Veterinary-formulated diets as protective factors against chronic kidney disease: A case-control study in domestic cats (*Felis catus*)

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Abstract

Chronic kidney disease (CKD) affects 30–40% of cats (*Felis catus*) over 10 years old, highlighting the need to identify modifiable dietary risk factors. This case-control study (2021–2023) evaluated pre-morbid diets in 194 client-owned cats (97 CKD cases, 97 controls) from southeastern Iran, excluding those with comorbidities and exclusively outdoor housing. CKD diagnosis was based on IRIS criteria (serum creatinine ≥1.6 mg/dL, urine specific gravity <1.030/proteinuria). Dietary intake was assessed using validated owner questionnaires, categorizing diets as commercial dry/wet, non-formulated homemade, or veterinary-formulated mixed diets. Cats with CKD had significantly higher creatinine levels (2.1 vs. 1.4 mg/dL, $p<0.001$), with 65% at IRIS Stage 2. Non-formulated homemade diets (28.9% vs. 16.5% controls; OR=2.1, $p=0.04$) and commercial wet foods (29.9% vs. 16.5%; OR=2.1, $p=0.027$) were associated with increased CKD risk, whereas veterinary-formulated mixed diets were protective (10.3% vs. 22.7%; OR=0.4, $p=0.02$). Subgroup analyses linked non-formulated diets to underweight status ($p=0.003$) and dry food consumption to obesity ($p=0.01$). These findings emphasize the critical role of diet formulation quality, particularly phosphorus-protein balance, in mitigating renal stress. Despite the observational design and potential residual confounders limiting causal inference, results support early nutritional counseling, IRIS-aligned diets, and routine screening to prevent CKD in aging cats. Future research should explore biomarker-guided dietary interventions to enhance feline renal health.

Keywords: Chronic kidney disease (CKD), Domestic cats, Veterinary-formulated diets, Dietary risk factors

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Introduction

Chronic kidney disease (CKD) is a leading cause of morbidity and mortality in domestic cats (*Felis catus*), affecting approximately 30–40% of individuals over 10 years of age (Brown *et al*., 2016). Characterized by irreversible nephron loss and progressive renal dysfunction, CKD imposes substantial burdens on feline welfare and veterinary healthcare systems, underscoring the urgency of identifying modifiable risk factors. While age and genetic predisposition are well-established contributors, the role of dietary patterns in CKD pathogenesis remains contentious, with conflicting evidence regarding the risks associated with commercial, homemade, and mixed diets (Greene *et al*., 2014). The International Renal Interest Society (IRIS) staging system provides a standardized framework for classifying CKD severity based on serum creatinine, proteinuria, and systemic blood pressure, enabling veterinarians to tailor management strategies, monitor progression, and prognosticate outcomes effectively. This evidence-based approach enhances clinical decision-making and fosters consistent communication among practitioners, ultimately improving patient care (https://www.iris-kidney.com/).

Existing studies have yielded paradoxical insights. For instance, while ad libitum feeding and nutrient imbalances (e.g., hyperphosphatemia) have been implicated in renal stress (Hughes *et al*., 2002), systematic reviews highlight inconsistencies in linking diet type—such as dry versus wet formulations—to CKD incidence (Freeman *et al*., 2016). Furthermore, improperly formulated homemade diets, often deficient in essential nutrients or excessive in phosphorus, have emerged as potential risk factors in experimental models, yet their clinical relevance in feline populations remains understudied(Freeman *et al*., 2016). Comorbidities, including hyperthyroidism and periodontal disease, further complicate these associations, as they frequently co-occur with CKD and may influence dietary practices (Greene *et al*., 2014).

To address these gaps, this case-control study investigates the relationship between pre-morbid dietary patterns and CKD incidence in domestic cats, while rigorously controlling for confounders such as comorbidities, age, and environmental factors. We hypothesize that non-formulated homemade diets and generic commercial wet foods elevate CKD risk due to nutrient imbalances, whereas veterinary-supervised mixed diets exert protective effects through optimized mineral and protein profiles.

By excluding cats with concurrent conditions and outdoor-only housing, this study enhances methodological rigor relative to prior work, offering novel insights into diet-driven renal pathophysiology. Our findings aim to refine evidence-based nutritional guidelines, empowering veterinarians to mitigate CKD prevalence through proactive dietary management and client education. This work aligns with global

veterinary priorities, as articulated by the American Association of Feline Practitioners (AAFP), which emphasizes early intervention and tailored nutrition to safeguard renal health in aging cats (Quimby *et al*., 2024).

Materials and methods

This study was conducted from 2021 to 2023 on 232 client-owned cats primarily presenting with renal-related concerns to veterinary teaching hospitals in southeastern Iran (Kerman and Zabol). The study protocol was approved by the Ethics Committee of the Faculty of Veterinary Medicine, University of Zabol (ID IR.UOZ.REC.1402.029). Blood samples were collected from all enrolled cats with no prior history of chronic kidney disease (CKD) for biochemical analysis.

Case inclusion criteria for CKD group

Cats were classified as CKD cases if they met both of the following criteria:

1.Serum creatinine ≥1.6 mg/dL (IRIS Stage 2 or higher).

2.Urine specific gravity (USG) <1.030 or presence of proteinuria.

Cats with a pre-existing CKD diagnosis in their medical records were also included but were required to answer questions regarding dietary and lifestyle habits prior to their CKD diagnosis.

Data collection via questionnaire

Owners of CKD-confirmed cats completed a multiple-choice questionnaire designed by the authors under the supervision of a board-certified specialist in companion animal internal medicine. The questionnaire focused on:

- Pre-CKD dietary patterns (commercial dry food, homemade diets, commercial wet food, or veterinarian-balanced mixed diets).
- Lifestyle factors (indoor/outdoor activity, vaccination status).
- Significant dietary changes from adoption to CKD diagnosis.

Questionnaire validation

A preliminary version was pilot-tested with 10 cat owners to assess clarity and coherence. Feedback was incorporated to refine phrasing. The final printed questionnaire was administered only to owners aged ≥18 years.

Control group

Cats were included in the control group if they met all of the following:

1. Serum creatinine <1.6 mg/dL.
2. USG ≥1.030.
3. Absence of proteinuria.

Cats meeting any CKD diagnostic criteria were excluded.

Comorbidities assessment

Medical records of both groups were reviewed for concurrent conditions (e.g., diabetes, hypertension, hyperthyroidism, dental disease, or polycystic kidney (PKD)).

Exclusion criteria

Cats with comorbidities or outdoor-only living conditions were excluded to minimize confounding factors.

Statistical analysis

- Normality of data distribution was assessed using the Kolmogorov-Smirnov test.
- The association between dietary patterns (dry food, wet food, homemade food, veterinary-formulated mixed diets) and CKD incidence was analyzed via Chi-square test.
- Post hoc pairwise Z-tests identified statistically significant differences between dietary groups.
- The analysis of the data was conducted using the computer program IBM SPSS statistics for Windows Version 29.

Results

Cohort characteristics and exclusion rationale

From an initial pool of 232 cats presenting to veterinary hospitals in southeastern Iran (2021–2023), **97 cats** met stringent inclusion criteria for the CKD group, while 97 age- and weight-matched controls were enrolled after excluding 38 cats. Exclusions were rigorously applied to minimize confounding:

- Comorbidities: 22 cats excluded for, hypertension, dental disease, diabetes, or hyperthyroidism.
- Outdoor Housing: 16 cats excluded due to uncontrolled environmental variables (e.g., toxin exposure, unknown diet history).

Demographic and metabolic homogeneity

The CKD and control groups demonstrated homogeneity in baseline parameters ($P > 0.05$):

- Age: CKD group: 8.36 ± 0.43 years; Control: 8.17 ± 0.62 years.
- Body Weight: CKD: 4.31 ± 0.18 kg; Control: 4.52 ± 0.20 kg.
- Body Condition Scores: CKD cats included 15 obese (BCS ≥7/9), 68 normal-weight (BCS 4–6/9), and 14 underweight (BCS ≤3/9) individuals.

Renal function stratification

CKD cats exhibited marked renal impairment:

- Serum Creatinine: Mean 2.1 mg/dL (vs. 1.4 mg/dL in controls; $P < 0.001$).
- IRIS CKD Staging:
  - Stage 2 (mild azotemia): 63 cats (65%), creatinine 1.6–2.8 mg/dL.
  - Stage 3 (moderate): 26 cats (26.4%), creatinine 2.9–5 mg/dL.
  - Stage 4 (severe): 8 cats (8.5%), creatinine ≥5 mg/dL.

Dietary patterns: Risk and protective associations

Analysis of dietary questionnaires (n=174) revealed distinct risk profiles:

1. Commercial Dry Food:
   - Most common diet in both groups but more prevalent in controls (44.3% vs. 30.9% in CKD; $P = 0.06$), suggesting a non-significant protective trend.
   - Dominated by 5 major brands of commercial dry food (82%).
2. Homemade Non-Formulated Diets:
   - Strongly associated with CKD (28.9% vs. 16.5% in controls; $P = 0.04$; OR=2.1, 95% CI: 1.1–4.0).

- Frequently lacked veterinary oversight (87% of owners reported no nutritional counseling).

3. Mixed Formulated Diets:
   - Protective effect: Only 10.3% of CKD cats vs. 22.7% of controls (*P = 0.02*; OR=0.4, 95% CI: 0.2–0.9).
   - All involved veterinary-prescribed homemade meals balanced with commercial dry food.

Key statistical outcomes

- Chi-square test: Dietary distribution differed significantly between groups ($\chi^2 = 12.7$, df=3, *P = 0.014*; Table 1).
- Pairwise Z-Tests:
  - Wet food: Higher CKD risk vs. dry food (*P = 0.027*; OR=2.1), potentially linked to phosphate additives in commercial wet diets.
  - Non-formulated homemade diets: Elevated CKD risk vs. mixed diets (*P = 0.032*; OR=3.2), likely due to imbalanced nutrient profiles (e.g., excessive protein, low moisture).
  - Mixed diets: Protective vs. wet food (*P = 0.025*; OR=0.36), underscoring the importance of veterinary-guided formulations.

Subgroup insights

- Obese CKD cats: Despite comparable caloric intake, 60% of obese CKD cats consumed high-carbohydrate dry foods vs. 28% in controls (*P = 0.01*).
- Underweight CKD cats: 71% relied on non-formulated homemade diets vs. 22% in controls (*P = 0.003*), highlighting malnutrition risks.

Table 1: Dietary pattern frequencies in domestic feline CKD and control groups.

		Diet							
		Home made		Dry food		Wet food		Mixed (Homemade and dry)	
		Count	Row N%	Count	Row N%	Count	Row N%	Count	Row N%
CKD status	+	28	28.9%	30	30.9%	29	29.9%	10	10.3%
	-	16	16.5%	43	44.3%	16	16.5%	22	22.7%

Table 2: Pairwise comparisons of dietary risk factors for CKD in cats.

		CKD status	
		+	-
		(A)	(B)
Diet	Home made	B(.040)	
	dry		
	wet	B(.027)	
	Mixed (Homemade and dry)		A(.020)

Discussion

The objective of this investigation was to explore the relationship between distinct dietary patterns and chronic kidney disease (CKD) risk in domestic cats, while rigorously accounting for confounders such as age, weight, and comorbidities. Our findings reveal statistically significant associations between non-formulated homemade

diets, generic commercial wet foods, and elevated CKD risk, whereas veterinary-formulated mixed diets demonstrated protective effects. These results both corroborate and challenge existing paradigms in feline renal health research, underscoring the need for precision in dietary formulation and client education.

Dietary patterns, nutrient imbalances, and mechanistic insights

The elevated CKD prevalence among cats fed non-formulated homemade diets (28.9% vs. 16.5% in controls; $P = 0.04$) aligns with experimental models demonstrating that nutrient imbalances—particularly hyperphosphatemia and potassium deficiency—exacerbate renal tubular oxidative stress and interstitial fibrosis (Ross *et al*., 2006, Freeman *et al*., 2016). In our cohort, 87% of owners providing homemade diets reported no veterinary nutritional counseling, suggesting that well-intentioned but uninformed dietary practices may inadvertently harm renal health. This underscores the necessity of veterinary oversight to mitigate risks associated with imbalanced nutrient profiles, as emphasized by (Larsen and Villaverde, 2016).

Paradoxically, commercial wet food—despite its hydration benefits—was associated with higher CKD risk (29.9% vs. 16.5%; $P = 0.027$). This finding challenges the conventional emphasis on moisture content as protective and instead highlights formulation quality as the critical determinant. (Jepson *et al*.) reported that 65% of non-prescription "renal support" wet diets exceeded IRIS phosphorus thresholds (>1.5 g/1000 kcal), a likely contributor to renal stress. While increased water intake improves renal perfusion (Paepe *et al*., 2015), our results suggest that unregulated phosphorus and sodium content in generic wet foods negate these benefits, necessitating stricter industry regulation. Conversely, veterinary-formulated mixed diets were protective (10.3% CKD vs. 22.7% controls; $P = 0.02$), likely due to optimized phosphorus restriction (<0.5% dry matter) and high-quality protein sources. These diets align with longitudinal studies showing delayed CKD progression in cats fed prescription formulations (Elliott and Geddes, 2022). The combination of commercial and homemade components may also enhance palatability, addressing adherence barriers noted in clinical settings (Laflamme *et al*., 2020).

Reconciling discrepancies with prior literature

Our results conflict with Greene *et al*. (2014), who found no association between diet type and CKD risk. However, their study did not exclude comorbidities such as hyperthyroidism, which may confound dietary effects. By contrast, our stringent exclusion criteria enhance internal validity, isolating diet-specific risks. Similarly, (Hughes *et al*., 2002) identified ad libitum feeding as a risk factor (OR = 4.1–5.5), but 95% of their cohort consumed dry food, suggesting that feeding practices—rather than dry food itself—may drive risk. Our data support this nuance: while

dry food prevalence was higher in controls (44.3% vs. 30.9%), its protective trend (*P = 0.06*) may reflect adherence to portion-controlled feeding protocols.

(Tang *et al*., 2022) identified phosphate-restricted diets (PRDs) as both a risk factor for nephrocalcinosis and a predictor of improved survival, illustrating the dual role of mineral metabolism in CKD. Our study extends these insights by demonstrating that veterinary-guided formulations mitigate risks associated with generic diets, likely through precise calcium-phosphate balance.

Methodological rigor and limitations

This study advances prior work by excluding outdoor-only cats and comorbidities, thereby reducing confounding from environmental toxins and systemic inflammation. However, observational designs cannot fully establish causality, and residual confounders such as undiagnosed hypertension may persist (Polzin, 2013). Regional recruitment from arid southeastern Iran may amplify dehydration-driven renal stress, limiting generalizability to temperate climates. Future studies should integrate climatic data with biomarkers like urine osmolality to clarify these interactions.

Clinical implications and future directions

1. Prescription Diets: Prioritize IRIS-aligned diets with phosphorus restriction (<0.4–0.6% dry matter) and omega-3 supplementation to reduce glomerular hypertension (Brown *et al*., 2016).
2. Client Education: Combat misconceptions about “natural” diets using tools like AAHA’s Nutritional Assessment Guidelines (Baldwin *et al*., 2010), emphasizing the dangers of unformulated homemade meals.
3. Early Screening: Annual creatinine and urine-specific gravity monitoring for cats ≥7 years, per AAFP guidelines (Quimby *et al*., 2021), enables early intervention.

Prospective studies should quantify nutrient intake via biomarkers (e.g., fecal phosphorus) and explore genetic susceptibilities to diet-sensitive nephropathies (Brown *et al*., 2024). Randomized trials comparing wet vs. dry prescription diets could resolve hydration-formulation trade-offs, as highlighted by (Freeman *et al*., 2016).

In conclusion, this study identifies dietary patterns as modifiable risk factors for CKD in domestic cats. Improperly formulated homemade diets and generic commercial wet foods were associated with elevated risk, while mixed diets formulated under veterinary guidance demonstrated significant protective effects. These findings align with emerging literature on feline renal health, yet refine current paradigms by emphasizing the critical role of precise diet formulation and client education. Clinically, proactive nutritional counseling, IRIS-aligned diets, and early screening are essential strategies to

mitigate CKD prevalence, underscoring the necessity of veterinary oversight in optimizing feline renal care.

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