

Comparative hematological and biochemical alterations associated with Gram-negative bacterial infections of lower urinary tract in dogs and cats

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Abstract

The aim of this study was to investigate hematological and biochemical alterations associated with gram-negative bacterial lower urinary tract infections (UTIs) in dogs and cats. For this purpose, 56 dogs and 36 cats were examined between October 2022 and May 2023. Twenty-eight dogs and twenty-two cats with clinical signs of lower UTIs were confirmed using ultrasonography, urinalysis, hematochemical analysis, and molecular identification of recovered pathogen. In dogs, UTIs were significantly associated with pyuria (82%), crystalluria (85.7%), and proteinuria. There was also significant decrease in total protein and globulin levels compared to those in the control. A significant increase in BUN, GGT, and CRP levels was recorded in comparison with healthy dogs. Neutrophils and monocytes showed a significant increase, whereas TLC showed no significant increase. Urinalysis revealed noticeable pyuria (82%), hematuria (57.1%), proteinuria (85.7%), and crystalluria (85.7%). However, the urinary ALP levels were significantly decreased. In cats, UTIs were significantly associated with pyuria (72.7%) and hematuria (81.8%). A significant increase in BUN, creatinine, and GGT levels was recorded in comparison with the controls. TLC significantly increased, with neutrophilia and relative lymphopenia. Urinalysis revealed noticeable pyuria (72.7%), hematuria (81.8%), proteinuria (54.5%), crystalluria (18%), and glucosuria (63.6%). Moreover, urinary ALP was significantly higher in cats with UTIs than in controls. The results of the present study indicate that Gram-negative infections of the urinary tract induce noticeable hematochemical alterations in dogs and cats. Dogs mainly showed systemic inflammation with mild renal effects, whereas cats showed severe renal impairment. The significant alterations in hematological and biochemical parameters emphasize their diagnostic significance in differentiating systemic inflammation from renal dysfunction.

Keywords: cystitis, pets, renal function, urinalysis, urinary tract infections

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Introduction

Bacterial urinary tract infections (UTIs) are among the most prevalent ailments in dogs and cats. They occur when the natural defense mechanisms of the urinary tract and pathogenic microbes are out of balance (Amphaiphan *et al.*, 2021). The infection can be localized to a single site, or it can be located in two or more of the urinary organs (Bartges, 2004). Pollakiuria, stranguria, and hematuria are typical symptoms of UTI. Fever is rare in animals without prostatitis or pyelonephritis (Byron, 2019). Gram-negative bacteria, especially *Escherichia coli*, are consistently reported as the predominant etiological agents of UTIs in small animals, followed by *Klebsiella* spp., *Proteus* spp., and *Pseudomonas* spp. (Dorsch *et al.*, 2019; Thassakorn *et al.*, 2025).

The lower urinary tract (LUT) contains a wide assortment of host defense mechanisms to combat UTIs (Litster *et al.*, 2011). In this context, physical barriers are examples of the first line of defense mechanisms (Bartges, 2004). This mechanism is supported by mucosal defense barriers, which include a glycosaminoglycan layer and vital antimicrobial characteristics, which help prevent bacterial migration and colonization (Blanco and Bartges, 2001). The urinary system of healthy cats, dogs, and humans contains different microorganisms that comprise the urinary microbiome or urobiome (Johnstone, 2020). Many of these organisms can only be identified by metagenomic methods that do not require culture to work (Wolfe and Brubaker, 2019). Even so, bacteria (mostly *E. coli*) have been found in up to 9% of healthy female dogs and 13% of older, non-azotemic cats that showed no signs of urinary tract disease using traditional culture methods (Johnstone, 2020).

Violation of the host's defense mechanisms allows an infectious agent to establish, multiply, and persist in the urinary tract, leading to potentially variable disorders requiring antibacterial therapy (Guardabassi *et al.*, 2004). However, improper selection or use of appropriate therapies can lead to antibiotic resistance and poor outcomes (Rampacci *et al.*, 2018).

The mechanism by which gram-negative bacteria can produce their effects includes both local infection and toxemia during multiplication, with the subsequent release of cytokines. Such an increase in cytokines results in hematological and biochemical changes that reflect both the host immune response and the degree of renal involvement. Hematological alterations, such as leukocytosis, neutrophilia, monocytosis, and anemia, are commonly observed, implying acute and chronic inflammatory processes (Punia *et al.*, 2018). Biochemical disturbances, including elevations in blood urea nitrogen (BUN) and serum creatinine levels, electrolyte imbalances, hypoalbuminemia, and hyperglobulinemia, are particularly evident in cases progressing to pyelonephritis or sepsis. These alterations provide valuable diagnostic and prognostic information, complementing urinalysis and microbiological cultures (Jasim, 2012).

The comparative response of dogs and cats to gram-negative bacterial infection of the urinary tract has not been clearly studied; therefore, the aim of the

current study was to determine the hematobiochemical changes and perform urine analysis in response to Gram-negative bacterial infection of the lower urinary tract in dogs and cats.

Materials and Methods

Animals: A total of 92 animals were included in this study. Of all, 56 dogs (44 mongrels, 12 other breeds) at 6 months to 4 years (average, 2 years were studied). The dogs weighed 10-30 kg (average 15 kg). Dogs included 16 males and 40 females. Thirty-six cats (14 Persian, 16 domestic short-haired, 6 Baladi) at 5 months to 5 years (average, 3 years) were also included. Cats weighed 1.5-6 kg (average, 3.5 kg). They included 26 males and 10 females. Twenty-two cats presented with clinical signs of lower UTIs, dysuria, stranguria, and hematuria were investigated. Cases were confirmed by ultrasonography, urine culture, urinalysis, and hematobiochemical tests according to the guidance provided (Yamanaka *et al.*, 2019). The complete demographic data and the contributing factors associated with UTIs were presented in Table 1. Additionally, 28 healthy dogs and 14 cats were included in the control group. The animals were examined between Oct 2022 and May 2023 and attended Mansoura University Teaching Hospital and private clinics (Dakahlia, Damietta). Owner consent was obtained for the study, which was conducted according to FASS guidelines and approved by the Mansoura University Ethics Committee (Code: MU-Vet.Med.127.03.2022).

Clinical examination: Complete medical history of each patient was obtained (Horwitz and Rodan, 2018). A complete physical examination of the animals was performed according to standard methods to detect abnormalities that help localize UTIs. Special attention was paid to the observation of abnormal urination, variations in daily urine flow, signs of abdominal pain, abnormal constituents of the urine, and evidence of systemic signs. Transabdominal palpation of the kidneys and abnormalities in the urinary bladder and urethra were also recorded (Bartges, 2004).

Ultrasound examination: Ultrasound images were obtained using a CHISON ultrasound system (iVis 60 EXPERT VET, CHISON Medical Imaging Co., Ltd., Wuxi, China) with a curved transducer (5-8 MHz). A standardized protocol was used in all cases. The patient was positioned in lateral or dorsal recumbency. The images were collected via the Linea alba to prevent near-field artifacts caused by the abdominal muscles and were optimized to minimize any artifacts caused by the nearby descending colon. For each patient, sagittal and transverse images of the urinary bladder and kidneys were obtained (Valls Sanchez *et al.*, 2019).

Samples and analysis: Two blood samples were collected from the cephalic and jugular veins. Whole blood was used for hematological examination, while the remaining blood was allowed to clot in plain tubes to obtain serum. The blood sera were separated and stored at -20°C for further biochemical analysis, including measurement of blood urea nitrogen, serum

creatinine, serum total proteins, serum albumin, serum globulin, ALP, GGT, and CRP. The total and differential leukocyte counts were determined according to standard methods (Radakovich *et al.*, 2017). Blood urea nitrogen, serum creatinine, serum total protein, serum albumin, and serum globulin levels were determined using a semiautomated analyzer according to the manufacturer's instructions

and using standard kits supplied by PIOCHEM (Chemical Manufacturing Company, Giza, Egypt). Serum C-reactive protein was also measured by a turbidimetric assay using standard kits (PIOCHEM, Chemical Manufacturing Company, Giza, Egypt) according to the standard protocol (Yogeshpriya *et al.*, 2018).

Table 1 Demographic data and contributing factors regarding UTIs in dogs and cats.

	Dogs	Cats
Age		
< 3 years	8	14
≥ 3 years	48	22
Sex		
Male	16	26
Female	40	10
Breed		
Mongrel	44	Persian (14)
Other breeds	12	Domestic Short Hair (16) Baladi (6)
Housing		
Indoor	8	22
Outdoor	48	14
Body condition		
Normal	8	20
Thin	48	16
Diet		
Dry	36	14
Homemade	20	22
Previous procedures		
Negative	16	32
Positive	40	4
Method of urine sample collection		
Cystocentesis	24	12
Catheterization	32	24
Concurrent diseases		
Negative	40	18
Positive	16	18

Urinalysis: Urine samples were collected from the studied animals by cystocentesis or catheterization, where two milliliters of urine were collected, stored in sterile vials, and processed within 1 hour according to the previously described method (Yamanaka *et al.*, 2019). The collected urine samples were subjected to Urinalysis, bacterial culture, and susceptibility testing were performed on collected urine samples. A complete physical examination of the urine was performed according to a previously described method (Echeverry *et al.*, 2010). Chemical urinalysis was performed using Multistix 10SG dipsticks supplied by PIOCHEM (Chemical Manufacturing Company, Giza, Egypt). Protein, glucose, and pH levels were recorded. Urine Gamma-glutamyl transferase (GGT) and alkaline phosphatase (ALP) levels were measured. All measurements were performed using standard methods, according to a previously described protocol (De Carvalho *et al.*, 2011). Microscopic analysis of uncentrifuged urine was performed manually in a disposable counting chamber to obtain a quantitative count of leukocytes and erythrocytes per milliliter of urine. A semi-quantitative assessment for the presence of casts and crystals in the specimen was performed (Litster *et al.*, 2007).

Urine culture and identification of bacterial isolates: The collected sample was placed directly in a sterile

test tube containing tryptone soy broth (TSB, Oxoid, Oxoid Ltd., UK) as an enrichment medium. The Step-by-Step Procedure of the Calibrated Loop/Surface Streak Method was performed according to a previously described protocol (Karah *et al.*, 2020). Bacterial isolates were identified based on colony type and morphology, Gram staining characteristics, and standard biochemical tests (Christopher and Bruno, 2003).

Molecular identification of bacteria: Genomic bacterial DNA was extracted from the purified bacterial isolates using the QIAGEN™ DNA extraction kit according to the manufacturer's instructions. The reactions were performed using a master mix reagent (Emerald Amp GT PCR; Takara, Code No: RR310A kit), with the following volumes: 12.5 µL (2x premix), 5.5 µL PCR grade water, 1 µL forward and reverse gene specific primers (Table 2), and 5 µL of different template DNA was added individually. Cycling conditions, including temperatures and time conditions of the two primers cPCR. The amplified products were stained with ethidium bromide dye and electrophoresed on an agarose gel (1%) (Molecular Grade, Boline). The gel was photographed with a gel documentation system, and the data were analyzed with computer software. Purification of the PCR products, sequencing reaction for *Klebsiella* and

Pseudomonas spp. following standard techniques (Altschul *et al.*, 1990). Phylogenetic analysis was assessed by comparative analysis of the sequences using the CLUSTAL W multiple sequence alignment program, version 12.1 of the MegAlign module of the Lasergene DNASTar software Pairwise (Madison, Wisconsin, USA).

Statistical analyses: Data were analyzed using the Statistical Software Program (SPSS for Windows, Version 21.0, SPSS Inc., USA). Data of hematological and biochemical analyses were subjected to a

normality distribution test (Shapiro-Wilk test). As the data were not normally distributed, normalization was performed according to standard statistical rules to reduce skewness and stabilize variance (Limpert and Stahel, 2011). The results of the data were presented as mean and standard deviation. Differences between mean values of variables in healthy controls and diseased animals were performed using an unpaired *t*-test. An association between the clinical signs and the occurrence of UTIs was performed using the Crosstabs (cross-tabulations) test. The results were considered significant when the *P*-value was < 0.05.

Table 2 Oligonucleotide primer sequences and target genes for amplified products in the identification of bacterial species.

Target gene	Primer sequence (5'-3')	Length of amplified product (bp)	Reference
<i>Klebsiella</i> spp.: 16S rRNA	AGAGTTTGATCMTGGCTCAG TACGGYTACCTTGTACGACTT	1485	(Lagacé <i>et al.</i> , 2004)
<i>E. coli</i> <i>phoA</i>	CGATTCTGGAAATGGCAAAAG CGTGATCAGCGGTGACTATGAC	720	(Hu <i>et al.</i> , 2011)
<i>Pseudomonas</i> spp.: 16S rRNA	AGAGTTTGATCMTGGCTCAG TACGGYTACCTTGTACGACTT		(Lagacé <i>et al.</i> , 2004)

Results

Clinical and ultrasonic findings: The results of clinical examination revealed that 16 dogs with lower UTIs were showing mild clinical signs without systemic signs. However, 9 dogs were showing moderate signs and 3 with severe signs. There was an association between UTIs and pyuria ($P = 0.001$). Where 23 dogs with UTIs (82%) had noticeable pyuria. There was also an association between lower UTIs and crystalluria ($P = 0.001$), and proteinuria ($P = 0.001$). Thus, 24 (85.7%) dogs with UTIs were showing crystalluria and proteinuria. However, non-significant association was recorded for gross haematuria ($n = 4$; 14.3%), polyuria ($n = 5$; 17.8%), anuria ($n = 3$; 10.7%), and pollakiuria ($n = 12$; 42.8%). Signs of abdominal pain, dysuria ($n = 16$; 57.1%), and stranguria ($n = 12$; 42.8%) were also recorded. Transabdominal palpation revealed gross enlargement of the urinary bladder ($n = 3$, 10.7%). For cats, the clinical signs were categorized as mild ($n=18$), and severe ($n = 4$). There was an association between UTIs and pyuria ($P = 0.001$) and haematuria ($P = 0.001$). Where 16 samples (72.7%) from diseased cats had a much higher of pyuria, with an average of 20 white blood cells per HPF. While 18 samples (81.8%) of the diseased cats had haematuria. Proteinuria and glucosuria occurred in only 12 (54.5%) and 14 (63.6%) samples of sick cats, respectively. Cats also showed polyuria ($n = 2$; 9%), anuria ($n = 8$; 36.3%), pollakiuria ($n = 10$; 45.5%), urinary incontinence ($n = 6$; 27.2%), dysuria ($n=12$; 54.5%), and stranguria ($n = 14$; 63.6%). Abdominal palpation showed gross enlargement of the urinary bladder ($n = 10$; 45.4%). Anorexia, vomiting, lethargy, and kidney failure were recorded in six cats.

Ultrasound examination: On ultrasound examination, increased bladder wall thickness with cloudy content ($n = 20$, 71.4%) was recorded in dogs and cats ($n = 14$; 63.6%) (Fig. 1).

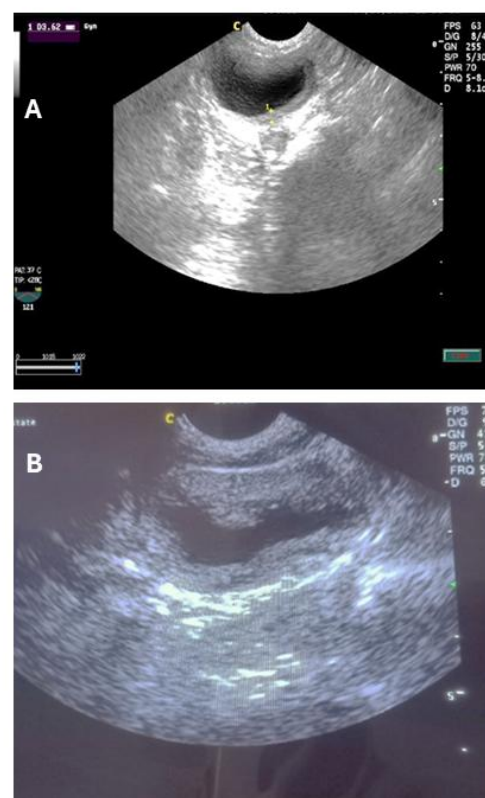


Figure 1 Ultrasonographic findings of UTIs in dog (A) and cat (B) showing diffuse bladder wall thickening exceeding 2 mm.

Bacterial isolates: Of the 92 urine samples from dogs and cats, 74 (80.4%) samples contained bacteria, of which 44 (78.6%) were from dogs, and 30 (83.3%) belonged to cats. Of the 30 samples collected from cats, 66.7% contained only a single bacterium, while 63.6% of the 44 urine samples collected from dogs contained a single bacterium. Conversely, 36.4% of the samples collected from dogs contained a mix of different bacteria, which are 2 different bacteria and more, while 33.3% of the samples collected from cats contained a

mix of bacteria. The frequency of *E. coli*, *Klebsiella* spp., and *Pseudomonas* spp. isolated from UTIs was 57.1%, 60% and 40%, respectively. However, in cats, it was 70%, 66.6%, and 40%, respectively.

Biochemical findings: In dogs with UTIs, there was a significant decrease in serum total protein and globulin levels compared to those in the control group ($P = 0.02$). Where the mean level of total protein was lowered in diseased dogs at 0.93 ± 0.17 mmol/L (Fig. 2). Similarly, the mean globulin level in the affected group was significantly lower at 0.28 ± 0.09 mmol/L ($P = 0.01$). However, in cats, there were no significant differences between diseased and healthy animals regarding these variables. The mean values of BUN, GGT activity, and CRP in healthy dogs were 10.07 ± 1.8 mmol/L, 0.2 ± 0.08 μ mol/L, and 25.69 ± 3.4 nmol/L, respectively. In contrast, dogs with UTIs had significantly ($P = 0.001$) higher values of BUN at 13.1 ± 2.1 mmol/L, GGT activity at 0.6 μ mol/L, and CRP at 62.9 nmol/L than those of healthy controls ($P = 0.002$) as shown in Figures 3–5.

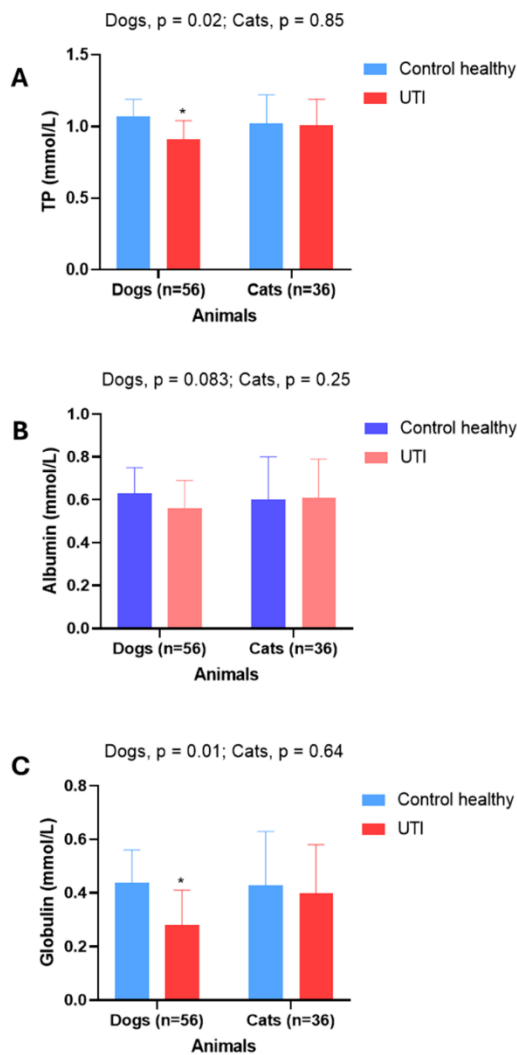


Figure 2 Serum total protein and fractions in dogs and cats suffering from UTIs and in healthy controls. (A) Total protein (TP) levels were significantly decreased in dogs ($P = 0.02$) but not in cats ($P = 0.85$). Globulin levels increased significantly in dogs ($P = 0.01$), while no significant changes were found in cats ($P = 0.64$).

Haematological findings: The mean TLC in healthy dogs was 14.6×10^9 /L. However, dogs with UTIs had a significantly ($P = 0.190$) higher mean TLC (17.6×10^9 /L) compared to controls. Neutrophil, eosinophil, and monocyte counts were also significantly ($P = 0.01$) higher in the affected dogs than in the control group, whereas lymphocyte counts showed non-significant ($P = 0.14$) changes between the two groups (Fig. 6). Also, neutrophil to lymphocyte ratio (NLR) and monocyte to lymphocyte ratio (MLR) showed non-significant increase in diseased dogs in comparison with control (2.71 vs 2.57 and 0.07 vs 0.06 , respectively). In cats with UTIs, there was a significant increase in serum BUN ($P = 0.001$), Cr ($P = 0.001$), and GGT activities ($P = 0.002$) in comparison to those of the control group (Figs. 3–5). The mean values of the remaining biochemical variables were not significantly different between the studied groups. The mean value of TLC in healthy cats was $9.4 \pm 0.95 \times 10^9$ /L. However, cats with UTIs had significantly ($P = 0.002$) higher values of TLC ($15.2 \pm 1.2 \times 10^9$ /L) than those in the control group (Fig. 6). Diseased cats also had a significantly $P = 0.01$ higher neutrophil count (63%) than the control group (60%). In contrast, the mean percentage of lymphocytes ($P = 0.98$) and eosinophils ($P = 0.98$) showed no significant variation between the two groups. NLR and MLR showed non-significant increases in diseased dogs in comparison with the control (1.9 vs 1.7 and 0.075 vs 0.071 , respectively). Moreover, the RBC count showed no significant variation between the groups.

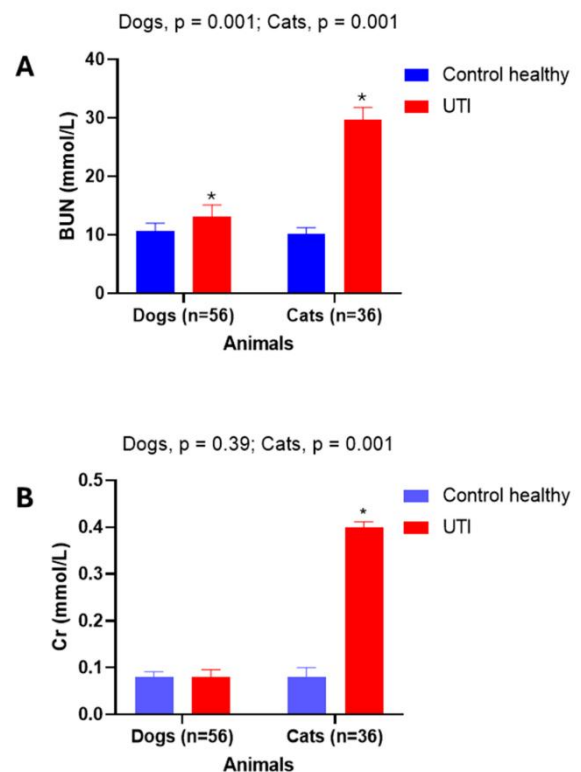


Figure 3 BUN (A) and creatinine (B) in dogs and cats with UTIs. *: denotes significant variation at $P < 0.05$.

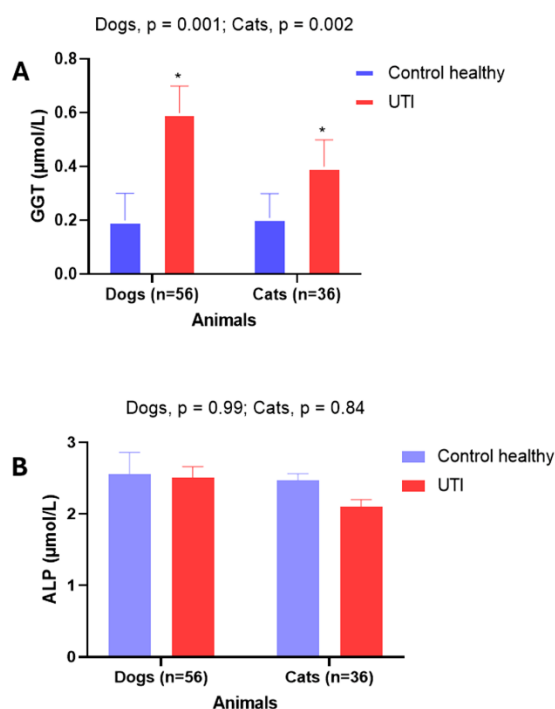


Figure 4 Serum GGT(A) and ALP (B) activities in dogs and cats with UTIs. (A) *: indicates significant variation at $P < 0.05$.

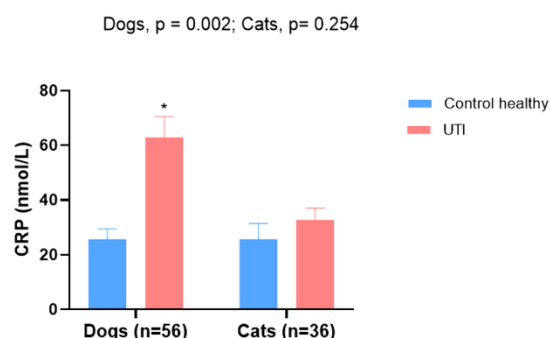


Figure 5 Serum CRP in Dogs and Cats with UTIs. CRP was significantly elevated in dogs ($P = 0.002$), but not in cats ($P = 0.254$).

Urinalysis: Like that recorded in haematological and serum biochemical parameters, urine parameters showed non-significant variations among specific bacterial infections in both dogs and cats. The urine pH was higher in dogs with UTIs than in controls (7.0 vs. 6.5), but the urine specific gravity was slightly lower in diseased dogs than in controls (1.020 ± 0.01 vs 1.025 ± 0.013). The mean GGT activity was significantly increased in dogs with UTIs (2.9 ± 0.31 vs 0.9 ± 0.14 $\mu\text{mol/L}$, $P = 0.001$), while ALP activity was significantly decreased at 1.6 ± 0.16 $\mu\text{mol/L}$ ($P = 0.02$) (Fig. 7). The mean urine specific gravity of the healthy cats was 1.020 ± 0.01 , while the mean value of ALP was 2.1 ± 0.58 $\mu\text{mol/L}$. However, in the group of sick cats, the values of USG and ALP showed significant variations compared to the control group. In this context, the mean value of urine specific gravity was significantly ($P = 0.039$) higher at 1.025 ± 0.016 , whereas

the mean value of ALP was significantly ($P = 0.001$) higher than 7.5 ± 1.0 $\mu\text{mol/L}$ compared to the control group. However, urine GGT did not show significant variation ($P = 0.67$).

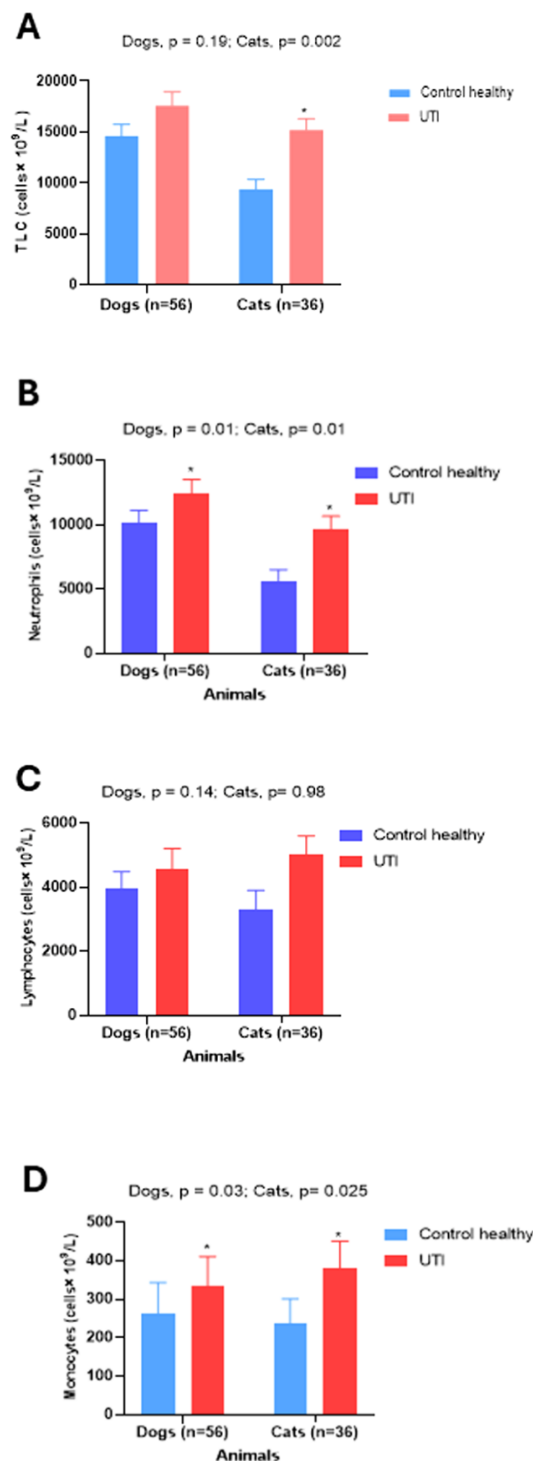


Figure 6 Hematological changes in dogs and cats with UTIs. (A) The total leukocyte count (A); Neutrophil numbers (B); lymphocytes(C) and monocytes (D) Monocytes. *: indicates significant variation at $P < 0.05$.

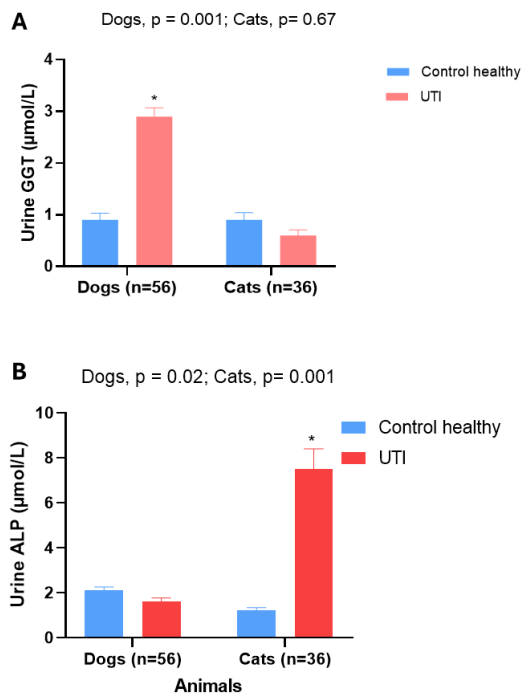


Figure 7 Urinary GGT (A) and ALP (B) activity in dogs and cats with UTIs.

Discussion

There have been discrepancies in research on the nature and response to UTIs in dogs and cats. Therefore, the present study aimed to highlight the comparative hematological and biochemical alterations associated with Gram-negative bacterial infections in dogs and cats.

In the present results, for dogs, dysuria, stranguria, and abdominal pain were common, while gross hematuria and changes in urine volume were less consistently associated with UTIs, reflecting that lower UTIs may present with variable and sometimes subtle signs (Thomas *et al.*, 2023; Taylor *et al.*, 2025). Similar variability is described in cats with feline lower urinary tract disease (FLUTD), where stranguria, pollakiuria, and hematuria dominate, but systemic signs occur mainly with obstruction or more severe disease (Kovářková *et al.*, 2020). The presence of anorexia, vomiting, lethargy and kidney failure in some cats suggests progression beyond uncomplicated lower UTI, consistent with reports that upper tract involvement and severe FLUTD can produce non-specific systemic illness (Dorsch *et al.*, 2019; Kaul *et al.*, 2019).

The strong association between UTIs and pyuria in both species agrees with data showing pyuria and hematuria are frequent, though not universal, in culture positive cases (Taylor *et al.*, 2025). High rates of crystalluria and proteinuria in dogs mirror studies where proteinuria and crystals commonly accompany bacterial cystitis and lower urinary tract disease (Novitasari *et al.*, 2023). In cats, the high prevalence of hematuria and moderate prevalence of proteinuria and glucosuria fit with FLUTD cohorts, where hematuria is the dominant sediment abnormality and pyuria is less consistent (Kovářková *et al.*, 2020). The lack of significant association for some clinical signs (polyuria,

pollakiuria, anuria) supports the notion that single signs are unreliable predictors of bacterial infection and must be interpreted with urinalysis and culture (Weese *et al.*, 2019; Aponrat *et al.*, 2025).

Bladder wall thickening with cloudy/sludgy content in most affected dogs and cats parallels report that thickened, often corrugated walls and intraluminal sludge or echogenic material are key ultrasonographic features of cystitis and other lower urinary tract affections (Yogeshpriya *et al.*, 2018). Similar thickening thresholds (> 3 mm) are used to recognize inflammatory bladder conditions in dogs and cats and in human/pediatric cystitis cystica (Elkewahy *et al.*, 2023). These findings support ultrasound as a useful adjunct to urinalysis for detecting and characterizing lower urinary tract diseases. In addition, the thickening of the urinary bladder wall observed on ultrasound (> 2 mm in diameter) was consistent with that reported later (Mantis, 2008), who stated that the thickness of the distended bladder wall should not exceed 2 mm in normal, healthy animals.

Diseased dogs had lower serum levels of total protein, albumin, and globulin than the control group. These results are consistent with those reported previously (Devaux *et al.*, 1996; Roopali *et al.*, 2018). However, an increase in the serum globulin concentration was observed in another study (Georgieva *et al.*, 2008). Hypoproteinemia can be attributed to the loss of protein in the urine (Roopali *et al.*, 2018). Decreased production and increased loss of albumin during inflammation can cause mild hypoalbuminemia, which may be accompanied by normal or elevated serum globulin concentrations (Throop *et al.*, 2004; Fransson *et al.*, 2007).

Dogs with UTIs had higher serum BUN, GGT, and CRP levels than dogs in the control group. A similar finding has been previously reported for BUN (Blanco and Bartges, 2001; Jeong *et al.*, 2006), GGT (Jasim, 2012), and CRP (Hindenberg *et al.*, 2020). The elevation of serum BUN levels could suggest impending azotemia. Increased GGT levels indicate kidney or hepatic injury, whereas increased CRP levels indicate inflammation (Hindenberg *et al.*, 2020). CRP has gained particular attention in veterinary medicine and in dogs with suspected inflammatory diseases (Yogeshpriya *et al.*, 2018).

Cats with UTIs had higher serum BUN, Cr, and GGT levels than those in the control group did. A similar finding was previously reported by several authors (Mayer-Roenne *et al.*, 2007) for BUN and Cr, and (Xavier Júnior *et al.*, 2022) for GGT. The elevation of serum BUN and Cr levels in diseased cats could suggest a decrease in GFR/renal blood flow due to several factors, such as hypovolemia, dehydration, acute or chronic renal failure, inflammation/infection, or lower urinary tract obstruction (Vaden *et al.*, 2011). The elevation of serum GGT levels in diseased cats could be linked to several factors, such as hepatorenal injury and corticosteroid administration (Vaden *et al.*, 2011). The pattern of total protein or globulin between dogs and cats suggests a different pattern of protein and acute-phase response compared with dogs. This speculation is supported by the results of previous studies, which indicate clear biochemical changes

(CRP, BUN, liver enzymes, proteins) in dogs and cats under similar urinary insults (Rana and Dighe, 2024).

The investigated dogs and cats had leukocytosis, neutrophilia, and relative lymphopenia compared with the control group. This finding is similar to that previously reported (Yogeshpriya *et al.*, 2018). Leukocytosis, neutrophilia, and lymphopenia may occur because of the variable extent of stress induced by bacterial organisms in the urinary tract, as well as a sign of manifestation of body defense mechanisms against bacterial infection (Senior *et al.*, 1986; Yogeshpriya *et al.*, 2018).

NLR and MLR only showed slight, non-significant increases in your dogs and cats. This matches larger feline and canine datasets where NLR/MLR shift with systemic inflammation or sepsis but are not strongly discriminatory within milder or localized urinary disease (Donato *et al.* 2023). Our findings were supported by those of a previous report (Tsouloufi *et al.* 2021).

Regarding urinalysis, in the present study, mean U-GGT activity was higher in diseased dogs than in clinically healthy controls. This result is consistent with the previous findings (Heiene *et al.*, 2001; Palviainen *et al.*, 2013) and can be attributed to tubular injury, severe GFR impairment, and extensive tubular necrosis (Rivers *et al.*, 1996; Mályusz and Braun, 2017). UGGT has been extensively investigated in aminoglycoside-induced AKI in dogs and has been shown to be a sensitive and early urinary biomarker. GGT is present on the brush border of the proximal renal convoluted tubules, and its detection in urine has been regarded as a good diagnostic method for detecting renal tubular injury or dysfunction in dogs (Lippi *et al.*, 2018).

The present study illustrates diverse findings regarding urine ALP levels in the investigated animals. In this context, diseased dogs had low urine ALP values, whereas diseased cats had higher values than the healthy controls. These findings in cats were consistent with those previously reported (D'Amico and Bazzi, 2003). The authors stated that the reason for such an elevation could be linked to proximal tubular injury, while the decrease in urinary ALP in diseased dogs remains elusive and requires further investigation. It has been reported that urine ALP could have unsatisfactory discriminatory power for diagnosing naturally occurring AKI in dogs, and therefore cannot be recommended as a sole screening test for canine AKI (Nivy *et al.*, 2017).

Here, diseased dogs had a lower USG value than controls, whereas in cats, it was higher in the diseased group than in the controls. These results are in agreement with those previously reported in dogs (Zambarbieri *et al.*, 2020), and cats (Defauw *et al.*, 2011). In contrast, our findings are consistent with those reported by other researchers (Tivapasi *et al.*, 2009; Lund *et al.*, 2013). In a previous study, the authors concluded that specimens of dogs with USG ≤ 1.013 could have a lower prevalence of clinically important bacterial growth than those of dogs in general. In a later study, the authors reported low USG in cats with FLUTD compared to the control group. In general, a low USG value likely indicates a reduced urine concentrating ability, possibly due to impaired renal function in diseased dogs, whereas a high USG in

diseased cats could be attributed to decreased water intake or stranguria (Defauw *et al.*, 2011).

The frequency of pyuria was much higher in diseased dogs and cats than in clinically healthy controls. This result is consistent with those reported in dogs (Forrester *et al.*, 1999), and cats (Bailiff *et al.*, 2008; Litster *et al.*, 2009). Pyuria can be attributed to an inflammatory response to bacterial infections in the urinary tract (Litster *et al.*, 2009). Despite this, a previous study reached different conclusions regarding WBC or pyuria as indicators of bacterial cystitis (Lund *et al.*, 2013). The results of hematuria are in accordance with those reported previously in dogs (Adamama-Moraitou *et al.*, 2017), and cats (Lund *et al.*, 2013). In addition to inflammation, cystocentesis has also been confirmed to cause transient microscopic hematuria, which can be differentiated from pathological hematuria (Kruger *et al.*, 1996).

Proteinuria is also more evident in diseased dogs and cats than in clinically healthy controls. These findings agree with those of previous studies (Vaden *et al.*, 2004), which implied that animals with pyuria due to UTIs are more likely to have abnormal urine protein concentrations, whereas other sources of urinary tract inflammation may be associated with proteinuria (Vaden *et al.*, 2004).

Cats with UTIs had a higher incidence of glucosuria than clinically healthy controls. This result is consistent with those previously reported (Heiene *et al.*, 2001; Palviainen *et al.*, 2013). Furthermore, severely affected cats demonstrated acute kidney injury. Glucose in urine can be fermented by glucose-fermenting bacteria, resulting in gas formation and emphysematous cystitis (Lippi *et al.*, 2019). In contrast, some researchers have reported no relationship between glucosuria and UTIs, and glucosuria is more common in healthy animals (Forrester *et al.*, 1999). Studies on the human urinary microbiome have identified the presence of microorganisms even in healthy populations (Burton *et al.*, 2017; Fouts *et al.*, 2012). Canine and feline urinary bladders have recently been found to be non-sterile environments (Burton *et al.*, 2017). However, as recorded in the present study, bacterial isolation is less frequent in healthy animals than in UTIs (Tang, 2017).

In conclusion, the results of the present study indicate that dogs with lower UTIs mainly show systemic inflammation without evidence of kidney dysfunction, but cats show marked signs. *E. coli* was the most frequently identified bacterium, emphasizing the necessity of culture-based diagnostics and adapted antimicrobial treatments. These findings emphasize species-specific variations in the clinical manifestations and pathophysiology of UTIs in dogs and cats.

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