2026, Scienceline Publication
World's Veterinary Journal
World Vet J, 16(2): 580-586.
ISSN 2322-4568

DOI: https://dx.doi.org/10.54203/scil.2026.wvj55
PII: S232245682600055-16

Association between Dietary Mineral Profiles and Hypercalcemia in Cats with Chronic Kidney Disease: A Retrospective Study

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ORIGINAL ARTICLE
Received: April 04, 2026
Revised: May 07, 2026
Accepted: June 08, 2026
Published: June 30, 2026

ABSTRACT

Hypercalcemia is an important clinical problem in feline veterinary medicine due to its association with a wide range of pathological conditions, particularly chronic kidney disease (CKD). The present study aimed to characterize the clinical and biochemical characteristics of hypercalcemic cats and to investigate the association between the dietary calcium-to-phosphorus (Ca:P) ratio and CKD, urolithiasis, and total and ionized calcium levels. A retrospective analysis was conducted of 50 hypercalcemic domestic cats presented to the Veterinary Clinic in Kyiv, Ukraine, between 2023 and 2025. For each cat, data on age, breed, total calcium, and ionized calcium were collected. Additionally, serum phosphorus levels and any concurrent diseases were documented from medical records. Dietary composition was assessed based on manufacturer-reported analytical values, including calcium, phosphorus, the Ca:P ratio, and vitamin D content. Cats were divided into two groups based on their dietary Ca:P ratio; one with a ratio of 1.4 or less (≤ 1.4) and the other with a ratio greater than 1.4. (>1.4). The majority of cats (70%) were over six years old. The median total calcium concentration was 3.05 mmol/L, while the median ionized calcium concentration was 1.60 mmol/L. Elevated ionized calcium levels, despite normal total calcium levels, was observed in 16% of cases. Chronic kidney disease was observed in 60% of cats with hypercalcemia, while 18% had urolithiasis, mainly calcium oxalate. Additionally, 18% of the cats had both conditions simultaneously. Comparative analysis demonstrated that cats fed diets with Ca:P ratios > 1.4 had a significantly higher prevalence of CKD (20/25, 80%) than cats fed diets with Ca:P ratios ≤ 1.4 (6/25, 24%). However, total and ionized calcium concentrations did not differ significantly between the groups. The current findings highlighted the diagnostic value of total calcium, the importance of measuring ionized calcium, and suggested a possible association between high dietary Ca:P ratios and concurrent CKD in hypercalcemic cats.

Keywords: Calcium-to-phosphorus ratio, Chronic kidney disease, Hypercalcemia, Ionized calcium, Vitamin D

INTRODUCTION

Disorders of calcium homeostasis are significant in feline veterinary medicine because hypercalcemia can be associated with different pathological conditions and may influence disease progression (de Brito Galvão et al., 2017; Coady et al., 2019). In cats, hypercalcemia frequently occurs concurrently with chronic kidney disease (CKD), which is one of the most common chronic conditions in felines and for which staging and treatment protocols are well established (IRIS, 2023). Tang et al. (2021) reported that changes in calcium-phosphorus balance in CKD are linked to a complex pathophysiological condition involving hormonal dysregulation and the development of extraosseous calcification. Disturbances in phosphorus and calcium regulation in CKD are associated with changes in parathyroid hormone and fibroblast growth factor 23 (FGF-23), which play key roles in maintaining mineral homeostasis. Geddes et al. (2013) and Lin et al. (2021) reported that FGF-23 levels gradually rise with advancing CKD stages in cats. Based on studies, elevations frequently precede improvement in hyperphosphatemia, suggesting that FGF-23 may play a role in early mineral imbalance.

Dietary modification plays an important role in the management of CKD in cats (Parker, 2021; Stockman, 2024). The calcium-to-phosphorus (Ca:P) ratio has been recognized as a key parameter influencing disease progression and mineral homeostasis in cats, and different studies have suggested that dietary adjustment may normalize ionized hypercalcemia in cats with idiopathic hypercalcemia or CKD (Ehrlich et al., 2024; Stockman, 2024). Recommendations for feline diets, including optimal Ca:P ratios, were provided in international nutritional guidelines, highlighting the importance of controlling dietary mineral composition in clinical practice (FEDIAF, 2024). Furthermore, dietary mineral composition has been recognized as a contributing factor in the development of feline urolithiasis, particularly calcium oxalate stones (FEDIAF, 2024). The American College of Veterinary Internal Medicine (ACVIM) guidelines identified dietary mineral composition as a contributing factor in calcium oxalate urolithiasis in cats (Lulich et al., 2016).

To cite this paper: Umanets M and Tsvilikhovskyi V (2026). Association between Dietary Mineral Profiles and Hypercalcemia in Cats with Chronic Kidney Disease: A Retrospective Study. *World Vet. J.*, 16(2): 580-586. DOI: https://dx.doi.org/10.54203/scil.2026.wvj55

Despite the availability of individual studies, the prevalence of hypercalcemia in cats and its association with feeding type, dietary Ca:P ratio, and concurrent diseases, particularly CKD, remain insufficiently studied in clinical practice. Additionally, there is limited data on isolated ionized hypercalcemia in cats with normal total calcium levels, which may lead to a missed diagnosis of a calcium ionization disturbance. The present study aimed to characterize the clinical and biochemical profiles of hypercalcemic cats and to evaluate the relationships among dietary mineral composition, particularly the Ca:P ratio and vitamin D content, concurrent diseases, and serum calcium parameters in clinical practice.

MATERIALS AND METHODS

Ethical approval

The present study was approved by the Bioethics Committee of the National University of Life and Environmental Sciences of Ukraine (Protocol No. 007/2024 dated 28 March 2024). The present study was conducted without any intervention in the treatment of animals. Data were collected from the medical records of animals at the Zoolux Veterinary Clinic (Kyiv, Ukraine), in strict accordance with confidentiality principles.

Study design

The study retrospectively analyzed medical records of cats with hypercalcemia that presented to the Veterinary Clinic in Kyiv, Ukraine, from 2023 to 2025. Cats of both sexes, different breeds, and aged between 3 and 19 years were considered for inclusion. To assess clinically relevant factors related to disturbances in calcium metabolism, data on breed, age, sex, biochemical results, dietary nutrients (calcium, phosphorus, Ca:P ratio, and vitamin D content), and the presence of concurrent diseases were extracted from clinical records. A total of 86 cats with confirmed hypercalcemia, characterized by elevated total and/or ionized serum calcium levels according to de Brito Galvão et al. (2017), presented to the clinic during the study period and were initially screened for inclusion.

Inclusion and exclusion criteria

Cats were included in the final study population for which the total and ionized serum calcium concentrations were available. Detailed dietary information, including the commercial product name and manufacturer-declared analytical composition (calcium, phosphorus, vitamin D content), was documented. Additionally, clinical history, encompassing data on concurrent diseases such as CKD, urolithiasis, polycystic kidney disease, and other systemic conditions, was recorded. Cats with a confirmed or suspected malignant neoplasm, those on calcium-containing phosphate binders, or those receiving systemic glucocorticosteroids were excluded because these factors independently influence calcium homeostasis and could confound the interpretation of dietary effects. Following the application of these criteria, 36 cats were excluded, leaving a final group of 50 cats.

Data extraction

The extracted parameters from clinical records included age (in years), breed (based on owner reports and confirmed through clinical examination), sex, body weight, total and ionized serum calcium levels, serum phosphorus levels, and the presence of any concurrent diseases. The dietary Ca:P ratio was calculated as the mass ratio of calcium to phosphorus, expressed as a percentage on a fed basis. Manufacturer-declared analytical values, as indicated on the product label, were used directly to calculate the Ca:P ratio. Serum total calcium and phosphorus levels were assessed in samples collected through jugular venipuncture and analyzed within four hours using an automated biochemistry analyzer (Mindray, China). Ionized calcium was measured separately on an electrolyte analyzer (High Technology, Inc., USA) using an ion-selective electrode method. Reference intervals for serum total calcium (2.2-2.7 mmol/L) and ionized calcium (1.10-1.38 mmol/L) were used, as described by de Brito Galvão et al. (2017). For comparative analysis, the cats were divided into two groups based on their dietary Ca:P ratio, one group with a ratio of 1.4 or less and the other with a ratio exceeding 1.4 (≤ 1.4 or > 1.4). The cutoff of 1.4 was selected based on the findings of Ehrlich et al. (2024) and Stockman (2024).

Statistical analysis

Categorical variables were compared using Fisher's exact test, while continuous variables were analyzed using the Mann-Whitney U test due to non-normal data distribution, as confirmed by the Shapiro-Wilk test ($p < 0.05$). Results were presented as absolute values, percentages, and median values. Differences were considered statistically significant at a p-value less than 5% ($p < 0.05$).

RESULTS

Study population characteristics

A total of 50 cats with hypercalcemia were included in the present study. Mixed-breed cats were the most prevalent in the study population (23/50, 46%), followed by Scottish Straight cats (11/50, 22%). British Shorthair and Exotic Shorthair cats accounted for 3/50 (6%) cases each, while other breeds, including Maine Coon, Persian, Bengal, Siamese, and Sphynx cats, were represented by isolated cases. The majority of cats (35/50, 70%) were older than six years, whereas cats younger than six years accounted for 15/50 (30%).

Renal and urinary disorders

In the total study population (2023-2025), the median concentrations were 3.05 mmol/L for total calcium (ranging from 2.27 to 3.74), 1.60 mmol/L for ionized calcium (ranging from 1.42 to 1.96), and 1.42 mmol/L for phosphorus (ranging from 0.73 to 2.71). Elevated ionized calcium levels with normal total calcium were observed in 8 out of 50 cases (16%). Chronic kidney disease was diagnosed in 30 out of 50 cats (60%), with 26 (52%) having CKD stages II-IV based on the International Renal Interest Society (IRIS) classification. Additionally, 4 cats (8%) had CKD stage I along with polycystic kidney disease. Urolithiasis, mainly calcium oxalate, was found in 9 out of 50 cats (18%). The distribution and co-occurrence of renal and urinary disorders are summarized in Table 1.

Dietary mineral composition

The dietary analysis revealed that the Ca:P ratio ranged from 1.00 to 2.33, with a median of 1.50. In 25 of the 50 cases (50%), the Ca:P ratio was greater than 1.4. Additionally, similar patterns in dietary mineral composition were identified. The most common commercial diets contained 0.6% calcium and 0.3% phosphorus (Ca:P ratio of 2.0), as well as diets with 0.6/0.33 (Ca:P ratio of 1.82) and 0.6/0.35 (Ca:P ratio of 1.71; Table 2).

To assess the effect of dietary mineral composition, animals were divided into two groups based on the Ca:P ratio, including a group with a ratio of 1.4 or less (≤ 1.4) and the other with a ratio exceeding 1.4 (> 1.4), with 25 cats in each group. The groups were evaluated based on total and ionized calcium levels, phosphorus concentration, the prevalence of CKD and urolithiasis, and dietary vitamin D intake (Table 3).

Dietary calcium-to-phosphorus ratio comparison

Comparison of biochemical and clinical parameters between the two groups was summarised in Table 3. Total calcium, ionized calcium, serum phosphorus, and dietary vitamin D levels were not significantly different between cats with a Ca:P ratio of ≤ 1.4 and those with > 1.4 ($p > 0.05$; Table 3). However, the prevalence of CKD was significantly higher in the Ca:P > 1.4 group than in the Ca:P ≤ 1.4 group ($p < 0.05$), whereas the prevalence of urolithiasis did not differ significantly between groups ($p > 0.05$). The degree of total calcium level exceeded the upper reference limit by about 13% in cases with Ca:P > 1.4 and by around 10% in cases with Ca:P ≤ 1.4. Median dietary vitamin D levels were similar between groups; however, a greater variability was observed in cats with Ca:P ≤ 1.4.

Table 1. Distribution of renal and urinary disorders in hypercalcemic cats during the study period from 2023 to 2025

Diagnostic category	Number of cats
CKD without urolithiasis	20
Urolithiasis without CKD	3
CKD with urolithiasis	6
CKD with polycystic kidney disease	4
No documented concurrent renal or urinary disease	17

CKD: Chronic kidney disease

Table 2. Most frequently observed commercial diets fed to hypercalcemic cats during the study period from 2023 to 2025

Diet (manufacturer)	Calcium	Phosphorus	Ca:P ratio	Number of cats
Renal feline (Royal Canin)	0.6	0.3	2.0	15
Renal function - advanced care (Purina)	0.6	0.33	1.82	6
Renal function early care feline (Purina)	0.6	0.35	1.71	3

Ca:P: Calcium-to-phosphorus ratio

Table 3. Comparison of serum calcium, phosphorus, vitamin D content, and prevalence of chronic kidney disease and urolithiasis according to dietary calcium-to-phosphorus ratio in hypercalcemic cats from 2023 to 2025

Parameter	Ca:P ratio (≤ 1.4)	Ca:P ratio (> 1.4)	p-value
Total calcium (mmol/L)	2.96 (2.44-3.55)	3.05 (2.27-3.74)	0.265
Ionized calcium (mmol/L)	1.64 (1.46-1.96)	1.63 (1.42-1.83)	0.741
Phosphorus (mmol/L)	1.41 (0.73-2.02)	1.55 (0.81-2.71)	0.201
Vitamin D (IU)	800 (190-1800)	800 (600-1200)	0.870
CKD	6 (24%)	20 (80%)	< 0.001
Urolithiasis	5 (20%)	4 (16%)	0.496

Ca:P: Calcium-to-phosphorus ratio, CKD: Chronic kidney disease, IU: International units. P-values were calculated using the Mann-Whitney U test for continuous variables and Fisher's exact test for categorical variables. Numbers in parentheses are presented as the median, ranging from minimum to maximum.

DISCUSSION

The high number of mixed-breed cats in this study probably indicated their greater overall presence in the general cat population, rather than a specific breed susceptibility to hypercalcemia. The relatively high number of Scottish Straight cats might be linked to the breed's popularity among owners and potential differences in management and feeding practices.

The observed age distribution, in which 70% of animals were older than six years, was consistent with previously reported data. Tang et al. (2021) reported that calcium metabolic disorders were more commonly observed in adult and senior cats, particularly in those with CKD. Other retrospective studies of feline hypercalcemia have reported a similar age distribution. Savary et al. (2000) reported a median age of 13 years among 71 cats. Meanwhile, Midkiff et al. (2000) observed idiopathic hypercalcemia mainly in adult and middle-aged animals, supporting the link between age and this condition.

Detecting isolated ionized hypercalcemia in 16% of cases suggested that measuring total calcium alone may not be sufficient to identify disturbances in calcium metabolism in cats, as some abnormalities may be limited to the ionized fraction. Similar findings were reported by Broughton et al. (2023), indicating that total calcium had limited sensitivity in detecting ionized hypercalcemia in cats. Schenck and Chew (2010), in an analysis of 434 feline serum samples, indicated that total calcium exhibited only a moderate correlation with the ionized fraction and that ionized hypercalcemia may occur despite normal total calcium levels. In a comprehensive review, de Brito Galvão et al. (2017) highlighted that ionized hypercalcemia was the primary diagnostic marker, reflecting the biologically active component rather than total calcium levels. Coady et al. (2019) established that the severity of the condition correlated with its etiology in a study with 1,373 cases of ionized hypercalcemia. Mild cases were most frequently associated with CKD and idiopathic hypercalcemia, while more severe forms were linked to paraneoplastic syndromes.

The high prevalence of hypercalcemia in CKD (52%) in the present study was consistent with current understanding of mineral metabolism disturbances in cats with CKD (Tang et al., 2021). Parker (2021) emphasized that alterations in calcium-phosphorus balance in cats with CKD were complex and predominantly influenced by dietary composition, a crucial factor in their management. Savary et al. (2000) found that the most frequent diagnoses were neoplasia, renal disease, and urolithiasis. The conditions mentioned largely aligned with the present results and highlighted the critical role of renal pathology among the associated diseases.

The detection of urolithiasis, especially calcium oxalate stones, in some cases might be linked to disruptions in calcium metabolism. According to ACVIM recommendations, calcium oxalate urolithiasis in cats is a multifactorial condition involving hypercalcemia, hypercalciuria, decreased urine volume, and dietary mineral composition (Lulich et al., 2016).

The data on dietary Ca:P ratios indicated that the majority of cases received diets with higher-than-normal Ca:P ratios. Similar findings have been reported by Pusoonthornthum et al. (2011), where increased Ca:P ratios were regarded as a factor influencing calcium-phosphorus homeostasis in felines, particularly within the context of renal disease. The identical Ca:P values observed in many cases suggested a dependence on a narrow range of diets with similar mineral compositions, likely because a few commercial manufacturers dominated the market.

The 1.4 threshold for group division was derived from Ehrlich et al.'s (2024) study, which indicated that switching hypercalcemic cats to diets with a Ca:P ratio below 1.4 generally normalized serum calcium levels within 3 to 20 weeks. Stockman (2024) further supported this threshold by examining the regulatory role of dietary Ca:P in feline mineral balance and highlighting the clinical significance of preventing excessive phosphate restrictions.

The similar ionized calcium levels observed between groups suggested a multifactorial nature of disturbances in calcium metabolism, indicating that dietary mineral composition alone, without consideration of additional factors, did not determine ionized calcium levels. However, the markedly higher prevalence of CKD in the Ca:P > 1.4 group (80%) may suggest an association between elevated dietary Ca:P ratios and concurrent renal pathology. Stockman (2024) described the Ca:P ratio as a dietary factor influencing mineral metabolism in cats, particularly in the context of kidney disease, consistent with the observed link between higher dietary Ca:P ratios and CKD in the present study. The observed tendency for higher total calcium levels in the Ca:P > 1.4 group, with 13% of animals exceeding the upper reference limit, suggested a possible association between dietary mineral ratios and calcium regulation. However, the influence of concurrent diseases and other confounding factors cannot be disregarded.

Since vitamin D plays an important role in calcium regulation, differences in dietary vitamin D intake might affect calcium levels in cats. Zafalon et al. (2020) emphasized that vitamin D is a key regulator of calcium homeostasis and may contribute to the development of mineral metabolism disorders in cats. Crossley et al. (2017) documented a series of cases of hypercalcemia accompanied by soft-tissue calcification in cats fed a commercial diet high in cholecalciferol, in which clinical signs completely resolved after dietary adjustment. The mentioned findings highlighted the importance of monitoring actual vitamin D levels in commercial diets and carefully assessing manufacturer-reported values.

It is important to note that the present study design differed mainly from previous retrospective studies that focused on identifying the causes of hypercalcemia. Savary et al. (2000) reported neoplasia (29.6%), renal failure (25.4%), and urolithiasis (15.5%) as the primary etiologies in 71 cats, whereas Coady et al. (2019) identified malignancy-associated (22.7%) and renal-associated (13.4%) forms as the most prevalent causes in 1,373 cats.

In the current study of 50 cats, the prevalence of CKD was 52%, and urolithiasis was 18%, both exceeding the referenced values. The observed distribution reflected the specific focus of the study, in which dietary mineral composition, particularly the Ca:P ratio, was the primary variable. Concurrent diseases were documented as clinically relevant conditions that could either occur before hypercalcemia or result from it, such as nephrocalcinosis and calcium oxalate urolithiasis (Lulich et al., 2016; de Brito Galvão et al., 2017).

CONCLUSION

A retrospective analysis of hypercalcemia in cats found that CKD (60%) and urolithiasis (18%) were common concurrent conditions, predominantly in older cats. A significant number of cases demonstrated isolated ionized hypercalcemia despite normal total calcium levels, highlighting the importance of measuring ionized calcium for accurate diagnosis. An elevated dietary Ca:P ratio (> 1.4) was associated with a significantly higher incidence of CKD; however, the elevated Ca:P ratio alone did not predict ionized calcium levels, highlighting the complex, multifactorial nature of calcium metabolic disorders. The significant variability in vitamin D levels among commercial diets could further affect calcium balance in cats, underscoring the need for laboratory monitoring. The retrospective single-center design, the relatively small sample size, and the reliance on manufacturer-declared dietary composition data without laboratory verification were limitations of the present study. In addition, hormonal markers of mineral metabolism, including FGF-23, parathyroid hormone, and 25-hydroxyvitamin D, were not evaluated. Further prospective multicenter studies with standardized dietary assessments and hormonal monitoring are necessary to understand the link between dietary mineral content and calcium metabolism in cats.

DECLARATIONS

Acknowledgements

The authors would like to express their gratitude to the Zoolux Veterinary Clinic (Kyiv, Ukraine) for providing access to clinical data.

Authors' contributions

Mykhailo Umanets participated in conducting the study, collecting and analyzing clinical data, and drafting the initial manuscript. Valerii Tsvilikhovskyi contributed to the conceptualization and design of the study, the methodology, supervision, and the review and editing of the manuscript. All authors have read and approved the final edition of the manuscript.

Availability of data and materials

The data supporting the findings of the present study are available from the corresponding author upon reasonable request.

Competing interests
The authors declared no competing interests.

Ethical considerations
The authors declared that the manuscript is original, has not been published elsewhere, and that the last edition was confirmed before publication. The authors confirmed that no AI tools were used for writing and preparing the article.

Funding
The present study did not receive any external financial support.

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