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CLINICOPATHOLOGICAL CHARACTERIZATION OF FELINE UROLITHIASIS IN PAKISTAN: URINALYSIS, SERUM ELECTROLYTES, RENAL FUNCTION AND RISK FACTOR PROFILE

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Abstract

Background: Urolithiasis is a clinically significant cause of lower urinary tract disease. Clinicopathological data from Pakistan is absent from the published literature.

Objective: To characterize the risk factor profile, clinical sign, urinalysis finding, and serum biochemical changes, in cats presenting with urolithiasis at veterinary facilities in Lahore and Islamabad, Pakistan.

Methods: A prospective observational study was conducted from August 2021 to January 2022 at the pet centre of University of Veterinary and Animal Sciences (UVAS), Lahore, and affiliated clinics in Islamabad. Twenty-four cats with confirmed urolithiasis were enrolled. Signalment, diet, housing, and clinical data were recorded. Urinalysis was performed by physical inspection, dipstick chemistry (Uric CF 10) and microscopic sediment examination. Serum biochemistry included blood urea nitrogen (BUN), creatinine, calcium and phosphorus. Catagorical variable were compared by Pearson chi-square. Significance was set at $p< 0.05$.

Results: Persian cats represented 45.83% of cases ($p\leq0.001$). Males compromised 91.67% of the cohort ($p<0.001$). The 1 to 3 year age group accounted for 66.67% of cases ($p<0.001$). Most

cats were non-neutered (75%). All 24 cats were dehydrated at presentation. Dysuria and stranguria were observed in 83.34% of cats. Alkaline urine was detected in 64% of cases ($p=0.021$). Crystalluria was present in 87.5% of cats ($p\leq0.001$); struvite was the most common single crystal type (25%), and 37.5% of cats exhibited multiple concurrent crystal types. Serum creatinine (mean 3.3±0.39 mg/dL) exceeded the upper reference limit in 15 of 24 cats (62.5%). Serum phosphorus (mean 7.08±0.21 mg/dL) exceeded the upper reference limit in 14 of 24 cats (58.3%). BUN and calcium remained within normal limits as a group.

Conclusion: Feline urolithiasis in Pakistan predominantly affects young, non-neutered, male Persian cats maintained indoors on commercial diets. Struvite crystalluria is the most frequent single crystal type and occurs commonly as part of a mixed-crystal presentation. Concurrent elevation of serum creatinine and phosphorus in the majority of cats indicates renal compromise at the time of initial presentation. These findings provide the first systematic clinicopathological description of feline urolithiasis in Pakistan.

1. Introduction

In feline veterinary medicine, the most frequent reasons for seeking an examination are urinary tract disease (Gerber et al. 2005). Urolithiasis is defined as the urolith or stone formation with in urinary system and it accounts for 10 to 23 percent cases of feline lower urinary tract disease (FLUTD) (Jone, 2009). Stone formation is predominantly in lower urinary tract with bladder involvement in more than 95% cases (Osborne et al., 1996). In male, urethral obstruction has life-threatening consequences, as urethra is anatomically narrow and long (Kopecny et al., 2021; Segev et al., 2011).

Various epidemiological studies from Europe and North America stated that, among felines uroliths struvite and calcium oxalate together accounts for approximately 90 percent (Houston et al., 2016; Kopecny et al.,2021). A change dietary reformulation causes significant shift in the composition of urolith that has been reported over time. Struvite increased from 41.8 percent in 2005 to 54.5 percent in 2018, while calcium oxalate decreased from 50.1 percent to 37.7 percent over the same period (Kopecny et al.,2021). Risk factors include gender, age, breed, housing and exclusively the diet given to the cats (Lekcharoensuk et al.,2000; Dorsch et al., 2014; Remichi et al.,2020).

Hematuria, stranguria, pollakiuria and dysuria are common symptoms in clinically presented with urolithiasis. Physical examination commonly reveals distension of bladder, dehydration and pyrexia (Remichi el al., 2020). Urinalysis provides important diagnostic information regarding urine pH, crystalluria, presence of leukocytes and blood. As obstructive urolithiasis can cause renal insufficiency and disturbance in electrolytes balance so serum biochemistry including calcium, phosphorus, blood urea nitrogen and creatinine is used as indicators (Bartges et al., 2016; Canei et al 2021).

Significant studies are present internationally, but published clinicopathological information from Pakistan is absent. The only available Pakistani report which described 5 Persian male cats but systemic urinalysis and serum biochemistry is absent in this study (Tariq et al., 2014). This lack of regional data hinders the clinical decision making which is evidence based. The present study was designed to characterize the risk factor profile, urinalysis findings and serum biochemical variation in cats presented at veterinary facilities in Islamabad and Lahore, Pakistan. The hypothesis was that affected cats would be predominantly male, persian breed, young, non-neutered, commercially

fed and kept in door, and that considerable proportion would show serum biochemical evidence of compromised renal activity when presented.

2. Materials and Methods

2.1 Study Design and Ethical Approval

A prospective study was carried out on cats presented at Pet Centre of University of Veterinary and Animal Sciences Lahore and private veterinary clinics, Islamabad, Pakistan with a problem of urine retention during August 2021 to January 2022. The study was conducted after the approval from the Ethical Committee for the care of Animals, UVAS, Lahore, (Alexandru-Flaviu and Cornel 2014), vide Notification no.335

2.2 Study Population

Of 2029 cats visiting above mentioned clinics during the study duration, those presenting cats which were suffering from urine retention, blood in urine, voiding small quantity of urine, abdominal distension and anorexia. Twenty-four cats with confirmed urolithiasis were enrolled. Diagnosis was established by history physical examination, urinalysis and imaging.

2.3 Signalment, History and Physical Examination

Owner interviews provide information of breed, age, gender, neutering status, housing management, and diet category. Physical examination included evaluation of body temperature (digital thermometer), respiratory rate (chest movements for 30 sec and then multiplied by 2), heart rate (auscultation) and dehydration (intrascapular skin tent test). Clinical signs were documented for each animal.

2.4 Radiography

By using Chison Medical Technologies, (China), ultrasonography was carried out in 11 cats, with a curvilinear probe having frequency 3 to 7 MHz. Position of animal was in dorsal or lateral recumbency. On shaved area gel was applied to perform ultrasonography. Abdominal Radiography was carried out in 3 cats to check presence of urolith, its location, size and number.

2.5 Sample Collection

Urine was collected by cystocentesis. Cat was restrained properly to avoid any harm to lab attendant and cat itself. Urinary bladder was located and the area was sterilized with alcohol swab. Sterilized 10cc syringe was inserted into bladder and minimum of 5ml urine was collected from each animal. The urine was collected in a separate urine collecting vacutainer and was labelled. Blood sample was collected from jugular vein following hair clipping and antiseptic preparation.

Blood is collected in gel and clot activator tube and centrifuged at 1,500rpm for 5 minutes to separate the serum. Thereafter, the serum samples were stored at -20^{o}C until analyzed later.

2.6 Urinalysis

Urinalysis was categorized as, physical analysis, chemical analysis and microscopy. In physical analysis, colour and turbidity of urine was observed. Chemical analysis was done by using commercially available dip strips of Uric 10 CF as per manufacture's recommendation. Change in colours of the strip was observed and compared with scale given with dip strips as per manufacturer- specific interval 30 to 120 sec. For microscopic analysis, urine was centrifuged at 1500 rpm for 5 minutes and sediment was taken on slide and observed under optical microscope to see the type of crystal present in urine.

2.7 Serum Biochemistry

Serum creatinine was measured by a kinetic photometric Jaffe method, (DiaSys Diagnostic System, Germany) at 510 nm. Serum urea was measured by a kinetic ultraviolet photometric method, (Biosystem, India) at 340nm. Serum phosphorus and calcium was measured by a photometric method, (Human Gesellschaft fur Biochemica and Diagnostica GmbH, India) at 340 nm and 570 nm, respectively.

2.8 Statistical Analysis

Collected data was analyzed by using the SPSS version 20 (SPSS, Inc., Armonk, NY, USA). The normality of the data was determined using the Kolmogorov–Smirnov test. Quantitative variables were presented as Means±SEM, while median and range were used to express the data that were not normally distributed. Qualitative data such as baseline characteristics excluding temperature, heart rate and respiration rate and hydration status) were presented as frequency and percentages. Categorical variables were compared using Pearson's Chi-square test. A probability value of less than 0.05 was considered significant.

3. Results

3.1 Study Population

Out of 2029 cats screened during study period, A total of 24 cats (1.18%) met the criteria of urolithiasis. Six cats were presented at UVAS Pet Centre Lahore and 18 cats at various veterinary clinics of Islamabad.

3.2 Breed, Age, Sex, Neutering, Housing and Diet

There was significant difference ($p \leq 0.001$) regarding the occurrence of urolithiasis in various breeds of cats. Also, significant difference ($p < 0.001$) regarding the frequency of occurrence of urolithiasis was noted when data were assorted at various ages. The disease was more prevalent ($p < 0.001$) in male cats compared to female cats. Out of 24 cats, 6 cats (25%) were neutered, while, rest of the18 cats were non-neutered ($p < 0.001$). As found from the record, majority ($p < 0.05$) of animals were kept indoor compared to those that spend most of the time as outdoor. Data shown significant difference ($p \leq 0.001$) based on the type of food offered to cats. These demographic and husbandry characteristics are summarized in table 1.

Table 1. Demographic and husbandry characteristics of 24 cats

Variable	Category	Number (%)	p-value
Breed	Persian	11 (45.83%)	≤0.001
	Short head domestic	6 (25.00%)	
	Arabian Cross	2 (8.34%)	
	Himalayan	2 (8.34%)	
	Persian cross	1 (4.16%)	
	Stray	1 (4.16%)	
Age (years)	<1	1 (4.16)	0.001
	1 to 3	16 (66.67)	
	4 to 6	6 (25.00)	
	>6	1 (4.16)	
Sex	Male	22 (91.67)	<0.001
	Female	2 (8.34)	
Neutering	Non-neutered	18 (75.00)	<0.001
	Neutered	6 (25.00)	
Housing	Indoor	19 (73.00)	<0.05
	Outdoor	5 (27.00)	
Diet	Homemade	3 (12.50)	≤0.001
	Commercial	18 (75.00)	

	Homemade and commercial	3 (12.50)	

3.3 Physical Examination and Clinical Signs

All 24 cats were dehydrated when presented to clinics as shown in table 2. Dysuria along with stranguria was most frequent clinical sign (n=20, 83.34%), followed by distended bladder (n=18, 75.00%), hematuria (n=14, 58.34%), pyrexia (n=18, 75.00%), tachypnea (n=4, 16.67%) and tachycardia (n=4, 16.67%).

Table 2. Physical examination of cats

Parameters	Median (Range)	Means±SEM
Temperature (°F)[1]	103.4 (101-104.6)	103.17±0.19
Heart rate (beats/min)[2]	132 (124-146)	133.83±1.24
Respiration (per min)[3]	34 (30-42)	35±0.74
Hydration status (%)[4]	5 (5-7)	5.25±0.12

3.4 Radiography

Ultrasonography is done in 21 cats to observe all paranchyma of kidneys and minor details. It confirms urinary crystals in 18 cats and cystitis in 3 cats.



Figure 1: Ultrasonographic image of cat (A) and (B) Urinary crystals are present (C) Cystitis

[1] Normal Temperature = 100.5-102.5°F
[2] Normal heart rate = 120-140 beats/minute
[3] Normal respiration rate = 16-40 per minute
[4] Healthy cats are hydrated having no dehydration

Radiographic examination in 3 cats confirm radio-opaque calculi in all 3 cats. There is retention of urine in these cats that might be due to obstruction of urethral plugs.

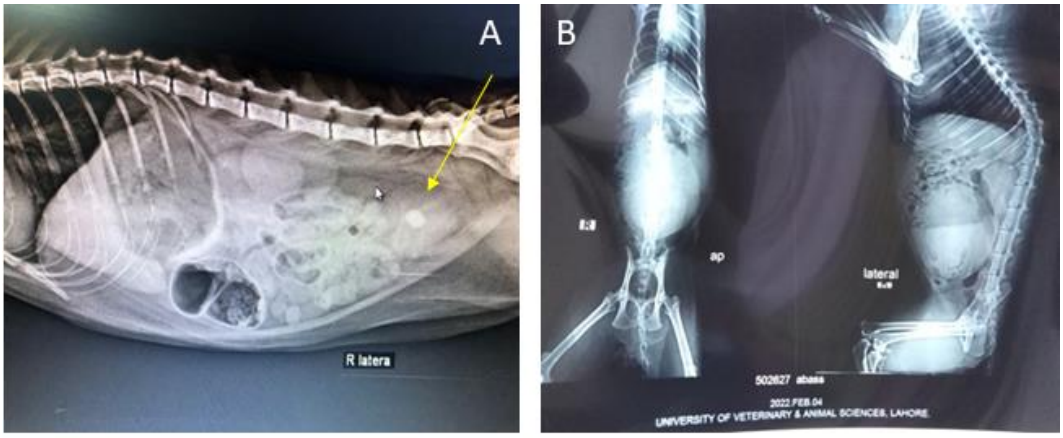


Figure 2: Radiographs (A) Showing bladder stone. (B) Illustrating urinary retention.

3.5 Urinalysis

Urine analysis showed a significant difference of ($p<0.05$) based on the color of urine of cats. Then turbidity of urine was analyzed physically ($p<0.149$). Among the observed cases, pH of urine was noted ($p\leq0.05$). Presence of blood in urine of cats showed significant results ($p<0.05$). Dip strip test showed no significant differences ($p > 0.05$) regarding the presence of leukocytes in urine. Urine of 24 cats was having normal level of glucose, bilirubin, ketone, and nitrate.

Microscopic examination showed that crystals were commonly observed in 21 cats (87.5%) with a significant value of ($p\leq0.001$). Under microscope, single type of crystal or more than one type of crystal was observed. In 3 cats, no crystal was observed. Results showed significant value ($p<0.05$). Regarding nature of crystal, struvite crystals were mostly observed later calcium oxalate and amorphous phosphate ($p>0.05$). Table 3 summaries the urinalysis of all 24 cats.

Table 3. Urinalysis Finding in 24 cats with urolithiasis.

Parameter	Category	Number (%)	p-value
Urine colour	Red	14 (58.00)	0.003
	Yellow	7 (29.00)	
	Pale Yellow	3 (12.00)	
Turbidity	Turbid	14 (58.00)	0.149

	Light turbid	9 (37.00)	
Urine pH	Alkaline	16 (64.00)	0.021
	Acidic	8 (29.00)	
Blood (dipstick)	Negative	4(16.67)	0.031
	Traces	1 (4.16)	
	++	5 (20.83)	
	+++	10 (41.67)	
	++++	4 (16.67)	
Leukocytes	Negative	3 (12.50)	0.306
	Traces	2 (8.34)	
	+	5 (20.83	
	++	5 (20.83)	
	+++	7 (29.16)	
	++++	2 (8.34)	
Crystal presence	Present	21 (87.50)	≤0.001
	Absent	3 (12.50)	
Crystal type	Mono crystal	12 (50.00)	0.019
	Multiple crystal	9 (37.50)	
	None	3 (12.50)	
Crystal composition	Struvite	6 (25.00)	0.300
	Calcium oxalate	3 (12.50)	
	Amorphous Phosphate	2 (8.34)	
	Calcium oxalate + Amorphous phosphate	5 (20.83)	
	Struvite + amorphous phosphate	1 (4.16)	
	Calcium oxalate + struvite + amorphous	1 (4.16)	

	phosphate		
	Nil	3 (12.50)	

3.6 Serum biochemistry

Serum creatinine and phosphorus was significantly high exceeding the upper reference values. While Blood Urea Nitrogen and serum calcium are almost in the range of reference values. Table 4 presents serum biochemical profile of 24 cats included in study.

Table 4. Serum biochemical profile of 24 cats with urolithiasis

Parameters	**Means±SEM**	**Median (range)**	**Number above upper limit (%)**
Blood Urea Nitrogen (mg/dl)[5]	34.75±1.99	36.45 (19.30-55.53)	0 (0 %)
Creatinine (mg/dl)[6]	3.3±0.39	3.7 (0.8-6.8)	15 (62.5 %)
Calcium (mg/dl)[7]	9.2±0.20	8.9 (8.15-12.71)	1 (4.2%)
Phosphorus (mg/dl)[8]	7.08±0.21	7.39 (5.02-8.9)	14 (58.3%)

3.7 Recommendation

The cats with complete urethral obstruction were recommended urinary catheterization after sedation with ketamine and diazepam. Intravenous fluid therapy was also recommended for dehydrated cats to correct dehydration. The catheter was recommended to maintain for 5 days along with antibiotic and analgesic therapy. Cystotomy was recommended in three cats with radiographically confirmed calculi, however no owner accepted surgical intervention. These cats were recommended prescription diet and analgesia and antibiotic for treating pain and bacterial infection, respectively.

Limitation of this study was diagnosing urolithiasis in cats no treatment was done during study.

4. Discussion

This study provides the first systemic clinicopathological characterization of feline urolithiasis in Pakistan. Twenty-four confirmed cases were prospectively enrolled and characterized by risk

[5] Normal value of Blood Urea Nitrogen = 32-64 mg/dl
[6] Normal value of Creatinine = 0.8-2.2 mg/dl
[7] Normal value of Calcium = 8-11 mg/dl
[8] Normal value of phosphorus = 3-6 mg/dl

factor profile, urinalysis and serum biochemistry. The principal findings are aligned with internal literature in several important aspect while also revealing regional clinical features.

4.1 Demographic and Risk Factor Profile

Male sex predominance (91.67%) was the most pronounced demographic finding. The male feline urethra is anatomically long and narrow, predisposing male to luminal obstruction by crystals, mucus plugs and cellular debris (Dorsch et al., 2014; Remichi et al., 2020; Segev et al., 2011). This anatomical vulnerability consistently produces male predominance across diverse geographic clinical populations. The finding emphasizes that male cats must be considered a primary clinical risk indicator in Pakistani veterinary practice.

Persian cats comprised 45.83% of cohort, consistent with the breed predisposition documented in large epidemiological studies in Europe and North America (Kirk et al., 1995; Thumchai et al., 1996; Lekcharoensuk et al., 2000). The high proportion of Persian cats in this cohort study also indicates the acceptance of this breed among urban cat owners in Pakistan.

The predominanace of cats aged 1 to 3 years (66.67%) is consistent with the known predilection of struvite urolithiasis for younger cats (Bartges et al., 2016; Kopecny et al., 2021). Struvite urolithiasis usually occurs in cats under 7 years of age, whereas calcium oxalate urolithiasis increases in prevalence with advancing age. It is observed that young age profile is consistent with the struvite dominant crystal composition.

A notable regional finding was the predominance of non-neutered cats (75%) among affected individuals. International datasets from Europe and North America reported higher rates of urinary calculi in neutered male cats, having calcium oxalate urolith in particular (Thumchai et al., 1996; Burggraaf et al., 2021). The non-neutered predominance in this series most probably reflects the considerably lower rate of elective neutering of companion animal in Pakistan relative to western veterinary practice, rather than a true biological association between intact status and urolithiasis. Owner should be given education regarding advantage of neutering to reduce the burden of this disease in Pakistani cats.

Indoor housing (73%) and exclusive commercial dry diet feeding (75%) were both significantly associated with care status. Indoor confinement reduces physical activity, discourages voluntary water intake, and promotes urinary stasis, all of which increase urinary supersaturation and crystal precipitation risk (Lund et al., 2016; Segev et al., 2011). Dry commercial diets produce more concentrated urine compared to wet food, increasing the risk of crystal formation (Segev et al.

2011; Palm and Westropp, 2011; Lulich et al., 2004). These findings underscore the importance of dietary modification and environmental enrichment for affected and at-risk cats in Pakistan.

4.2 Clinical signs

The clinical signs of dysuria and stranguria (83.34%), hematuria (58.34%), bladder distension (75%), and dehydration (100%) are consistent with international literature of feline lower urinary tract urolithiasis and urethral obstruction (Lund et al., 2016; Wightman et al., 2016). Pyrexia in 75% of cats indicates a systemic inflammation response, consistent with possible secondary bacterial involvement and urothelial injury. Recognition of these clinical signs should prompt immediate urological evaluation in Pakistani veterinary practice.

4.3 Urinalysis

Alkaline urine in 64 cats ($p=0.021$) is consistent with struvite-dominant crystalluria. Struvite precipitation is favored by neutral to alkaline urine pH, and alkaline nature of urine is associated with commercial diet high in certain mineral profile (Remichi et al., 2020). The minority of cats with acidic urine (29%) corresponded to those with calcium oxalate components in their crystal composition. The urinary pH distribution therefore maps coherently onto the observed crystal composition.

Crystalluria was identified in 87.5% of cases ($p\leq0.001$), confirming that microscopic sediment examination is a high-yield diagnostic procedure in cats with lower urinary tract signs. Struvite was the most common single type (25%), consistent with studies by Kopecny et al. (2021).

A clinically important observation was that 37.5% of cats harbored multiple concurrent crystal types. Mixed crystalluria has been reported in other clinical populations (Nururrozi et al., 2020), but has not previously been characterized as a feature of urolithiasis presentations in Pakistan. The clinical significance of mixed crystalluria is relevant to treatment planning, dissolving protocols and dietary management strategies are crystal-type specific, and mixed presentation may require tailored, combined approach.

4.4 Serum Biochemistry

Concurrent elevation of serum creatinine and phosphorus in the majority of cats was the most clinically significant biochemical finding of this study. Serum creatinine exceeded the upper reference limit in 62.5% cats (mean 3.3±0.39 mg/dL) and serum phosphorus exceeded the upper reference limit in 58.3% (mean 7.08 ±0.21 mg/dL) of cats. These finding indicate a pattern consistent with reduced glomerular filtration rate at time of clinical presentation.

In serum, concurrent presence of increased creatinine and phosphorus level in majority of cats is best interpreted in context of urethral obstruction, which was confirmed in 15 of 24 cats recommended catheterization. Urethral obstruction impairs urine flow, generate retrograde hydrostatic pressure on renal tubules and glomeruli, and reduces glomerular filtration rate. The consequent retention of creatinine and phosphorus in the circulation produces biochemical changes consistent with postrenal azotemia (Canei et al., 2021; Bartges, 2016). The interpretation is supported by chronological association between obstruction and biochemical instability, and is consistent with the finding of Canei et al (2021), who documented normal level of creatinine and electrolyte values following relief of obstruction in 33 similarly affected cats.

BUN remained with in normal limits as a group, which may reflect that BUN is influenced by protein catabolism and hydration status in addition to renal filtration, proceeding greater variability between individuals (Cleroux et al., 2017). The in ability to perform serial biochemical measurement before and after catheterization is a limitation of the present study that prevents definitive distinction between reversible postrenal azotemia and concurrent intrinsic renal disease.

Serum calcium was with in normal limits in 23 of 24 cats. This contrast with international reports in which idiopathic hypercalcemia is identified in approximately 35% of cats with calcium oxalate uroliths (Midkiff et al., 2000). The low prevalence of hypercalcemia in this cohort may reflect the predominance of struvite over calcium oxalate, the relatively young age of affected cats, or differences in dietary mineral composition in Pakistani commercial cat foods.

From a clinical practice perspective, the high prevalence of elevated serum creatinine and phosphorus at presentation supports routine inclusion of serum biochemistry in the initial diagnosis of all cats presenting with urinary retention or urolithiasis in Pakistan. These biochemical markers provide objective evidence of renal compromise and help in deciding the line of treatment.

5. Limitations

The study enrolled 24 cats. This sample is adequate for descriptive characterization but insufficient for subgroup comparisons by crystal type, urine pH, or biochemical category.

The absence of concurrent healthy control prevents calculation of relative risk and precludes case-control inference. The frequencies of risk factors reported here reflects the clinical cases population and cannot be directly compared to a background healthy population.

Serum biochemistry was measured once at initial presentation, not after recommended treatment. This design does not permit distinction between reversible postrenal azotemia and intrinsic chronic

renal disease.

Urolith composition was determined by microscopic examination of urine sediment crystals. Qualitative infrared spectroscopy or X-ray diffraction of surgically retrieved urolith specimens would provide more definitive results about mineral characterization of urolith. Crystal in sediment does not consistently predict urolith composition.

Urine culture was not performed. The contribution of urease- producing bacteria to struvite formation therefore cannot be assessed.

6. Conclusion

Feline urolithiasis in Pakistan predominantly affects young, non-neutered, male Persian cats maintained indoor on commercial diets. Struvite is the most common single crystal type, frequently occurring alongside calcium oxalate and amorphous phosphate in a mixed-crystal pattern. Concurrent elevation of serum creatinine and phosphorus in majority of cats at initial presentation indicates renal compromise of probable postrenal origin. Serum biochemistry should be included in the routine diagnostic workup of all cats presenting with urolithiasis in Pakistan. Veterinary practitioners should counsel owner of young, non-neutered, male, indoor Persian cats regarding urological risk, the benefits of dietary modification and adequate hydration, and the clinical signs warranting urgent veterinary evaluation. Future controlled studies with larger sample size, qualitative mineral analysis, and biochemical measurements are necessary to advance the regional evidence base.

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