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Feline Interstitial Cystitis - Analysis of Clinical-epidemiological Findings and Inflammatory Biomarkers

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ABSTRACT

***Background*:** Feline Interstitial Cystitis (FIC) is a prevalent condition within Feline Lower Urinary Tract Diseases (FLUTD), frequently affecting male, mixed-breed cats aged 1-10 years. Despite its high incidence, data on FIC in Ceará, Brazil, remain limited. This study evaluates the prevalence of FIC among cats treated at the Veterinary Hospital of Ceará State University (UECE) and explores the utility of inflammatory biomarkers, including the serum albumin/creatinine ratio (SACR) and urine specific gravity/albumin ratio, as potential diagnostic and prognostic tools for disease monitoring.

***Materials, Methods & Results*:** This study evaluated 227 cats diagnosed with FIC among 3,900 treated at the Veterinary Hospital of Ceará State University, indicating a prevalence of 5.82%. Data were collected on sex, age, reproductive status, diet, clinical signs, urinalysis results, and laboratory parameters including urine specific gravity (USG), creatinine, albumin, and inflammatory biomarker ratios (SACR and USG/albumin). Of the 227 cats, 102 presented with the obstructive form (OC) and 125 with the non-obstructive form (NOC). All OC cats were male, 75% were intact, and 25% neutered, while 56% of NOC cats were female. The clinical signs observed in OC cats included hematuria (69.6%), dysuria (50%), periuria (19.6%), stranguria (18.6%), and polyuria (4.9%). Dry food predominated as the primary diet in 80% of OC and 83% of NOC cats. Urinalysis showed struvite crystals in 41% of OC and 28% of NOC cats, while 55.8% of OC and 69.6% of NOC cats had no crystals. Laboratory analysis revealed no significant differences between groups for USG, creatinine, and albumin levels. However, SACR values were lower in OC cats compared to NOC cats, and the USG/albumin ratio showed no statistical difference between groups.

***Discussion*:** This study highlights the prevalence of FIC at 5.82% in cats treated at the Veterinary Hospital of Ceará State University, providing important insights into its clinical and epidemiological characteristics. The findings confirm that male cats are disproportionately affected by the obstructive form (OC), with 100% of cases occurring in males, of which 75% were intact. Hematuria, dysuria, and periuria were the most frequent clinical signs in OC cases, aligning with previous studies. The predominance of dry food as the primary diet in both OC and NOC groups underscores its potential role in urinary health, although no direct causation was established. Urinalysis revealed a higher occurrence of struvite crystals in OC cases (41%) compared to NOC (28%), while more NOC cats had no crystals (69.6%). These findings suggest that other factors, beyond crystalluria, contribute to the inflammatory processes underlying FIC. The significant reduction in serum albumin/creatinine ratio (SACR) in OC cats emphasizes its potential as a biomarker for inflammation and impaired renal function. However, the lack of difference in USG/albumin ratio between groups suggests that additional studies are needed to validate its clinical utility. In conclusion, the study underscores the epidemiological and clinical relevance of FIC, emphasizing the potential of SACR as a diagnostic and monitoring tool. Further prospective studies are encouraged to deepen the understanding of the disease's pathophysiology and explore the role of inflammatory biomarkers in its management.

Keywords: lower urinary tract disease, urine specific gravity, epidemiology, albumin to creatinine ratio.

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INTRODUCTION

Feline Lower Urinary Tract Disease (FLUTD) comprises a range of conditions affecting the urinary bladder and urethra, representing a common issue in feline veterinary practice [1,22]. It includes clinical conditions like Feline Interstitial Cystitis (FIC), urolithiasis, and urinary tract infections (UTI), with FIC diagnosed when no other specific causes of FLUTD are identified [16]. Cats affected by FIC often exhibit polyuria, stranguria, hematuria, periuria, dysuria, or ischuria [11], with a higher prevalence in male, mixed-breed cats aged 1-10 years, especially those on dry diets with low water intake [21].

FIC occurs in obstructive and non-obstructive forms. Obstructive FIC involves urinary blockage, while non-obstructive FIC is marked by urinary signs without flow interruption. Diagnosis relies on clinical evaluation, patient history, and complementary exams such as biochemical tests, like serum creatinine and albumin, and ultrasonography [4,5,23]. Additionally, urine specific gravity (USG) is important for assessing potential renal injury linked to inflammation [24].

Human medicine emphasizes inflammatory biomarkers, with analyte ratios offering detailed insights into clinical conditions. Serum albumin/creatinine ratio (SACR) is one such biomarker, used to evaluate prognosis in acute myocardial infarction [15]. However, data on SACR in veterinary contexts are scarce.

Considering the high prevalence of FIC [6] and lack of regional data in Ceará, this study assesses FIC prevalence at the Ceará State University Veterinary Hospital (UECE). Additionally, we aimed to examine SACR and USG/albumin ratio as indicators of FIC's inflammatory nature.

MATERIALS AND METHODS

Study design

This prospective study was conducted at the Hospital Veterinário Sylvio Barbosa Cardoso (HVSBC/UECE) during 2 years.

Study population and group distribution

A total of 3,900 cats were treated at HVSBC during the specified period, and from these, 227 animals were selected and distributed into 2 groups: the obstructive FIC group (OC), comprising 102 animals clinically diagnosed with urinary obstruction (and no evidence of uroliths), and the non-obstructive FIC group (NOC), comprising 125 animals with cystitis without clinical signs of obstruction. For comparative evaluation of the serum albumin/creatinine ratio (SACR), a control group (CG) of 20 healthy male cats, aged between 1-3 years, who attended routine consultations at HVSBC, was included (Figure 1).

Assessment criteria

The enrolled cats were assessed based on sex, age, breed, reproductive status, clinical signs (polyuria, stranguria, hematuria, dysuria, and periuria), type of diet, presence and type of urinary crystals, bacteriuria, and isolated bacterial species. In addition, laboratory tests and ultrasonography were conducted.

Laboratory analysis

Laboratory analysis focused on urine specific gravity (USG), creatinine, and albumin values, alongside derived inflammatory biomarkers such as the serum albumin/creatinine ratio (SACR) and the USG/albumin ratio (Figure 1). Ultrasonographic evaluations determined the presence or absence of uroliths. Notably, all laboratory tests were performed within 7 days of clinical evaluation for both the OC and NOC groups, ensuring consistency and relevance of the data collected.

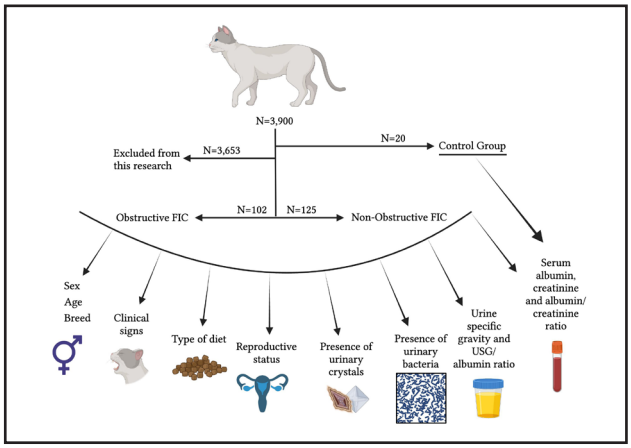

Figure 1. Flowchart summarizing the study design and methodology. A total of 3,900 cats were assessed, with 3,653 excluded based on inclusion criteria. The final sample included 102 cats diagnosed with obstructive feline idiopathic cystitis (OC), 125 with non-obstructive feline idiopathic cystitis (NOC), and 20 healthy control cats. The variables evaluated included sex, age, breed, clinical signs, type of diet, reproductive status, presence of urinary crystals, urinary bacteria, urine specific gravity (USG), and serum markers (albumin, creatinine, and albumin/creatinine ratio).

Statistical analysis

Statistical analysis were performed using GraphPad Prism[1] software. Qualitative variables were expressed descriptively and analyzed using Fisher's Exact Test for comparison between the OC and NOC groups. Quantitative data were expressed as mean and standard deviation. Albumin, USG, creatinine, and the USG/albumin ratio between groups were compared using the Mann-Whitney test ($P < 0.05$). The serum albumin/creatinine ratio between groups was compared using the Kruskal-Wallis test, followed by Dunn's post hoc test ($P < 0.05$).

RESULTS

In the present study, a total of 227 cats were included, revealing a prevalence of 5.82% of FIC cases. All cats evaluated were of mixed breed, aged between 1 and 10 years, with an average age of 4 years. Among the 102 cats in the OC group, all were male, with 75% being intact (76/102) and 25% neutered (26/102). Regarding the frequency of clinical signs, 69.6% exhibited hematuria (71/102), 19.6% periuria (20/102), 50% dysuria (51/102), 18.6% stranguria (19/102), and 4.9% polyuria (5/102). In terms of diet, 80.3% (82/102) were fed exclusively dry food, while 20% (22/102) also received wet food. Urinalysis revealed that 41.1% (42/102) of the animals had struvite crystals, 2.9% (3/102) had calcium oxalate crystals, and 55.8% (57/102) had no crystals (Table 1).

Urinalysis in the OC group further demonstrated that 6.8% (7/102) of the animals had bacteriuria. Urine culture was performed in only 17 animals, revealing bacterial growth in 7 samples, with the isolated agents being: *Proteus mirabilis* (n=3), *Escherichia coli* (n=2), and *Staphylococcus pseudintermedius* (n=2).

The NOC group consisted of 125 animals, with 42.4% (53/125) being males and 57.6% (72/125) females; 85.6% (107/125) were neutered, and 14.4% (18/125) were intact. Hematuria was observed in 33.6% (42/125) of the cases, polydipsia in 24.8% (31/125), stranguria in 22.4% (28/125), dysuria in 29.6% (37/125), and periuria in 25.6% (32/125). Dry food was provided exclusively to 83.2% (104/125) of the animals, while 16.8% (21/125) received wet food. Urine analysis revealed that 28% (35/125) had struvite crystals, 2.4% (3/125) had calcium oxalate crystals, 69.6% (87/125) had no crystals, and 10.4% (13/125) had bacteriuria (Table 1). Urine culture was performed in 44 animals, with positive results in only 10 cases. The isolated agents were *Staphylococcus pseudintermedius* (n=3), *Escherichia coli* (n=5), and *Streptococcus intermedius* (n=2).

The obstructed cats had a mean SACR of 1.54 ± 0.65, while the non-obstructed cats had a mean value of 1.81 ± 0.56, and the control group had a mean value of 2.16 ± 0.48. SACR values were statistically different between the OC and CG groups, as well as between the OC and NOC groups. In the analysis of the USG/Albumin ratio, a mean of 441 ± 86 was observed in OC and 420 ± 83 in NOC. Regarding urine specific gravity, the mean values were 1.040 ± 15.8 in OC and 1.043 ± 12.56 in NOC. Finally, the mean values of creatinine and albumin in OC were 2.35 ± 2.48 and 2.44 ± 0.44, respectively, while in NOC they were 1.61 ± 1.1 and 2.56 ± 0.45. It is noteworthy that no statistical differences were observed in any of these parameters (Figure 2).

Table 1. Qualitative variables associated with FIC in a population of domestic cats treated at HVSBC during 2 years.

		OC (n = 102)	NOC (n = 125)	*P*	Odds ratio
Sex	Male	102	53	$P < 0.0001$	277.8
	Female	0	72		
Reproductive Status	Intact	76	18	$P < 0.0001$	17.38
	Neutered	26	107		
Clinical Signs	Hematuria	71	42	$P < 0.0001$	4.5
	Periuria	20	32	$P = 0.34$	-
	Dysuria	51	37	$P = 0.002$	2.3
	Stranguria	19	28	$P = 0.51$	-
	Pollakiuria	5	31	$P < 0.0001$	0.15
Diet	Dry	82	104	$P = 0.49$	-
	Wet	22	21		
Urinary Crystals[1]	Struvite	42	35	$P = 0.038$	1.80
	Calcium Oxalate	3	3		
	No Crystals	57	87		

[1]Cats from OC and NOC groups were compared regarding the presence and absence of urinary crystals.

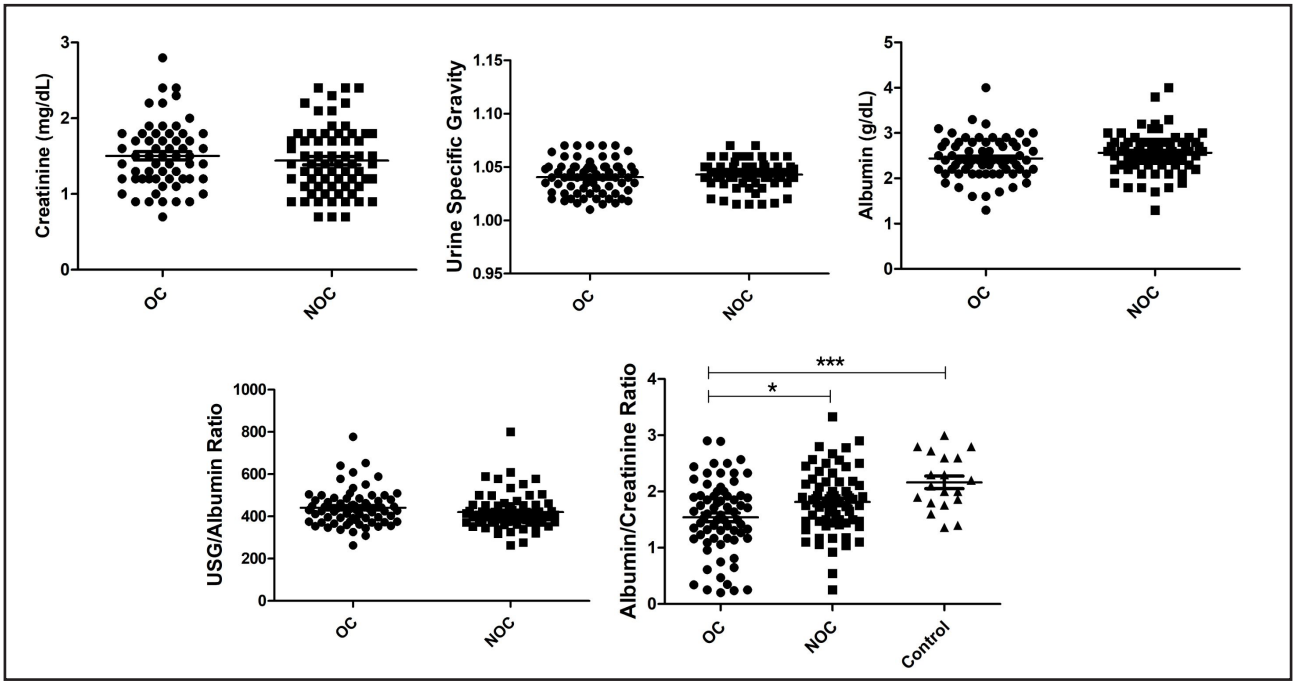

Figure 2. Laboratory parameters (urine specific gravity, albumin, creatinine, albumin/creatinine ratio, and USG/albumin ratio) in cats with FIC.

DISCUSSION

Feline idiopathic cystitis (FIC) is associated with a range of clinical and laboratory changes resulting from inflammation of the urinary bladder [12,17]. The high incidence of FIC in clinical practice underscores the importance of studies focused on its epidemiology and clinical management [13,17]. In the present study, a prevalence of 5.82% (227/3,900) of FIC cases was observed among all cats treated at HVSBC during 2 years of monitoring.

Although FIC can affect both male and female cats [9], its obstructive form is more frequently observed in males due to their smaller urethral diameter compared to females [17,18]. This observation aligns with our findings, where all obstructed cats were male. Among the clinical forms of this disease, however, the non-obstructive form of FIC is more common [9], which is consistent with the data obtained in the present study. These findings may be related to environmental factors and management practices, which can initiate an inflammatory process in the bladder that begins with the non-obstructive form of FIC and, through chronic progression [12], may advance to the obstructive form.

It was previously believed that neutering could be among the risk factors for the development of FIC in both obstructive and non-obstructive forms, due to morphological changes in the urethral and penile regions [9,10]. However, in our study, the obstructive condition was more commonly observed in intact animals, corroborating other data in the literature [18]. The frequency of non-neutered and obstructed cats may be related to a combination of predisposing factors, such as type of diet, routine changes, confinement, and sedentary lifestyle [9,10,20]. Nonetheless, given the methods applied to this study, a detailed causal analysis could not be performed.

It is well known that an exclusively dry diet is one of the risk factors for the development of obstructive FLUTD, considering that it can alter urinary pH and predispose cats to the formation of crystals and uroliths [16,19]. However, the relationship between the type of food and FIC still needs to be elucidated. In the present study, the dietary profile analysis of cats affected by FIC, in both obstructive (OC) and non-obstructive (NOC) forms, revealed a predominance of dry food consumption. Despite this, the majority of cats affected by FIC did not have crystals in their urine, suggesting that if dry food plays a role in the pathogenesis of FIC, it may do so through other mechanisms. Therefore, conducting prospective studies that include healthy animals, as well as those with obstruc-

tive and non-obstructive FIC, is encouraged to further understand the causal relationship between diet type and disease development.

In our study, there was a higher occurrence of struvite (triple phosphate) crystals in the urine of animals in both the OC and NOC groups, although they did not have urolith formation. The formation of these crystals is related to factors such as diet type, low water intake, and alkaline urinary pH [21]; however, the exact correlation of these variables could not be evaluated in the present study. Notably, the NOC group had a significantly lower occurrence of crystalluria compared to the OC group ($P = 0.038$), with an odds ratio of 1.80 indicating that cats in the OC group were 1.8 times more likely to have struvite crystals. Despite this, the majority of animals in both the OC and NOC groups did not have crystals, reinforcing the idea that while crystals may contribute to bladder irritation [2], other factors are likely involved in the development of the disease.

Hematuria and dysuria were the main clinical signs observed in the OC group and can occur due to intense bladder distension and local inflammation, leading to the release of blood in the urine and the manifestation of pain during urination. This local inflammation is often the result of damage to the bladder wall, which can be exacerbated by the presence of crystalline debris that irritate the bladder lining [2]. In addition to these factors, the influence of manual bladder compression, cystocentesis, and catheterization [15] can also be considered as possible causes of hematuria/dysuria in the OC group, especially since some of these animals had a history of recurrent obstruction. The clinical implications of these findings highlight the importance of careful handling and minimally invasive techniques in the management of cats with FIC to reduce the risk of exacerbating hematuria and dysuria.

In the NOC group, we observed a higher number of animals with pollakiuria, which is also related to the inflammatory process and pain, causing urgency to urinate [9]. It is believed that the low number of animals with pollakiuria in the OC group is related to the interruption of urinary flow that occurs in this form of FIC.

In our study, it was also possible to evaluate and compare the values of urine specific gravity (USG), creatinine, albumin, and their interrelationships. No significant differences were observed in USG, creatinine, and albumin between the OC and NOC groups, although the mean values in the OC group for albumin were lower and for creatinine were higher compared to the NOC group. Considering that the assessment of these parameters was performed within 7 days of the clinical consultation, and that the OC animals were de-obstructed at the time of initial treatment, it is believed that the cats in this group mostly showed a trend towards improvement in the evaluated parameters, which approximated those of the NOC group.

Finally, our data allowed us to propose an approach to this disease using the relationships between these markers. In medicine, biomarker ratios are used to enhance test performance compared to individual analysis [25]. The serum albumin/creatinine ratio (SACR) is a prognostic biomarker in cardiology, with lower values associated with worse outcomes [14]. In this study, the OC group showed reduced SACR values, suggesting activation of inflammatory responses that decrease albumin and increase creatinine levels [6]. Notably, while individual creatinine and albumin values did not differ significantly between groups, SACR did, indicating its potential for detecting inflammation and reduced glomerular filtration. Prospective studies should evaluate SACR behavior as the disease progresses or improves to validate its use as a prognostic and monitoring tool.

In the context of evaluating relationships, we propose the combined assessment of urine specific gravity (USG) and serum albumin. USG is an important indicator of renal concentrating ability [24], and when combined with albumin levels, can provide valuable information about renal health and the inflammatory state of the animal. Albumin is an essential protein, and its decrease may be associated with inflammatory processes [7], hepatic [3] and renal diseases [8]. The relationship between USG and albumin could help identify changes in renal function and vascular integrity, reducing the interference of pre-analytical factors such as age, dehydration, and fasting status [24], thus providing a more comprehensive health assessment. Although an increase in the USG/albumin ratio was expected in obstructed animals, no statistical difference was observed between the OC and NOC groups. This finding may also be related to the timing of the post-deobstruction exams, which likely brought the results of the OC group closer to those of the NOC group. Future studies should explore the clinical utility of this relationship, as well as validate it, to better

understand how these variables interact in the context of FLUTD and FIC.

This study has several limitations that should be considered when interpreting the results. Firstly, the sample size, although adequate, may not fully represent the broader population of cats with FIC, and further studies with larger and more diverse populations are needed to confirm these findings. Furthermore, the study did not control for all environmental and dietary factors that could influence the development and progression of FIC, limiting the ability to draw definitive conclusions about causality. Other prospective, longitudinal studies are recommended to better understand the complex interactions between various risk factors and FIC.

CONCLUSION

In conclusion, FIC has a high prevalence in animals treated at HVSBC-UECE. Factors such as sex and reproductive status are important in the epidemiology of the disease, and the serum albumin/creatinine ratio (SACR) is altered in cats with obstructive FIC. Further studies are recommended to evaluate the use of this inflammatory biomarker in monitoring and prognosis of affected patients. Additionally, this study introduces the novel approach of assessing the relationship between urine specific gravity and serum albumin, suggesting it as a biomarker to be explored in FIC and other urinary system diseases.

MANUFACTURER

[1]GraphPad® Software. San Diego, CA, USA.

***Ethical approval*.** The experimental protocol for this study was approved by the UECE Ethics Committee for the Use of Animals under the number NUP 31032.001187/2023-10.

***Declaration of interest*.** The authors declare no conflicts of interest. The authors were responsible for the content and writing of the paper.

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