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Pathogens isolated from clinical cases of lower urinary tract disorders in dogs and their antibiogram

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Abstract
The main objective of this study was to isolate the pathogens from lower urinary disorders of infectious origin and to study the antibiogram pattern of those pathogens among the dogs that were presented to Veterinary College, Bangalore during the period from March 2018 to September 2019. A total of 9780 dogs were presented to the Veterinary hospital during study period, out of these 276 were suspected for having lower urinary tract disorder based on history and clinical symptoms and were taken for detailed study. Among 276 dogs, 226 were diagnosed with lower urinary tract disorders of infectious origin *viz*., bacterial urinary tract infection (BUTI) of lower urinary tract (cystitis and/ urethritis), urolithiasis, transitional cell carcinoma (TCC) of urinary bladder with concurrent infections and prostate diseases. The most common bacterial pathogens isolated from urine sample were *E. coli* followed by *Staphylococcus* spp., *Proteus* spp., *Pseudomonas* spp., and *Streptococci* spp.
Antibacterial sensitivity pattern of *E. coli* isolates showed highest sensitivity for ceftriaxone-tazobactam (89.47%), *Staphylococcus* spp. showed highest sensitivity to enrofloxacin (91.49%). Higher antibacterial sensitivity pattern of *Proteus* spp. was showed towards amoxycillin with clavulanic acid (94.12%), *Pseudomonas* spp. isolates were sensitive to enrofloxacinin (100%) and *Streptococcus* spp. showed 100% sensitivity towards amoxicillin+clavulanic acid and ceftriaxone+tazobactam followed by doxycycline (83.33%), cefixime (66.66%).

Keywords: Lower urinary tract, UTI, Urolithiasis, TCC of bladder

Introduction
Lower urinary tract disorders include various diseases that affect bladder, urethra and prostate (Bartges 2004). Among them lower urinary tract infections (cystitis and or urethritis) and uroliths were most commonly seen with more of struviteliths (Bartges and Kirk 2012).
Frequently observed infections of lower urinary tract in the present study were bacterial UTI (cystitis and/ urthritis), complicated UTI with urolithiasis and transitional cell carcinoma, prostatitis and prostatic abscess. Ascending infection from normal skin and gastrointestinal tract flora which may overcome the normal urinary tract defences that prevent colonization and causes infections in lower urinary tract (Barsanti, 2006) [2].

Materials and Methods
A total of 9780 cases, 276 cases with clinical signs suggestive urinary tract infections were selected taken for the detailed study and 226 were confirmed as lower urinary tract disorders, based on urinalysis, haematobiochemical findings, imaging techniques and cultural studies. Among 226 lower urinary tract disorders, 125 were of infectious cause which included UTI (115), urolithiasis with concurrent UTI (6) and TCC with concurrent UTI (2), prostatic abscess and prostatitis (2 each).
Urine samples from the affected animals were collected aseptically in a sterile container.Samples were inoculated on different growth media and isolates were identified on the basis of Gram's reaction, morphology, and colony characteristics and confirmed by biochemical tests. Different bacteria isolated from urine samples of the infected animals were subjected to *in vitro* drug sensitivity testing, using fourteen antimicrobials by the disc-diffusion method.

Results and Discussion
Among the suspected dogs for lower urinary tract disorders, different bacteria were isolated from dogs with UTI (Uncomplicated and complicated), urolithiasis and TCC with concurrent UTI, prostatitis and prostatic abscess.

Bacterial isolates in UTI

Among 115 dogs with UTI, 100 were single isolates, 15 were mixed culture and no growth was observed in the 13 samples. From the present study, most of UTI cases are monomicrobial (86.96%) and polymicrobial isolates were found in 13.04% dogs. This is in agreement with Chew *et al*. (2011) [4] who worked on cystitis and recorded single organism isolated in 75% of cases, multiple bacteria were isolated in 25% dogs. The present findings are also in concordance with Way *et al.* (2013) [23] who reported that most of the lower UTI infections are monomicrobial (92%) and multiple bacterial isolates in 8% of samples. In the present study, among polymicrobic infections 86.66% isolates were from female dogs and13.33% isolates were from males indicating UTI with multiple bacteria are common in female dogs, which could be due to wider and shorter urethra in female dogs conceivably making it easier for bacteria to ascend into the bladder.

In the present study, among single isolates, 64.61% were gram negative with of *E. coli* (47.61%) as common uropathogen and 35.38% were gram positive isolates with S*taphylococcus* spp. (60.87%) as frequently seen uropathogen among gram positive bacteria. The findings of present study are similar to Barsanti (2006) [2], Johnson *et al*. (2003) and Chew *et al*. (2011) [4] who reported that Gram- negative bacteria cause UTI in 75% of cases.

Among dogs with UTI the distribution of isolates was *E. coli* in 40 (34.78%), *Staphylococcus* spp. in 28 (24.35%), *Proteus* spp. in 14(12.17%), *Pseudomonas* spp. in 12 (10.43%), *Streptococcus* spp. in 6 (5.22%) and *mixed infections in* 15 (13.04%) urine samples. Among mixed infections, ten samples were found positive for combination of *E. coli*+ *Staphylococcus* spp., *E. coli* + *Pseudomonas* spp. in three samples, *Staphylococcus* spp. + *Proteus* spp. in two samples. In the present study, *E. coli*was the major causative agent of urinary tract infection followed by *Staphylococcus* spp. The findings of the present study are in agreement with McGuire *et al.* (2002) [11], Seguin *et al.* (2003) [19], Papini *et al.* (2006) [14], Prescott *et al.* (2002) [17], Westropp (2012), Wong *et al.* (2015) [24] and Srikanth*et al.* (2017) [20] who reported that *E. coli*, *Staphylococci* spp, *Proteus Streptococci* spp, *Enterococus* spp, *Pseudomonas* spp. were the common pathogens associated with urinary tract infections in dogs.

In the present study, *E.coli*was the major pathogen of urinary tract infection followed by *Staphylococcus* spp. which is inconsistent with the findings of Ling *et al*. (2001) [1], Hall *et al.* (2013), Ulrika *et al*. (2014), Wong *et al.* (2015) [24] and Colakoglu *et al.* (2017) [5]. *E. coli* is the most common bacterial uropathogen in humans, dogs and cats. Most of the lower UTIs are presumptively caused by ascending migration of pathogens from the external genitalia and urethra to the bladder. Rectal, perineal and genital bacteria serve as the principal reservoirs for infection. Intrinsic motility of some bacteria like *E. coli* assist with retrograde migration from the distal urogenital tract and Brownian motion is the primary mechanism for ascending infection. Pili of *E. coli* easily adhere to the uroepithelial surface, develops colonization and results in establishment of UTI (Ettinger and Feldman, 2010). In the present study higher incidence (70%) of *E.coli* seen in female dogs which could be due proximity of anus to urethral orifice.*Staphylococcus* spp. constitute a major component of the normal microflora of human beings, dogs and cats, as they are opportunistic pathogens, cause UTI when there is altered host defensive mechanism (Wagenlehner *et al*. 2008 and Penna *et al*. 2010) [22, 16]. In the present study, proportion of *E.coli* (92.9%) was higher in uncomplicated infections when compared with isolates from dogs with complicated UTI, which could be due to larger proportion (83.47%) of uncomplicated UTI in the present study, andsimilar finding was reported by Wong *et al.* (2015) [24].

Bacterial isolates in urolithiasis

Among seventy dogs with urolithiasis, only six dogs (8.57%) with struvitecrystalluria had bacterial growth on cultural studies, which were also considered under complicated UTI, as urolithiasis is one of the main comorbidity in urinary tract infection. Out of six dogs with positive cultures, *Staphylococcus* spp. isolates seen in five dogs (83.33%) and one dog’s (16.66%) urine sample was found positive for *Proteus* spp which is in accordance with the previous study conducted by Houston and Eaglesome (1999) [7]. In the present study concurrent infection with urolithiasis was very less, asurine volume, frequency of urination, therapeutic agents and genetics also influence the formation of urolith (Scott 2013)[18]. The findings of the present study are in contrast to Koehler *et al*. 2008 who stated that 95% of dogs with struviteurolithiasis have infection. In the present study only 8.57% dogs showed infection which is supported by Chew *et al*. 2011[4] who opined that struvite solubility is decreased in animals with persistently alkaline urine even in the absence of UTI.

Bacterial isolates in TCC

Out of eighteen dogs with transitional cell carcinoma, two dogs had bacterial urinary tract infection associated with *E. coli* and *Staphylococcus* spp. TCC may cause a failure of host barriers as a result of abnormal patterns of voiding, decreased mucosal defences caused by changes in the uroepithelium, and by decreased antibacterial properties caused by alterations of urine pH or host defence peptides, thereby predisposing to UTI (Ettinger and Feldman, 2010). In support of our findings, the most common bacteria isolated in urinary tract infections associated with transitional cell carcinoma in dogs as documented by Budreckis *et al.* (2015) were *Staphylococcus* spp. And *E. coli.* followed by *Streptococcus* spp., *Enterococcus* spp., *Pseudomonas* spp., *Pasteurella* spp., *Mycoplasma* spp *Proteus* spp., *Bacillus* spp., *Enteric* spp., *Actinomyces* spp. and *Aerococcus* spp

Bacterial isolates in prostate diseases

In the present study twenty three dogs were diagnosed with prostatic diseases, which includes benign prostatic hyperplasia (19), prostatitis (2) and prostatic abscess (2) which were confirmed by history, clinical symptoms, ultrasonographic findings and cultural studies of urine and prostatic fluid samples. Krawiec (1994) [9] emphasized that prostatic fluid evaluation as a mandatory for definitive diagnosis of prostate disease and secondary complications, if any. In a normal prostate the lavage does not yield growth on culture media (Barsanti *et al.* 1980) [2]. The dogs having UTI along with prostatitis may or may not yield the same species from urine and prostate lavage sample (Ling *et al* 1983).

Among dogs with prostate disorders *E. coli* was isolated from two dogs with prostatic abscess and from one dog with prostatitis. *Staphylococcus* spp. was isolated from a case of prostatitis. Similar findings were reported by Fonseca-Alves *et al.* (2012) [6] who conducted clinical, haemato biochemical, and cultural studies in fifteen dogs with prostatic abscess and reported that the most commonly isolated bacterial pathogen was *E. coli* followed by *Staphylococcus* spp. and *Proteus* spp. Parry (2006) [15] who identified *E. coli* as the most common bacterial organism in dogs with bacterial prostatitis followed by *Staphylococcus aureus, Klebsiella spp., Proteus mirabilis, Mycoplasma canis and Pseudomonas aeruginosa.*

Urine sample from dogs with prostatic infections also yielded similar bacterial growth on culture media but there was no concurrent cystitis observed by clinical examination and other diagnostic techniques.Same bacterial isolates from both urine and prostatic samples from prostatic infections could be due to constant drips retrograde from the prostatic urethra into the urinary bladder in the intact male dog yields bacterial growth from urine samples though there was no cystitis (Johnston *et al.* 2000) [8]. This finding is supported by Krawiec and Heflin (1992) [9] and Basinger and Luther (1993) who opined that prostatic infections in dogs are often ascending of urethral origin and rarely due to bacterial contamination of the bladder, renal or testicular origin.

ABST pattern of bacterial isolates

Overall sensitivity pattern of 142 bacterial isolates from urine samples and few prostatic fluid samples of dogs with lower urinary tract disorders was higher in enrofloxacin followed by ceftriaxone+tazobactam, amoxycillin+clavulanic acid and gentamicin. Least sensitivity was towards cefpodoxime and penicillins (Ampicillin and amoxycilin).

The present study is in agreement with the findings of Nicolle (2005) who reported that the causative organisms associated with UTI in dogs were *E.coli, Staphylococcus* spp., and *Enterococcus* spp. and *in vitro* susceptibility of those isolates for commonly prescribed antimicrobials was amoxicillin (59%), amoxicillin/clavulanic acid (76%), cephalexin (66%), enrofloxacin (74%) and trimethoprim-sulfamethoxazole (86%). Similarly, Weese*et al*. (2011) stated that enrofloxacin had good activity against many common urinary pathogens as it is excreted in the urine. Further Dowling (1996) stated that cephalosporins have excellent activity against UTI pathogens *Staphylococci* spp, *Streptococci* spp, *E. coli, Proteus* spp., and *Klebsiella* spp. in dogs. Bacterial pathogens like *E. coli, Staphylococcus* spp. and *Streptococcus* spp were sensitive to fluoroquinolones and amoxicillin/clavulanic acid which was isolated from the urine sample (Peery 2010 and Westropp *et al*. 2012). Tirunavukkarasu *et al*. (2010) documented that all the ten bacterial isolates (*E.coli*-6, *Staphylococcus* spp, *Pseudomonas* spp., *Klebsiella* spp., and *Streptococcus* spp one each) from urine sample of dogs with cystitis were sensitive for ceftriaxone +tazobatam. The antibiotic sensitivity of *E. coli* and *Streptococcus* from dogs with UTI were highly sensitive to enrofloxacin as reported by Lautzenhiser and Bjorling (2002). Srikanth*et al.* (2017) [20] conducted anibiogram patterns on isolates from cystitis *viz*., *E. coli*, *StaphylococcusI* spp *and Pseudomonas* spp. and reported that enroflaxacin and amoxicillin were highly effective antibiotics. Antibiotic sensitivity pattern of our study is similar to the above discussed findings of different authors. The variation in the sensitivity pattern may be attributed to difference in the selection of antibiotics for primary use and indiscriminate use of antimicrobial drugs, which contribute to the increased resistance of different bacterial strains. Further the isolates showed higher sensitivity to gentamicin which could be due to lesser use of this antibiotic due to nephrotoxic nature of these drugs. This finding is in agreement with the authors Chang *et al*. (2014) and Windahl *et al*. (2015) who also reported gentamicin to be effective on *in vitro* antibiotic testing.

Antibiogram of *E. coli*isolates

The results of antibacterial sensitivity pattern of *E.coli*isolates showed higher sensitivity for ceftriaxone-tazobactam followed by enrofloxacin and amikacin. *E. coli* was found to be most sensitive to ceftriaxone-tazobactam which is in agreement with Tirunavukkarasu*et al*. (2010), Wagenlehner*et al.* (2008) [22] and Chang *et al.* (2015. In contrary to our study, Chang *et al*. (2014), Windahl*et al*. (2014) and Moyaert *et al.* (2017) reported higher sensitivity of *E.coli*towards amoxycillin andampicillin. This variation could due to indiscriminate use of these drugs, which contribute to reduced sensitivity and increased resistance of bacterial strains.

Antibiogram of *Staphylococcus* spp

Staphylococcus spp. isolates showed higher sensitivity to enrofloxacin followed by amoxicillin with clavulanic acid andgentamicin. *Staphylococcus* spp. were most sensitive to enrofloxacin followed by amoxicillin with clavulanicacid and gentamicin. Least sensitivity was seen for synthetic penicillins. The findings of present study are similar to the reports of many researchers Penna *et al*. (2010) [16], Windahl *et al*. (2014) and McMeekin *et al*. (2016) who also found higher sensitivity of *Staphylococcus* spp. for enrofloxacin and amoxycillin with clavulanic acid.

Antibiogram of *Proteus* spp

In the present study, higher antibacterial sensitivity pattern of *Proteus* spp. was showed for amoxycillin with clavulanic acid followed by gentamicin and cefixime. This is in aggriment with Moyaert *et al.* (2017) who observed *Proteus* spp. isolates from dogs with UTI had high antimicrobial susceptibility (90%) to amoxicillin/clavulanic acid, enrofloxacin, and marbofloxacin and slightly lower susceptibility to ampicillin and orbifloxacin.

Antibiogram of *Pseudomonas* spp

In the present study all fifteen *Pseudomonas* spp. isolates were sensitive (100%) for enrofloxacin. Fluoroquinolones are among the few drugs of choice for treatment of bacterial urinary tract infections in dogs, including those due to *Pseudomonas* (Cohn, *et al.* 2003).

Antibiogram of *Streptococcus spp*

Results of antibiotic sensitivity pattern for *Streptococcus* spp. showed 100% sensitivity towards amoxicillin+clavulanic acid and ceftriaxone+tazobactam followed by doxycycline. Similar to present study findings, higher sensitivity (100%) of *Streptococcus* isolates towards amoxicillin/clavulanic acid combination had been reported by Windahl *et al*. (2014). The findings are also similar to the reports of Manisha *et al.* (2018) who documented that *Streptococcus* spp. showed maximum sensitivity (100%) towards ceftriaxone-tazobactam, ceftriaxone, cefoperazone, followed by amoxicillin-clavulanic acid.

Table 1: Distribution of bacterial isolates in LUTD

Isolates	Bacterial UTI	Urolithiasis	TCC	Prostate diseases
E.coli	40 (34.78%)	0	1 (5.56%)	2 (prostatic abscess) 1 (prostatitis)
*Staphylococcus*spp.	28 (24.35%)	5 (7.14%)	1 (5.56%)	1(4.35%) (prostatitis
Proteus spp.	14 (12.17%)	1 (1.43%)	0	0
Pseudomonas spp.	12(10.43%)	0	0	0
Streptococcus spp.	6 (5.22%)	0	0	0
*Mixed infections**	15 (13.04%)	0	0	0

*Sample size = 142: single isolates =112 and mixed isolates= 30

Table 2: Overall antibiotic sensitivity pattern of bacterial isolates from dog urine sample and prostatic fluid sample (*142 isolates)

Antibiotics	Sensitivity (%)	95% CI
Ampicillin	13 (9.15)	8.55-18.34
Amikacin	84 (59.15)	45.32- 67.2
Amoxycillin	12 (8.45)	22.21-59.27
Amoxycillin + clavulanic acid	102 (71.83)	12.41-46.85
Cephalexin	58 (40.85)	12.41-46.85
Cefpodoxime	25 (17.61)	15.55-51.11
Ceftriaxone	46 (32.39)	36.81-74.30
Ceftriaxone + tazobactam	106 (74.65)	52.64-82.12
Cefixime	82 (57.75)	18.82-55.25
Doxycycline	75 (52.82)	19.56-58.32
Enrofloxacin	110 (77.46)	53.15-87.59
Gentamicin	96 (67.61)	29.30-67.00
Tetracycline	36 (25.35)	36.81-74.30
Trimethoprim/sulfamethoxazole	50 (35.21)	25.70-63.19

Table3: *In vitro* antibiotic sensitivity pattern of different bacterial isolates (n=142, including pure and mixed cultures)

Sl. No.	Antibiotics used	*E. coli* (n=57)	*Staphylococcus* spp.(n=47)	*Proteus* spp. (n=17)	*Pseudomonas* spp (n=15)	*Streptococcus* spp.(n=6)
1.	Ampicillin	6 (10.53%)	5 (10.63%)	1 (5.88%)	0 (0%)	1 (16.67%)
2.	Amikacin	41 (71.92%)	29 (61.7%)	3 (17.65%)	11 (73.33%)	0
3.	Amoxicillin	6 (10.53%)	4 (8.51%)	1 (5.88%)	0	1 (16.67%)
4.	Amoxicillin + clavulanic acid	36 (63.16%)	41 (87.23%)	16 (94.12%)	3 (20%)	6 (100%)
5.	Cephalexin	25 (43.86%)	19 (40.43%)	4 (23.53%)	7 (46.67%)	3 (50%)
6.	Cefpodoxime	10 (17.54%)	9 (19.15%)	4 (23.53%)	0	2 (33.33%)
7.	Ceftriaxone	22 (38.6%)	10 (21.28%)	3 (17.65%)	9 (60%)	2 (33.33%)
8.	Ceftriaxone + tazobactam	51 (89.47%)	29 (61.7%)	9 (52.94%)	11 (73.33%)	6 (100%)
9.	Cefixime	30 (52.63%)	25 (53.19%)	12 (70.59%)	11 (73.33%)	4 (66.66%)
10.	Doxycycline	35 (61.40%)	27 (57.45%)	8 (47.06%)	0 (0%)	5 (83.33%)
11.	Enrofloxacin	40 (70.17%)	43 (91.49%)	10 (58.82%)	15 (100%)	2 (33.33%)
12.	Gentamicin	36 (63.16%)	33 (70.21%)	14 (82.35%)	13 (80.66%)	0
13.	Tetracycline	18 (31.58%)	15 (31.91%)	2 (11.76%)	0 (0%)	1 (16.67%)
14.	Trimethoprim+sulfamethoxazole	26 (45.61%)	15 (31.91%)	6 (35.29%)	3 (20%)	0

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