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THE IMPACT OF AGE ON SOME BIOCHEMICAL PARAMETERS IN FELINES WITH CHRONIC KIDNEY DISEASE

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Abstract

According to specialty literature, the incidence of chronic kidney disease in felines had substantially risen in the recent years. This research is intended to show a correlation between the increasing age of felines (over 10 years) and the variations of some biochemical parameters (urea, creatinine, phosphorus and also symmetric dimethylarginine) in the progression of the chronic kidney disease. The research was performed over a period of two years at the University Emergency Hospital "Prof. univ. dr. Alin Bîrțoiu", Bucharest, on a total of 20 cases of felines suspected of chronic kidney disease, 10 of them older than 10 years were considered suitable for this study. One feline, an 11-year-old patient in uremic coma (n = 1) had the highest serum phosphorus, urea, creatinine and symmetric dimethylarginine levels. The other nine patients (n = 9) between 11 and 15 age had urea levels higher than 79.2 mg/dl, creatinine levels above 2 mg/dl and serum phosphorus levels higher than 7.35 mg/dl.

Key words*: felines, chronic kidney disease, biochemical parameters.*

INTRODUCTION

Chronic kidney disease (CKD) is the most frequent metabolic disease in domestic felines, especially in senior cats (>10 years old). In older felines, chronic kidney disease (CKD) is a common diagnosis (Reynolds & Lefebvre, 2013). The prevalence of chronic kidney disease is approximately 2-4% overall, in felines aged 1 and 2 years old and increases to 30-40% in felines older than 10 years. The prevalence of CKD in felines is higher than in dogs and the incidence of CKD diagnoses in felines has increased over the past few decades (Brown & Elliott, 2016; Markovich et al., 2015).

Additional risk factors for developing CKD, other than age have not been identified in felines, but weight loss or poor body condition, polyuria/polydipsia (PU/PD), higher creatinine concentrations, dehydration and potentially lower urine specific gravity (USG) may indicate the presence, or predict development of CKD (Bartlett P.C. et al., 2010).

The classical biomarker of chronic kidney disease (CKD) in felines - the serum creatinine concentration has significant limitations that reduce its value as an early CKD biomarker. New serum biomarkers, such as symmetric dimethylarginine (SDMA), could help in identifying felines with chronic kidney disease (CKD) before traditional indicators of glomerular filtration rate (GFR), such as urea and creatinine, would show significant increase, above the normal reference range (Syme & Elliot, 2016). Symmetric dimethylarginine (SDMA), also highlights the deviation from the normal functioning of the glomerular filtration rate, when 25% of the nephrons are damaged or destroyed. However, it is important to note that significant nephron loss has already occurred by the time, symmetric dimethylarginine (SDMA) is persistently above the reference range (Hall & Yerramilli, 2014).

It is possible to stage chronic kidney disease based on creatinine and SDMA levels. Therefore, in stage 1, creatinine will be 1.6 mg/dl and symmetric dimethylarginine <18 µg/dl; in stage 2, creatinine will be 1.6-2.8 mg/dl and symmetric dimethylarginine 18-25 µg/dl; in stage 3, creatinine will be 2.9-5 mg/dl and symmetric dimethylarginine 26-38 µg/dl and in the final stage, creatinine will be >5 mg/dl and symmetric dimethylarginine >38 µg/dl. Other researchers characterize the evolution and stage of the chronic kidney

disease just based on creatinine levels (Kidder & Chew, 2009).
Phosphorus retention during chronic renal failure has negative effects on renal function, renal histopathology and soft tissue mineralization in the kidneys (Syme & Elliot, 2016).

MATERIALS AND METHODS

This study was performed over a two-year period at the University Emergency Hospital "Prof. univ. dr. Alin Bîrțoiu" in Bucharest and at the Vietatis - The Vets Clinic of Bucharest, on a total of 20 felines suspected of chronic kidney disease; 10 of these felines, older than 10 years old were considered suitable for this research, all of them belonging to the European race. Each patient was clinical and paraclinical examined, by general methods and special methods, such as biochemical investigations (urea, creatinine, phosphorus, symmetric dimethylarginine).
Symmetric dimethylarginine test was performed in 5 of the 10 patients.
All study participants were in the third or fourth stage of chronic kidney disease.
Patients were classified into one of four CKD stages based on the creatinine and symmetric dimethylarginine levels, as well as creatinine levels independently.
The results obtained from the paraclinical examinations and the physiological interval values were specified in each individual case.
Skyla, IDEXX and Spotchem SP devices were used to perform the biochemical examinations.

RESULTS AND DISCUSSIONS

In this study, the biochemical examination results of 10 felines of varying ages are analysed: two patients aged 10 years, three aged 15 years, two aged 12 years, one feline aged 11 years, one aged 13 years and one feline aged 18 years. All of these patients had extremely elevated creatinine and urea levels compared to the physiological values for their species. Only one patient presented a serum phosphorus level within the physiological range; the rest presented elevated levels, which may be associated with chronic kidney disease. Regarding the symmetric dimethylarginine, which was performed on only half of the studied patients, it revealed a significant decrease in the glomerular filtration rate; this result was obtained before the other biochemical parameters were measured. The values of creatinine and symmetric dimethylarginine are highly correlated. The relationship between the two parameters is displayed in the table below (Table 1):

Table 1. The values of creatinine and symmetric dimethylarginine (SDMA) in patients classified in fourth stage of chronic kidney disease

Pacient's age	Creatinine (mg/dl)	SDMA (µg/dl)
15 years old	7.2	26
10 years old	19.01	35
18 years old	8.8	27
13 years old	10.2	28
12 years old	8.34	28

The normal range for creatinine is between 0.4 and 1.6 mg/dL and the normal range for symmetric dimethylarginine is less than 15 ug/mL. The only 10-year-old patient had a creatinine value of 19.01 mg/dl and a symmetric dimethylarginine value of 25 µg/dL and was presented in a uremic coma upon entering the clinic. Based on the values in Table 1, all five patients are classified as having stage 4 chronic kidney disease. Two additional 15-year-old patients were classified as being in the third stage of chronic kidney disease, despite having only creatinine determined and symmetric dimethylarginine not, their results are presented in Table 2:

Table 2. The values of creatinine in patients classified in third stage of chronic kidney disease

Patient's age	Creatinine mg/dl
15 years old	3.45
15 years old	3.64
11 years old	4.25

Having the lowest creatinine levels, these three patients had a more favourable evolution over a shorter period of time than the rest of the patients in the study, whose creatinine levels were well above the reference range (0.4-1.6 mg/dL).
All cats participating in this study had their levels of creatinine, urea and phosphorus

measured. These values varied according to age, with all patients being over 10 years old except for one who presented with uremic coma. The parameters' values are presented in Table 3.

Table 3. Biochemical parameters values (creatinine, urea and phosphorus) in all studied patients

Number of patient	Patient's age	Creatinine (mg/dl)	Urea (mg/dl)	Phosphorus (mg/dl)
1	10 years old	19.01	637	27.21
2	11 years old	4.26	168	8.2
3	12 years old	8.34	291	15.2
4	12 years old	5.5	188	7.8
5	13 years old	10.2	272	>18
6	15 years old	3.45	191	7.35
7	15 years old	3.64	134	6.76
8	15 years old	7.2	197	8.5
9	18 years old	8.8	290	10.7
10	18 years old	7.3	185	8.7

In this study, 10 female felines were examined; one was 10 years old one was 11 years old, two were 12 years old, one was 13 years old, three were 15 years old and two were 18 years old. Regarding the biochemical parameters, the highest values were recorded in the 10-year-old patient, who presented in a uremic coma (presented increased values above the limit that the analyser could register: creatinine - 19.01 mg/dl; urea - 637 mg/dl; phosphorus - 27.21 mg/dl and as symptoms presented: hypothermia, apathy, lethargy, depression, severe dehydration, uraemic breath, elevated serum urea nitrogen and creatinine concentrations and possibly seizures and coma prior to death) and in the 13-year-old patient (creatinine - 10.2 mg/dl; urea - 272 mg/dl; phosphorus - >18 mg/dl), who presented with severe hyperphosphatemia.

Patients classified as being in the third stage of chronic kidney disease, two cats aged 15 years (creatinine - 3.45 mg/dl; urea - 191 mg/dl; phosphorus - 7.35 mg/dl/ creatinine - 3.64 mg/dl; urea - 134 mg/dl; phosphorus - 6.76 mg/dl) and one aged 11 years (creatinine - 4.26 mg/dl; urea - 168mg/dl; phosphorus - 8.2 mg/dl), presented with urinary sediment and feline urological syndrome in the past and their diet consisted of special urinary care diet. They presented urinary sediment, which was analysed at a different clinic, where it was discovered to contain struvites, requiring specific treatment for dissolution. The two 18-year-old cats had high creatinine and urea levels (creatinine - 8.8 mg/dl; urea – 290 mg/dl/ creatinine - 7.3 mg/dl; urea - 185 mg/dl) due to a history of chronic kidney disease in their mother's lineage. However, they didn't present hyperphosphatemia (phosphorus - 10.7 mg/dl; phosphorus - 8.7mg/dl) and these levels could be decreased using the appropriate treatment.

The 12-year-old patient (creatinine - 5.5 mg/dl, urea -188 mg/dl, phosphorus - 7.8 mg/dl) is on the limit between the third and fourth stages of chronic kidney disease (creatinine values > 5 mg/dl are considered to be in the fourth stage), but had the best evolution of the general condition and implicitly of the creatinine and urea values, after the initiation of treatment. The second patient aged 12 years (creatinine - 8.34, urea - 291 mg/dl, phosphorus - 15.2 mg/dl) who was administered the same treatment showed decreases in values after a longer period of time than the first patient aged 12 years, also presenting hyperphosphatemia. Phosphate retention is a major contributor to the progression of chronic kidney disease in many species and it is well known that hyperphosphatemia is associated with a significant mortality risk in humans with end-stage renal disease.

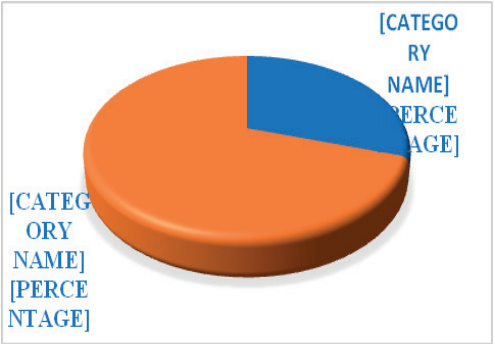

Figure 1. Identifying patients by gender

As concerning the gender, it can be observed in Figure 1 that more than half of the patients are

male (70%), with 50% of them being neutered (the scientific literature indicates that this could be a risk factor for developing chronic kidney disease), and 30% of the subjects being spayed females.
Also, the two felines aged 15 years and one aged 11 years that had previously presented feline urological syndrome and sediment were neutered males.

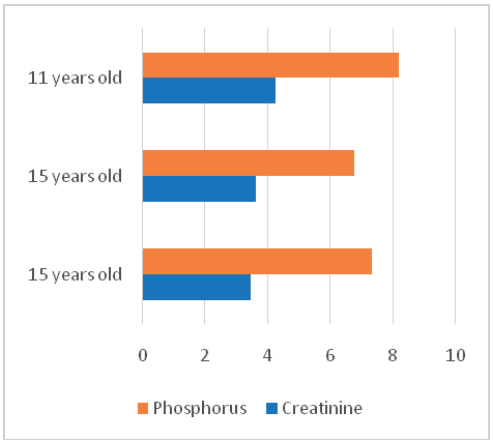

Figure 2. Creatinine and phosphorus levels in patients with third stage chronic kidney disease

Frequently, the third stage of chronic kidney disease is accompanied by hyperphosphatemia. The second 15-year-old patient presented a serum phosphorus value of 6.76 mg/dl (the reference range is 2.7-6.5 mg/dl), which cannot be considered hyperphosphatemia, unlike the first 15-year-old patient, who had a slightly elevated phosphorus level compared to the maximum value (7.35 mg/dl). Throughout their lives, the two cats consumed food with a low phosphorus content and high-quality protein, which played a crucial role in maintaining the phosphorus level within normal or close to normal limits.
The 11-year-old patient's phosphorus level was 8.2 mg/dl, also due to its diet that did not consist of high-quality food.

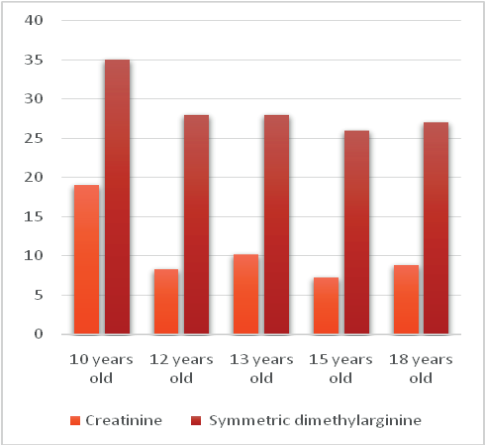

Figure 3. Creatinine and symmetric dimethylarginine values in patients with chronic kidney disease in the fourth stage

According to IRIS, based on the results of creatinine and SDMA in this study, 5 of the patients could be classified as being in the fourth stage of chronic kidney disease (CREA >5 mg/dl, SDMA >35 µg/dl). Although not all patients presented SDMA levels significantly above the normal range, they received the therapeutic protocol for stage 4 CKD, because they have creatinine levels that are significantly above the normal range.

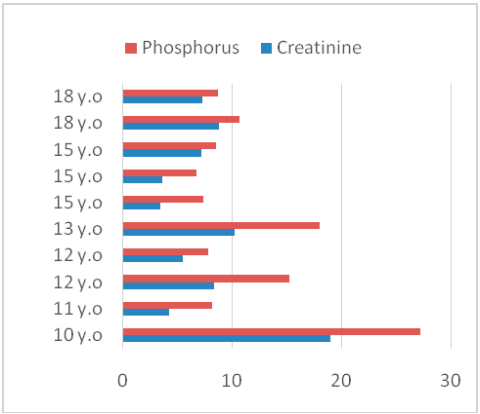

Figure 4. Graphic representation of creatinine and phosphorus levels, in all the studied patients

The highest serum phosphorus concentrations were found in patients aged 10 (27.21 mg/dl), 12 (15.2 mg/dl), 13 (>18 mg/dl) and 18 years, with concentrations indicating a severe hyperphosphatemia.
Shortly after reaching the clinic, the 10-year-old died of uremic coma.
However, with treatment, the phosphorus levels of the 12 and 13-year-olds were reduced to 7.5-8 mg/dL in two weeks. As concerning the 18-year-old patient with elevated phosphorus levels, it received long term (approximately one month) hyperphosphatemia treatment.

CONCLUSIONS

Age, particularly after 10 years, has a crucial role in the occurrence and progression of chronic kidney disease in felines, associated with food and other renal or urinary pathologies (feline urological syndrome).
The results of biochemical examination (creatinine, urea, phosphorus and symmetric dimethylarginine (SDMA) elevated levels were detected in three of the studied patients, indicating the extent of glomerular filtration damage.
These cats had a pathological history of feline urological syndrome and their diet consisted of low-quality protein and high phosphorus dry or canned food.

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