MCV), lymphocytes count, albumin to globulin ratio (A:G), and the concentrations of hemoglobin, albumin, globulin and mean corpuscular hemoglobin (MCHC) were analysed using one-way ANOVA; data that were not normally distributed including the total counts of red (RBC) and white (WBC) blood cells, band and segmented neutrophils, monocytes, eosinophils and reticulocytes, the concentrations of serum sodium (Na), potassium (K), chloride (Cl), calcium (Ca), BUN, creatinine, total protein, and the urine specific gravity (USG) were analysed using Kruskal-Wallis Test. The tests were done to compare the mean or median of clinicopathological parameters with the CKD stages, respectively. When there is statistical significance, corresponding post hoc Fisher's LSD and pairwise comparison were then performed. Results with a p value of less than 0.05 were considered statistically significant.

RESULTS

Breed, Sex, and Age Distribution

There was no significant association found ($p>0.05$) between CKD stages and breed, sex, and age.

Breed

Among 136 cats that were suspected with CKD, Domestic Shorthair represented the majority of the study population, followed by Persian and Cross/Mixed as shown in Table 1.

Table 1
B*reeds of cats that were suspected with chronic kidney disease*

Breed	CKD Stage (n)			Frequency (n)	Prevalence (%)	95 % CI	
	II (%)	III (%)	IV (%)			Lower limit	Upper limit
Domestic Shorthair	47 (34.6%)	22 (16.2%)	36 (26.5%)	105	77.2	69.6	83.6
Persian	2 (1.5%)	1 (0.7%)	5 (3.7%)	8	5.9	2.8	10.8
Cross/Mixed	2 (1.5%)	2 (1.5%)	4 (2.9%)	8	5.9	2.8	10.8

Table 1 *(continued)*

Breed	CKD Stage (n)			Frequency (n)	Prevalence (%)	95 % CI	
	II (%)	III (%)	IV (%)			Lower limit	Upper limit
Domestic Longhair	4 (2.9%)	1 (0.7%)	2 (1.5%)	7	5.1	2.3	9.8
Siamese	2 (1.5%)	1 0.7%)	1 (0.7%)	4	2.9	1.0	6.8
Maine Coon	0 (0.0%)	1 (0.7%)	0 (0.0%)	1	0.7	0.1	3.4
Norwegian Forest	1 (0.7%)	0 (0.0%)	0 (0.0%)	1	0.7	0.1	3.4
Unknown	1 (0.7%)	1 (0.7%)	0 (0.0%)	2	1.5	0.3	4.6
Total	59 (43.4%)	29 (21.3%)	48 (35.3%)	136	100.0		

Sex

Male cats have a higher proportion of CKD than female cats. Among toms, 44 were castrated, while among queens, 39 were spayed as shown in Table 2.

Table 2
Sex distribution of cats that were suspected with chronic kidney disease

Sex	CKD Stage (n)			Frequency (n)	Prevalence (%)	95 % CI	
	II (%)	III (%)	IV (%)			Lower limit	Upper limit
Intact Male	14 (10.3%)	7 (5.1%)	17 (12/5%)	38	27.9	20.9	35.9
Castrated Male	18 (13.2%)	9 (6.6%)	17 (12.5%)	44	32.4	24.9	40.5
Intact Female	6 (4.4%)	4 (2.9%)	2 (1.5%)	12	8.8	4.9	14.5
Spayed Female	20 (14.7%)	8 (5.9%)	11 (8.1%)	39	28.7	21.6	36.7
Unknown	1 (0.7%)	1 (0.7%)	1 (0/7%)	3	2.2	0.6	5.8
Total	59 (43.4%)	29 (21.3%)	48 (35.3%)	136	100.0		

Age

The age of cats that were suspected with CKD were categorised into several age groups (Table 3). Age group with the highest frequency was 5-8 years, followed by 9-12 years and 13-16 years. Cats aged 5-8 years also represented the most prevalent age group across all CKD stages.

Table 3
Age distribution of cats that were suspected with chronic kidney disease

Age (Year-old)	CKD Stage (n)			Total	Prevalence (%)	95% CI	
	II (%)	III (%)	IV (%)			Lower limit	Upper limit
0 - 4	10 (7.4%)	2 (1.5%)	6 (4.4%)	18	13.2	8.3	19.7
5 - 8	18 (13.2%)	10 (7.4%)	20 (14.7%)	48	35.3	27.6	43.6
9 - 12	12 (8.8%)	6 (4.4%)	13 (9.6%)	31	22.8	16.4	30.4
13 - 16	11 (8.1%)	7 (5.1%)	5 (3.7%)	23	16.9	11.3	23.9
17 - 20	4 (2.9%)	1 (0.7%)	2 (1.5%)	7	5.1	2.3	9.8
Uncertain	4 (2.9%)	3 (2.2%)	2 (1.5%)	9	6.6	3.3	11.7
Total	59 (43.4%)	29 21.3%)	48 (35.3%)	136	100.0		

CKD = Chronic kidney disease

Clinicopathological Parameters

Haemogram

Overall, the RBC, haemoglobin and PCV decreased from stage II to IV in CKD cats (Table 4). The stage II cats had RBC and haemoglobin concentration significantly higher ($p<0.05$) than stage IV cats. Meanwhile, the PCV of stage II cats was found significantly higher ($p<0.05$) than stages III and IV CKD cats.

The reticulocyte count in stage II cats was significantly higher ($p<0.05$) than cats with CKD stages III and IV. Nevertheless, the reticulocyte count median at all stages were below the normal range. There was no significant difference of MCV and MCHC between CKD stages.

Leukogram

The WBC, band and segmented neutrophils, and monocytes increased with stage, in which values at stage IV were significantly higher ($p<0.05$) than stage II (Table 5). The eosinophil count was significantly lower ($p<0.05$) at stage IV than stages II and III.

Table 4
Haemogram of cats with chronic kidney disease according to stages

Parameter	CKD Stage	n	Mean	Median ± SD
RBC (5-10 × 10^{12}/L)	II	57	7.15	7.19^{a} ± 1.54
	III	28	6.59	6.51^{ab} ± 1.92
	IV	47	6.19	5.93^{b} ± 2.15
Haemoglobin (80-150 g/L)	II	57	116.16^{a}	119.00 ± 25.73
	III	28	103.86^{ab}	98.55 ± 32.48
	IV	47	93.89^{b}	89.60 ± 28.86
PCV (0.24-0.45 L/L)	II	59	0.31^{a}	0.31 ± 0.06
	III	29	0.28^{b}	0.26 ± 0.07
	IV	28	0.26^{b}	0.25 ± 0.07
MCV (39-55 fL)	II	57	43.96	44.00 ± 4.20
	III	28	42.32	43.00 ± 4.73
	IV	47	43.06	44.00 ± 4.67
MCHC (300-360 g/L);	II	57	371.88	367.00 ± 35.40
	III	28	375.57	375.00 ± 34.56
	IV	47	366.30	360.00 ± 35.33
Reticulocytes (0.5-1.5/100RBC)	II	44	1.06	0.20^{a} ± 1.61
	III	26	0.28	0.10^{b} ± 0.68
	IV	43	0.52	0.10^{b} ± 1.17

CKD = Chronic kidney disease; RBC = Red blood cells; PCV = Packed cell volume;
MCV = Mean corpuscular volume; MCHC = Mean corpuscular haemoglobin concentration
^{ab} = Mean or median within column with different superscripts are significantly different ($p<0.05$)

Table 5
Leukogram of cats with chronic kidney disease according to stages

Parameter	CKD Stage	n	Mean	Median ± SD
WBC (5.5-19.5 × 10^{9}/L)	II	57	12.41	10.30^{a} ± 7.26
	III	28	14.39	12.70^{ab} ± 8.49
	IV	47	17.80	14.10^{b} ± 11.29
Band Neutrophils (<0.3 × 10^{9}/L)	II	57	0.20	0.11^{a} ± 0.18
	III	27	0.27	0.13^{ab} ± 0.27
	IV	47	0.32	0.21^{b} ± 0.28
Neutrophils (2.5-12.5 × 10^{9}/L)	II	57	8.74	7.21^{a} ± 5.43
	III	27	10.97	9.73^{ab} ± 6.08
	IV	47	14.09	11.18^{b} ± 9.20
Lymphocytes (1.5-7.0 × 10^{9}/L)	II	57	2.08	1.81 ± 1.07
	III	27	2.35	2.02 ± 1.68
	IV	47	2.09	1.75 ± 1.57
Monocytes (0.2-0.8 × 10^{9}/L)	II	57	0.55	0.37^{a} ± 0.50
	III	27	0.74	0.51^{ab} ± 0.55
	IV	47	0.99	0.66^{b} ± 0.99
Eosinophils (0.1-1.5 × 10^{9}/L)	II	57	0.80	0.61^{a} ± 0.71
	III	27	0.72	0.66^{a} ± 0.54
	IV	47	0.36	0.23^{b} ± 0.54

CKD = Chronic kidney disease; WBC = White blood cells
^{ab} = medians within column with different superscripts are significantly different ($p<0.05$)

Although WBC were within normal range in all stages, the mean of band and segmented neutrophils and monocytes in stage IV were above normal. Meanwhile the lymphocyte count was at low normal in all CKD cats.

Biochemistry

The median of phosphate concentration in stage IV was above normal range and significantly higher ($p<0.05$) than stages II and III CKD cats (Table 6). The sodium concentration was at high normal while chloride was at low normal in all stages. The potassium level was within normal range across all stages of CKD.

The concentration of BUN and creatinine increased with stages in which stage IV values were approximately four times higher when compared with stage II.

The median of serum protein concentration was 22 to 26% above normal range in all stages of CKD. The albumin and globulin concentrations across all stages were within and above normal range respectively. The median of A:G was at low normal in stages II and IV, while stage III was lower than normal. There were no significant differences in the median of serum protein, albumin and globulin concentration between all stages.

Table 6
Serum biochemistry parameters of cats with chronic kidney disease according to stages

Parameter	CKD Stage	n	Mean	Median ± SD
Sodium (146-156 mmol/L)	II	54	151.52	152.00 ± 6.42
	III	28	152.64	152.50 ± 6.22
	IV	46	152.73	151.55 ± 10.52
Potassium (3.9-5.5 mmol/L)	II	54	4.74	4.70 ± 0.78
	III	28	4.65	4.65 ± 0.97
	IV	46	5.05	4.50 ± 1.43
Chloride (110-132 mmol/L)	II	54	115.15	114.50 ± 6.00
	III	28	115.74	115.50 ± 7.90
	IV	46	112.46	112.50 ± 11.20
Calcium (2.2-2.9 mmol/L)	II	17	2.56	2.60 ± 0.21
	III	6	2.67	2.73 ± 0.13
	IV	5	2.33	2.57 ± 0.77
Phosphate (1.1-2.8 mmol/L)	II	43	1.61	1.60^{a} ± 0.44
	III	26	2.38	1.95^{a} ± 1.75
	IV	35	5.06	5.40^{b} ± 2.48
Urea (3.0-10.0 mmol/L)	II	59	16.92	15.10^{a} ± 13.89
	III	29	27.27	24.60^{b} ± 12.99
	IV	48	56.33	50.50^{c} ± 22.97

Table 6 *(continued)*

Parameter	CKD Stage	n	Mean	Median ± SD
Creatinine (60-193 µmol/L)	II	59	186.73	186.00[a] ± 31.90
	III	29	328.31	319.00[b] ± 54.25
	IV	48	782.27	653.50[c] ± 348.84
Serum Protein (55-75 g/L)	II	48	94.04	94.05 ± 11.02
	III	26	92.32	91.80 ± 9.61
	IV	45	94.89	93.00 ± 16.39
Albumin g/L (25-40 g/L)	II	48	30.28	30.75 ± 4.45
	III	26	28.40	28.20 ± 4.93
	IV	45	30.48	28.60 ± 7.41
Globulin (25-45 g/L)	II	48	63.76	63.70 ± 13.04
	III	26	63.92	63.10 ± 11.47
	IV	45	64.40	64.50 ± 15.14
A:G (0.5-1.4)	II	48	0.49	0.50 ± 0.15
	III	26	0.47	0.45 ± 0.12
	IV	45	0.50	0.50 ± 0.16

CKD = Chronic kidney disease; A:G = Albumin to globulin ratio
[ab] = medians within column with different superscripts are significantly different ($p<0.05$)

Urinalysis

The median of USG of stage II CKD cats was significantly higher ($p<0.05$) than stages III and IV cats (Table 7).

Table 7
Urine specific gravity of cats with chronic kidney disease according to stages

Parameter	CKD Stage	n	Mean	Median ± SD
USG	II	59	1.026	1.022[a] ± 0.013
	III	29	1.015	1.015[b] ± 0.004
	IV	48	1.015	1.015[b] ± 0.006

CKD = Chronic kidney disease; USG = Urine specific gravity
[ab] = median within column with different superscripts are significantly different ($p<0.05$)

There was significant association ($p<0.05$) between CKD stages and urine protein concentration (Table 8). No evidence of proteinuria (negative) was the most common finding in stages III (15/29; 52%) and IV cats (22/48; 46%). Stage II cats had proteinuria of 1+ concentration as the highest frequency (21/59; 36%), followed by no proteinuria (16/59; 27%).

Table 8
Protein concentration in urine of cats with chronic kidney disease according to stages

Protein	CKD Stage			Total	Percentage
	II	III	IV		
Negative	16	15	22	53	39.0
1+	21	7	7	36	25.7
2+	10	1	8	19	14.0
3+	11	2	11	24	17.6
4+	1	4	0	5	3.7
Total	59	29	48	136	100.0

CKD = Chronic kidney disease

DISCUSSION

This study provides a comprehensive profile of clinicopathological changes across various stages of feline CKD. A higher proportion of male than female cats suspected with CKD found in the current study is consistent with other studies (Greene et al, 2014; Piyarungsri & Pusoonthornthum, 2016). The prevalence of CKD was notably higher in neutered cats than in intact cats. This finding could be supported by another study whereby absence of testosterone or oestrogen in neutered cats was reported to have smaller kidney size than intact cats, which could be related to higher risk of getting CKD (Shiroma et al., 1999).

The prevalence of CKD cats that were younger than 16 years old were higher than geriatrics, in contrast with Lulich et al. (1992). Young cats below five years of age with CKD could be a progression of acute kidney injury (AKI) into CKD (Schmiedt et al., 2016). However, due to limited access to confirmatory reports such as diagnostic images by the clinicians, AKI cases may have been included in the analysis.

Hemogram results revealed that the RBC, haemoglobin and PCV declined from stage II to stage IV, a consistent observation with a previous study by King et al. (2007). In addition, the reticulocyte count, MCV and MCHC values were also suggestive of non-regenerative normocytic normochromic anaemia. These results suggest there is a positive correlation between the progression of CKD stages and the prevalence of non-regenerative anaemia in feline patients. A previous study reported that anaemia was more often seen in patients with terminal stage of CKD due to decreased or total absence of erythropoietin (Lawson & Jepson, 2021). However, the high MCHC values can be due to haemolysis during blood sampling.

Leukogram analysis revealed that cats with stage IV CKD frequently exhibit systemic inflammation or concurrent infection. Cats with CKD tend to have a leukocyte profile characterised by neutrophilia, lymphopaenia and eosinopaenia when compared with healthy cats, more pronounced in the end-stage of the disease (Kralova et al., 2016). This

leukogram pattern was also seen in CKD dogs (Kralova et al., 2009). It was suggested that decreased lymphocytes particularly T cells, is common in CKD cats especially at the end-stage, compromising patients' immunity, which then results in increased susceptibility to infection or inflammation (Kralova et al., 2016).

Inflammation or infection of the renal system such as tubulointerstitial nephritis and lower urinary tract bacterial infection have been reported as common features in CKD (Brown et al., 2016; Reynolds & Lefebvre, 2013). Cats with CKD have a lower antioxidant capacity due to oxidative stress, which increases the risk of infection and inflammation (Keegan & Webb, 2010). Oxidative stress can accelerate apoptosis of neutrophils and decrease neutrophil functions as seen in dogs (Silva et al., 2013). In humans, it was reported that oxidative stress can cause scarring of the kidneys and systemic inflammation in later stages of CKD (Vaziri, 2004). Leukocyte counts provide critical insights into CKD staging and may serve as a prognostic predictor of patients' survival time (King et al., 2007). This supports the findings of the current study where there was an ascending trend of leukocytosis observed as the CKD stages advances.

Typical electrolyte imbalances in serum biochemistry of CKD cats were not observed in the present study. Instead of hyponatraemia, the sodium concentration was found to be at high normal. This finding is likely attributable to reduced fluid intake, profuse polyuria, or a combination thereof that results in dehydration and subsequently haemoconcentration (Elliott & Barber, 1998). Vomiting, polyuria and anorexia were more likely seen in CKD cats at the time of diagnosis, which can lead to haemoconcentration (Greene et al., 2014). However, in depth clinical assessment of hydration status like mucous membrane and skin turgor elasticity were not obtained due to limited access to clinical information, hence other causes of high normal sodium including hemoconcentration cannot be ruled out.

The normokalaemia observed is contrary to previous studies that reported hyperkalaemia at end-stage CKD (Elliot & Barber, 1998; King et al., 2007). Hyperkalaemia is typically seen in CKD due to reduced GFR and the presence of tubular injury, which causes impaired compensatory mechanism of potassium excretion by the tubules (DiBartola, 2016). Nevertheless, it was reported by Reynolds and Lefebvre (2013) that hyperkalaemia is rather uncommon in CKD cats (prevalence 5.8%) compared with hypokalaemia (prevalence 18-30%), although the latter mostly applies to CKD IRIS stages II-III. While the exact mechanisms of hypokalaemia in CKD cats are not fully understood, it is likely multifactorial, involving insufficient dietary potassium intake, excessive urinary excretion, and stimulation of renin-angiotensin-aldosterone system resulting from sodium-restricted renal diets (Adams et al., 1993; Polzin, 2013). Episodes of vomiting in CKD that leads to metabolic alkalosis may cause exchange of hydrogen ions with potassium, which leads to hypokalaemia (DiBartola, 201 6). Conversely, hyperphosphataemia was observed in stage IV patients, a finding that corroborates previous research that reported seven out of eight

cats developed hyperphosphataemia with the greatest severity noted at terminal stages of the disease (Schaefer et al., 2021). This observation might be due to poorer glomerular excretion and tubular reabsorption as the disease worsens (Kidder & Chew, 2009).

The progressive elevation of BUN and creatinine from stage II through stage IV reflects the declination of GFR as the disease severity advances. The increased prevalence of infection and inflammation in the CKD patients may likely to cause hyperglobulinaemia and concomitant rise of serum protein. In CKD, affected glomerular filtration barrier will cause leakage of albumin into the urine (Kovarikova, 2015) and consequently develop hypoalbuminemia (Rayhel et al., 2020). The normal value of albumin observed could be explained with the possibility of dehydration leading to false elevation of albumin concentration whilst the actual concentration may be lower. However, as mentioned earlier, the clinical presentation of hydration status was not confirmed due to limited data to be included in this study.

The observed progressive decline in USG from stage II to stage IV indicates that the renal tubular concentration capacity undergoes significant deterioration as feline CKD advances. The USG in stages III and IV were also approaching isosthenuria (USG 1.008-1.012) suggesting that the urine osmolality was almost isotonic with plasma, which aligns with observations of Elliott and Barber (1998). Another study also reported that the mean of USG in CKD cats was 1.009 whereas in normal cats was 1.050 which was sufficiently concentrated (Deguchi & Akuzawa, 1997). Consequently, failure of the renal concentrating mechanism drives a polyuric state that necessitates a corresponding increase in water intake. Without this sufficient compensatory intake, dehydration ensues (Greene et al., 2014).

Since serum albumin concentration were found to be within normal range, it is expected to find that most of the cases presented showed no signs of proteinuria. Cases that had low concentration of protein in the urine could be due to insensitivity of the urine dipstick to detect protein (Grauer, 2011). Although these findings may also suggest that glomerular functions were not as compromised as the tubules in CKD cats presented to UVH (Hokamp & Nabity, 2016). Nevertheless, it is widely recognised that urine dipstick analysis lacks the precision required for a definitive diagnosis of proteinuria. Assessment of the urine protein to creatinine ratio (UP:C) and detection of microalbuminuria would represent more robust diagnostic modalities for evaluating kidney disease patients. Other forms of diagnosis such as histopathology can further identify the affected and damaged kidney structures and their level of severity.

CONCLUSION

This study demonstrates that the clinicopathological hallmarks of feline CKD significantly influenced by age and hydration status, often leading to non-classical biochemical presentations. The prevalence of high-normal sodium and normal albumin concentrations likely reflects masked hemoconcentration, underscoring the necessity of standardised

hydration status in tropical climates. Nevertheless, the clinicopathological profile of the cats involved in this study suggests that the severity of CKD worsens from stages II to IV. The emergence of non-regenerative anaemia and impaired tubular concentrating ability are pathognomonic of advanced stages. Furthermore, increased inflammatory markers identified suggest that CKD cats were more susceptible to inflammation or infection.

It is acknowledged that this study largely focused on stage II to stage IV CKD as the bias is inherently linked to the reliance of serum creatinine as a primary diagnostic marker. Stage I cases is attributed to the subclinical nature of early-stage of renal insufficiency. Azotaemia becomes detectable only after 50 to 75% of the functional renal mass becomes compromised. Consequently, Stage I patients often evade clinical detection. This also highlights inclusion of SDMA testing could have mitigated this limitation.

Another major limitation in this study is that the confirmatory diagnosis of CKD by the clinicians was not obtained, which may lead to inclusion of AKI cases. It is highly recommended that further studies such as prospective designs with more comprehensive information including confirmatory diagnosis and staging of CKD inclusive of SDMA concentration and UP:C, clinical assessment of hydration status and diet, to better delineate the clinicopathological changes in each stage of CKD in feline patients.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest regarding this study.

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