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Causes of lower urinary tract disease in Czech cat population

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Abstract

This study was done to investigate epidemiological data and to report causes of lower urinary tract disease in a population of cats presented at the Small Animal Clinic of the University of Veterinary and Pharmaceutical Sciences Brno. Cats presented with lower urinary tract disease signs that had undergone a thorough physical examination and urinalysis (dipstick, urine specific gravity, urine sediment and dipslide urine culture) were included in the study. Urine samples were collected only by cystocentesis or sterile catheterization. Bloodwork, abdominal ultrasound, and abdominal radiographs were performed in 118 (66%), 170 (96%) and 9 (5%) patients, respectively. Cats that were treated with antibiotics or glucocorticoids during an episode of feline lower urinary tract disease (FLUTD) or during the foregoing month and which had undergone perineal urethrostomy or catheterization in private practice, were excluded. The study population consisted of 177 cats. Forty-one (23%) cats were diagnosed with a urethral plug, 26 cats (14%) with a urinary tract infection (UTI), 9 cats (5%) with urolithiasis and 101 cats (57%) with feline idiopathic cystitis (FIC). The cats diagnosed with UTI were significantly older than the cats with FIC, urethral plugs and urolithiasis. Urinary tract infection was diagnosed significantly more often in patients older than 10 years, and in female cats. The diagnosis of urethral plug was made significantly more often in males. Feline idiopathic cystitis and urethral plugs are the most common causes of FLUTD, and the causes are significantly age and sex-related.

FLUTD, UTI, LUTS, urethral plug, urolithiasis, feline

The term "Feline Lower Urinary Tract Disease" (FLUTD) summarizes a spectrum of clinical signs related to diseases of the urinary bladder and/or urethra. By aetiology, FLUTD covers multiple disorders such as urolithiasis, urinary tract infections (UTI), neoplasia, congenital or acquired morphological abnormalities, and feline idiopathic cystitis (FIC). Cats with FLUTD are often presented for stranguria, haematuria, periuria, pollakiuria, overgrooming of the genital area and inner thighs, and behavioral changes (i.e. aggression) (Gunn-Moore 2003). These lower urinary tract signs (LUTS) or their combinations are not specific for any particular disease as lower urinary tract reacts to all kinds of irritation in the same manner (Osborne et al. 1996).

Feline idiopathic cystitis is a diagnosis of exclusion (Forrester and Towell 2015). A diagnostic work-up including urinalysis (dipstick, urine sediment examination and urine culture), survey radiographs for identification of radiodense urethrolits/cystoliths and/or ultrasonographic examination for the identification of radiolucent uroliths or neoplastic changes should be performed to rule out other specific causes (Kruger et al. 2009). Many authors agree that FIC is the most common cause of LUTS (Kruger et al. 1991; Lekcharoensuk et al. 2001).

Significant differences regarding the prevalence of UTI in cats presenting for FLUTD were found. European studies (Netherlands, Switzerland, Norway, Germany and Poland) revealed a higher occurrence of FLUTD cases due to bacterial infection, ranging from 7.8%

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to 22% (Kraijer et al. 2003; Gerber et al. 2005; Eggertsdottir et al. 2007; Dorsch et al. 2014; Lew-Kojrys et al. 2017) compared to studies from USA which had a prevalence up to 3% in cats less than 10 years of age (Kruger et al. 1991; Lekcharoensuk et al. 2001). Older female cats are generally at increased risk for the development of urinary tract infection (George 1996; Litster et al. 2009). The aging process and/or concurrent diseases, which are commonly seen in geriatricpatients, could contribute to reduction of natural urinary tract defense mechanisms against infection in older cats (George 1996). The occurrence of UTI is also increasing in cats with concurrent disorders such as chronic kidney disease, diabetes mellitus, or hyperthyroidism (Bailiff et al. 2006; Mayer-Roenne et al. 2007), after repeated catheterizations and perineal urethrostomy (Lekcharoensuk et al. 2001). Mayer-Roenne et al. (2007) found an association between decreasing urine specific gravity (USG) and increasing frequency of UTI in cats with diabetes mellitus. However, another study failed to prove this association (Bailiff et al. 2008).

Urethral plugs are believed to be the most common cause of urethral obstruction. In one study, urethral plugs were found to be the cause of obstruction in 55% of patients, with urolithiasis in 12%, and the cause remaining unknown in 30% of cats (Kruger et al. 1991).

The aim of this retrospective study was to investigate epidemiological data and to report causes of lower urinary tract disease in a population of cats presented at the Small Animal Clinic, University of Veterinary and Pharmaceutical Sciences Brno (UVPS).

Materials and Methods

Medical records of cats which had been admitted to the Small Animal Clinic at UVPS from January 2013 to February 2019 with LUTS (pollakiuria, stranguria, haematuria, periuria, abnormal grooming of the genital area, vocalization on urination, straining to urinate) and diagnosed with FLUTD (obstructive or non-obstructive form) were reviewed and included in the study. Data retrieved from medical records included: breed, age, sex, neutering status, season of presentation (winter [December, January, February] spring [March, April, May] summer [June, July, August] autumn [September, October, November]), presence of urethral obstruction, urinalysis results, and final diagnosis. Cases were identified by searching medical records for "FLUTD", "FIC", "dysuria", "haematuria", "periuria" and "urethral obstruction". Cats that presented with their first episode were included along with cats with previous episodes of FLUTD. Animals that had been treated with antibiotics or glucocorticoids during the episode of FLUTD or during the foregoing month and that had undergone perineal urethrostomy or catheterization in private practice, were excluded. A thorough physical examination and dipslide urine culture were performed in all of the included cats. Bloodwork, abdominal ultrasound, and abdominal radiographs were performed in 118 (66%), 170 (96%) and 9 (5%) of the patients, respectively.

The patients were divided into four groups (FIC, UTI, urethral plug, urolithiasis) based on defined diagnostic criteria. A diagnosis of UTI was made when urine culture was positive with significant bacterial growth ($\geq 10^3$ colony forming units per ml), and no concurrent uroliths were identified. A urolithiasis was diagnosed via abdominal ultrasound or radiographs. Obstructive FLUTD was considered in cats with overdistended, rigid, and painful urinary bladder that was unable to express by gentle palpation. In cats which had obstructive FLUTD caused by urethral plugs detected on radiographs or during catheterization, uroliths or significant bacterial growth had to be eliminated. If no urolith was identified on abdominal ultrasound/radiographs, no urethral plug was observed and urine culture returned negative, the diagnosis of FIC was made.

Urinalysis

Only cats with urine samples collected by cystocentesis or sterile catheterization were included. Urine specific gravity measurement by refractometer (A. KRÜSS Optronic, GmbH, Hamburg, Germany), urine dipstick analysis (HeptaPhan, Erba Lachema, s.r.o., Brno, Czech Republic), microscopical examination of native urine sediment, and dipslide urine culture were performed in all cats. Dipslide urine bacteriology was performed on cysteine-, lactose-, and electrolyte-deficient and MacConkey medium (Uricult, Orion Diagnostica, Espoo, Finland) according to the manufacturer's instructions. Microbiological culture with sensitivity testing was performed at the Department of Infectious Diseases and Microbiology, UVPS. The samples were plated onto blood agar and MacConkey agar (Oxoid, Hampshire, United Kingdom) and incubated at 37 °C for 24 h. Isolates were identified using MALDI-TOF Mass Spectrometry (Bruker Daltonic, Germany).

A standard volume of urine (4 ml) was used for urine sediment examination and the urine sediment was examined within 20 min after collection. After centrifugation of urine at 350 *g* for 5 min, the supernatant was removed and the sediment was resuspended in 0.4 ml of supernatant. Haematuria was diagnosed if more than 10 erythrocytes were counted per × 400 field. Pyuria was diagnosed when more than 5 white blood cells (WBC) were recorded per × 400 field in sediment sample. The amount of crystals was rated as one, two, or three crosses.

Statistical analysis

For all statistical tests and box plot investigation of age and urine specific gravity among groups, a commercial software (Prism, version 7, GraphPad, La Jolla, CA, USA) was used. Descriptive statistics were generated to report continuous data (age, USG; median, minimum, maximum, mean and standard deviation). Based on an assessment of normality (Shapiro-Wilk test) and homoscedasticity (Levene's test), Kruskal-Wallis test followed by Dunn's post hoc test were performed to compare continuous variables between groups. Fisher's exact test was used for the comparison of categorical parameters between groups and odds ratios and 95% confidence intervals were calculated. Significance was set at $P < 0.05$.

Results

Search of the small animal clinic's records revealed 185 patients with clinical signs consistent with LUTS. Previous catheterization in private practice was performed in 3 cases, 3 cats had undergone perineal urethrostomy, one cat had been treated with glucocorticoids because of atopic dermatitis, and one cat had been treated with antibiotics without a previously performed urine culture. This resulted in a study population of 177 cats.

One hundred and sixty-eight (95%) of all patients were first opinion cases and eight patients (5%) were referred from private practices. The studied population consisted of 133 domestic shorthair cats (75%), 23 (13%) British shorthair cats, 5 (3%) Ragdolls, 4 (2%) Persian and 4 (2%) Siberian cats and 2 (1%) Russian cats. The other breeds were Ocicat, Norwegian forest cat, Abyssinian cat, Main coon cat, Chartreux cat and Neva masquerade cat each with one representative. Data regarding age and sex are presented in Table 1.

Table 1. Age, sex and urine specific gravity findings of all cats with FLUTD and within the four diagnosis groups (number of cats, %).

	All cats (n = 177)	FIC (n = 101)	Urethral plug (n = 41)	UTI (n = 26)	Urolithiasis (n = 9)	*P*
Age (years)						
Mean ± SD	5.90 ± 4.45	5.40 ± 3.93	5.03 ± 3.46	10.10 ± 5.76	3.33 ± 1.63	0.0005
Median, range	5, 0.4–20	5, 1–17	5, 0.4–16	10.5, 0.5–20	3, 1–6	
Sex	104 (59%) mc, 48 (27%) fs, 20 (11%) mi, 5 (3%) fi	61 (60%) mc, 27 (27%) fs, 10 (10%) mi, 3 (3%) fi	34 (83%) mc, 6 (15%) mi, 1 (2%) fi	5 (19%) mc, 18 (69%) fs, 2 (8%) mi, 1 (4%) fi	4 (44%) mc, 3 (33%) fs, 2 (22%) mi,	
USG						
Mean ± SD	1042.83 ± 16.56	1048.61 ± 15.62	1037.66 ± 11.49	1027.50 ± 14.56	1050 ± 13.26	< 0.0001
Median, range	1045, 1008–1080	1050, 1008–1080	1039, 1008–1055	1021.5, 1011–1075	1046, 1037–1080	
Proportion of DSH	75%	74%	78%	76%	66%	

FLUTD – feline lower urinary tract disease, FIC – feline idiopathic cystitis, UTI – urinary tract infections, mc - male castrated; fs - female spayed; mi - male intact; fi - female intact, USG – urine specific gravity, DSH – domestic shorthair cats

Forty-one (23%) cats were diagnosed with a urethral plug, 26 (14%) with UTI, 9 (5%) patients with urolithiasis and 101 cats (57%) with FIC. In 156 (88%) cases, urine samples were collected via cystocentesis, and 21 (12%) via sterile catheterization.

Cats diagnosed with UTI were significantly older than cats with feline idiopathic cystitis ($P = 0.0015$), urethral plugs ($P = 0.0038$) and urolithiasis ($P = 0.0059$) (Fig. 1). Urinary tract infection was diagnosed significantly more often in patients older than 10 years ($P < 0.0001$), FIC was less frequent in cats older than 10 years, but the difference was not significant ($P = 0.1641$) (Table 2). Urinary tract infection was more frequently

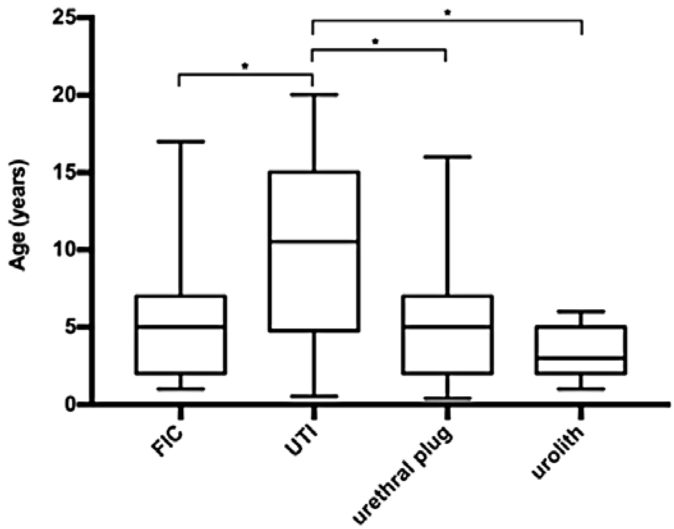

Fig. 1. Data regarding age within groups based on the diagnosis. Significant differences between groups are marked by * ($P = 0.0005$).
FIC – feline idiopathic cystitis, UTI – urinary tract infections

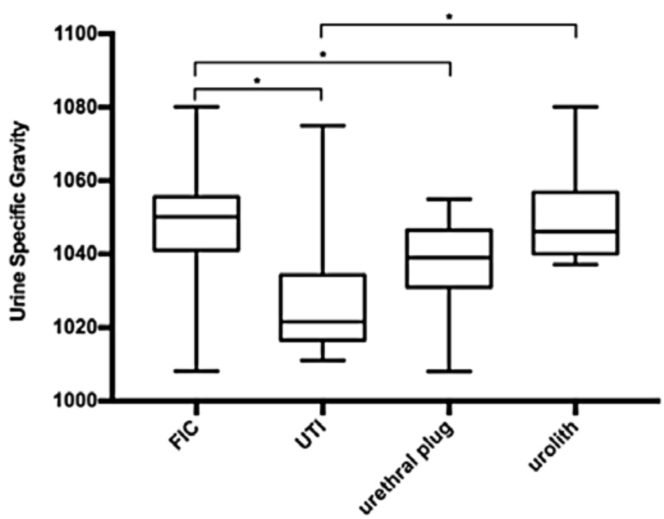

Fig. 2. Urine specific gravity within groups based on the diagnosis. Significant differences between groups are marked by * ($P < 0.0001$)
FIC – feline idiopathic cystitis, UTI – urinary tract infections

diagnosed in female cats ($P < 0.0001$) and the diagnosis of urethral plug was made significantly more often in males ($P < 0.0001$) (Table 3). Relationships between the castration status and most frequent diagnoses are presented in Table 4.

Table 2. Incidence of the four most common causes of FLUTD in cats below 10 years of age and cats aged 10 years or older

Diagnosis	Cats < 10 years (n = 146)	Cats ≥ 10 years (n = 31)	*P*	Odds ratio
FIC	87	14	0.1641	0.558
Urethral plug	38	3	0.0606	0.304
UTI	12	14	< 0.0001	9.196
Urolithiasis	9	0		

FLUTD – feline lower urinary tract disease, FIC – feline idiopathic cystitis, UTI – urinary tract infections

Table 3. Incidence of the four most common causes of FLUTD in male and female cats.

Diagnosis	Male	Female	*P*	Odds ratio
FIC	71	30	> 0.9999	1.027
Urethral plug	40	1	< 0.0001	24.76
UTI	7	19	< 0.0001	0.107
Urolithiasis	6	3	> 0.9999	0.848

FLUTD – feline lower urinary tract disease, FIC – feline idiopathic cystitis, UTI – urinary tract infections

Table 4. Incidence of the four most common causes of FLUTD in castrated and intact cats.

Diagnosis	Spayed/castrated	Sexually intact	*P*	Odds ratio
FIC	88	13	0.6645	1.269
Urethral plug	34	7	0.6093	0.741
UTI	23	3	> 0.9999	1.307
Urolithiasis	7	2	0.6166	0.555

FLUTD – feline lower urinary tract disease, FIC – feline idiopathic cystitis, UTI – urinary tract infections

Table 5. Incidence of pyuria within the diagnosis groups of cats.

Diagnosis	WBC < 5/hpf	WBC > 5/hpf	*P*	Odds ratio
FIC	92	5	0.0055	0.221
Urethral plug	35	2	0.2519	0.383
UTI	13	12	< 0.0001	17.93
Urolithiasis	9	0		

FIC – feline idiopathic cystitis, UTI – urinary tract infections, WBC – white blood cells, hpf – high power field

The urine specific gravity was significantly lower in cats diagnosed with UTI compared to cats from the FIC group ($P < 0.0001$), and cats with urolithiasis ($P = 0.0083$). Cats from the UTI group had lower USG than cats with urethral plugs, but the difference was not significant ($P = 0.1912$). Data regarding urine specific gravity in different groups are noted in Table 1 and Fig. 2. Cats diagnosed with an infection of *Staphylococcus felis* had a significantly higher urine specific gravity ($P = 0.0137$) than cats having another isolate identified. Pyuria occurred significantly more often in the UTI group ($P < 0.0001$) than in the other studied groups (Table 5). Struvite crystals were identified significantly more often in cats diagnosed with a urethral plug ($P = 0.0155$) (Table 6). Crystals were identified in 15 of 41 cats with the urethral plug, struviteswere identified in all cases,and in two of these, struvites were found together with calcium oxalate crystaluria.

Table 6. Incidence of crystalluria within the diagnosis groups of cats.

Diagnosis	Crystals	No crystals	*P*	Odds Ratio
FIC	20	81	0.5815	0.796
Urethral plug	15	26	0.0155	2.834
UTI	1	25	0.0181	0.123
Urolithiasis	2	7	> 0.999	1.048

FIC – feline idiopathic cystitis, UTI – urinary tract infections

Of the 26 patients with positive displide urine culture, aerobic bacteriology was performed in 18 patients and infections with single isolate were detected. The identified isolates having significant bacterial growth were *Escherichia coli* from 9 of the cases, *Staphylococcus felis* from 4 cases, *Staphylococcus intermedius* from one patient, *Klebsiella* spp.from one patient, *Enterococcus* spp. from one patient, *Bacillus* spp. from one patient and *Achromobacter* spp. from one patient. Microbial culture was not performed in 8 patients due to owners' disapproval. Urine culture was positive in 24/156 samples (15.4%) from cystocentesis and in 2/21 samples (9.5%) collected by sterile catheterization.

Discussion

In the present study, 75% of presented cats were domestic shorthair cats, which is in accordance with the population of our patients at UVPS. The majority (70%) of patients in our study were male cats, as in previous studies (Gerber et al. 2005; Saevik et al. 2011; Dorsch et al. 2014). One possible explanation is the predisposition of male cats to urinary tract obstruction because of the narrow penile part of the urethra. The urgent nature of urethral obstruction could be the reason why owners contact veterinarian immediately unlike in non-obstructive cases with possible higher rates of spontaneous recovery (Hostutler et al. 2005). Male cats were presented dominantly in all diagnostic groups with the exception of the UTI group, which agrees with the hypothesis that female cats are more prone to UTI because of their shorter urethra (Litster et al. 2009).

Some previous studies indicate that FLUTD occurs more commonly during the winter season (Lekcharoensuk et al. 2001; Eggertsdottir et al. 2007), however, for unknown reason. Cats in our studywere presented more frequently during winter (30%) and summer (30%) seasons than during autumn (21%) and spring (19%).

Feline idiopathic cystitis was the most common diagnosis made in 57% of patients in our study investigating the Czech population of cats with FLUTD. This is in agreement with results of previous studies with an estimated prevalence of FIC at 51 to 63% (Kruger et al. 1991; Lekcharoensuk et al. 2001; Gerber et al. 2005; Saevik et al. 2011; Dorsch et al. 2014).

The second most common diagnosis in our study were urethral plugs (23% of cases). Clinically, it is difficult to differentiate between obstructive uropathy caused by urethral inflammation, swelling and/or sphincter contraction from a urethral plug (Kruger et al. 2009). Therefore, for a safe identification of a urethral plug, contrast radiography and/or cystoscopy is necessary (Chew et al. 1996). However, these procedures were not routinely performed inthe presentstudy, mainly because of the acute nature of urethral obstruction and the need of prompt intervention. This might have led to misdiagnosis of urethral plugs and an underestimation of FIC. The cause of plug formation is still not completely known. Osborne et al. (1992) proposed that crystalluria with concomitant inflammation leads to formation of matrix-crystalline plugs. Interestingly, struvite crystals as the mineral component in urethral plugs still predominate, despite the increase in prevalence of feline calcium oxalate urolithiasis. It is believed that leakage of plasma proteins into urine during the inflammatory process leads to an increase of urinary pH which promotes further precipitation of struvite crystals. Crystalluria has been shown to occur more frequently in cats with FIC than in cats with other forms of FLUTD (Kruger et al. 1991). In our study, only cats from the urethral plug group had struvites identified more frequently on urinalysis than cats with other diagnoses. Higher incidence of crystalluria in cats with plugs confirms that crystalluria is one of the important predisposition factors in obstructive FLUTD.

The most noticeable disagreement was found in the prevalence of UTI in the population of Czech cats. The previously reported incidence rate of UTI in the USA was determined to be below 3% (Kruger et al. 1991; Buffington et al. 1997). European researchers determined higher prevalence of UTI in cats. Incidence rate of 22.2% was described by Kraijer et al. (2003), 8% by Gerber et al. (2005), 11.8% by Saevik et al. (2011) and 18.9% by Dorsch et al. (2014). In our study, 14% of patients had primary UTI, which is in agreement with other European researchers. Studies in the USA were performed at referral institutions and included mainly referred cases; in contrast, most European studies comprised predominantly first-opinion cases with only a minor portion of referred patients, which makes the main difference in the studied population. The mean age of all patients in our study was 5.9 years, which was similar to studies from the USA (5.1 years) (Buffington et al. 1997) and Norway (5.6 years) (Saevik et al. 2011). The incidence of UTI in cats <10 years in our study was 8.2%. This finding supports the clinical experience that infections should be considered as a possible cause of FLUTD not only in older but even in young and middle-aged cats with LUTS.

Collecting the urine sample by cystocentesis is the gold standard for bacteriological testing (Pressler and Bartges 2009). Twenty-one urine samples were collected by sterile catheterization in our study, to prevent possible complications after performed cystocentesis in obstructed patients with overdistended bladder. Cystocentesis was performed in 92.3% (24/26) of cases in cats diagnosed with primary UTI.

The distribution of bacterial species is in accordance with previously published reports, with *Escherichia coli* being the most commonly found microorganism (Wooley and Blue 1976; Litster et al. 2007; Passmore et al. 2008). It was identified in 50% of our patients, and the second most common isolate identified in 22% of cases was *Staphyloccocus felis*. Staphylococcal species are commonly urease producing organisms.Urease alkalizes urine and, especially in combination with higher urine specific gravity, leads to the formation of struvite crystals (Litster et al. 2007). Infection of *Staphyloccocus felis* was associated with higher urine specific gravity in our study, as previously noted by Litster et al. (2007), and resulted in crystalluria in 25% of patients, but did not result in urolithiasis in any of our patients. Two of the isolates identified (*Achromobacter* spp., *Bacillus* spp.) are not common primary urinary tract pathogens. Urinary tract infections caused by *Achromobacter* spp. and *Bacillus* spp. are rarely noted in humans. Both of these isolates are recognized as opportunistic pathogens that can cause systemic or local infections including urinary tract infections in immunocompromised patients and patients with urological or other underlying diseases in humans (Tena et al. 2008; Pérez Barragán et al. 2018; Ehling-Schulz et al. 2019). Both feline patients suffered from a concurrent chronic kidney disease. Their urine samples were collected by cystocentesis, but we cannot rule out with certainty the possibility of contamination during the handling and processing of the urine sample.

The results of our study confirm previous findings of the American and European studies regarding FIC being the most frequent cause of LUTS in feline patients. The prevalence of UTI in our study was higher than in the American patients, but in agreement with the European population of cats. Even though the risk of UTI is higher in females and increases with age, UTI should always be considered as a possible cause and eliminated during the diagnostic work-up even in younger and middle-aged cats presented with LUTS.

Conflict of Interest

The authors disclose no conflict of interest. None of the authors have any financial or personal relationships that could inappropriately influence or bias the content of the paper.

Off-label Antimicrobial Declaration

The authors declare that there was no off-label use of antimicrobials.

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