Review Article

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The role of Uropathogenic *Escherichia coli* (UPEC) virulence genes in Urinary Tract Infection (UTI) cases in cats

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ABSTRACT

Urinary Tract Infection (UTI) is a common urogenital disease in cats, with uropathogenic *Escherichia coli* (UPEC) being the primary cause. UPEC originates from the normal gastrointestinal flora but is opportunistic, possessing the ability to adhere, invade, and persist in the urinary tract, leading to recurrent infections and clinical complications. These infections can range from mild to severe, including dysuria, hematuria, pollakiuria, stranguria, and urinary retention. The prevalence of UTI in cats varies across countries, ranging from 17.5–46.5%, with UPEC being the dominant pathogen. UPEC virulence is determined by genes encoding adhesion factors (*fim*A, *pap*, *sfa*, and *csg*A), iron acquisition systems (*ent*, *fyu*A, and *iut*A), outer membrane proteins (*Omp*A), and toxins (*hly* and *cnf*1), which support colonization, biofilm formation, invasiveness, and tissue damage. These virulence mechanisms allow the bacteria to survive urinary flow, pH, and host immune defenses, as well as to form intracellular bacterial communities and dormant reservoirs, increasing the risk of persistent and difficult-to-treat infections. In addition to its impact on feline health, UPEC also has zoonotic potential due to its close interaction with humans and the presence of antimicrobial resistance factors. Therefore, identifying UPEC virulence genes is crucial for understanding the pathogenesis of UTIs in cats and anticipating the risk of transmission to humans. This study reviews the scientific evidence regarding the distribution of UPEC virulence genes in cats, their implications for clinical infection, and the urgency of a One Health approach to infection prevention, diagnosis, and control. Understanding UPEC genetics provides the basis for more effective therapeutic strategies, the development of antibacterial interventions, and the mitigation of zoonotic risk.

Introduction

Urinary Tract Infection (UTI) is a urinary tract disease caused by the most common *Escherichia coli* bacteria in cats and can cause significant morbidity and recurrent clinical complications (Hutton *et al*., 2018). *E. coli* is a normal flora in the gastrointestinal tract, but is an opportunistic pathogen because it can cause various diseases, in the urinary tract infection is caused by a strain called uropathogenic *Escherichia coli* (UPEC) (Hasan and Ajeel, 2024). According to Osugui *et al*. (2014), that UPEC is included in the ExPEC group, is the bacteria most often isolated from UTI cases in cats. Urinary Tract Infection is one of the urogenital disorders often found in cats, both male and female, with clinical symptoms such as dysuria, hematuria, pollakiuria, periuria or urethral obstruction, and stranguria, to urinary retention (Dorsch *et al*., 2019). According to Nittayasut *et al*. (2021), UPEC is responsible for more than 80% of UTIs in humans and between 30 and 69% of UTIs in pets. The gastrointestinal tract serves as the primary reservoir for UPEC, where urinary tract infections typically occur due to urogenital contamination by fecal flora, accompanied by a failure of host defense mechanisms to eliminate uropathogens (Whelan *et al*., 2023). This condition places patients with UTIs at high risk for re-colonization.

The ability of UPEC to cause symptomatic urinary tract infections is closely related to the presence of various virulence genes. These genes include various adhesion factors, invasion proteins, toxins, and other proteins that play a key role in pathogenesis outside the gastrointestinal tract (Bunduki *et al*., 2021). The presence of virulence genes along with resistance determinants increases the risk of persistent and difficult-to-treat infections (Beceiro *et al*., 2013). Virulence genes identified in UPEC, which causes urinary tract infections in cats, include adhesion factors, persistence, iron acquisition systems, and toxins (García-García *et al*., 2025). The most dominant adhesion factors are type 1 fimbriae (*fim*ACDH), flagella (flgBCDEFGHIJ), and curli fimbriae (*csg*), which play a key role in colonization and biofilm formation on urinary tract epithelium (Aurich *et al*., 2023). Persistence factors such as MalX, which plays a role in glucose and maltose transport, and the outer membrane protein *Omp*A, which supports continued colonization in the urinary bladder, were found consistently across all isolates (Cook *et al*., 2009). In the iron acquisition system, feline UPEC showed a high prevalence of siderophore genes, including enterobactin, yersiniabactin, salmochelin, and aerobactin (Valdebenito *et al*., 2005). Toxin factors such as hemolysin *hly* and cytotoxic necrotizing factor 1 (*cnf*1) were also detected and contributed to tissue damage and modulation of the host immune response (Jousserand *et al*., 2025).

The distribution of these genes indicates that UPEC in cats has a complex virulence potential, thus supporting persistent colonization and worsening the clinical course of urinary tract infections. The combination

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of virulence factors allows this strain to have a greater ability to migrate upward through the urinary tract, colonizing, penetrating, and spreading to the bladder mucosa (Johnson, 1991). From there, the bacteria can further develop until they reach the kidneys, causing pyelonephritis, and even enter the bloodstream, causing bacteremia (Huang *et al*., 2020). This condition not only threatens the cat's health but also poses a potential zoonotic risk due to the close interaction between cats and humans (Bubpamala *et al*., 2018; Flament-Simon *et al*., 2020). Therefore, identifying UPEC genetic factors that play a role in pathogenesis is crucial not only for understanding the dynamics of infection in cats but also in a public health context. Studying the distribution of virulence genes can provide the basis for developing more effective strategies for the prevention, diagnosis, and treatment of UTIs caused by UPEC. The aim of this review was to synthesize and evaluate the current scientific evidence regarding the role of UPEC virulence genes in the pathogenesis of UTIs in cats.

The role of *E. coli* as an opportunistic pathogen

E. coli is a normal flora, but it also has the ability to act as an opportunistic pathogen when there is a change in the microbiota environment, decreased host immunity, or migration to organs outside the gastrointestinal tract (Riley, 2020). One form of opportunistic pathogenicity of *E. coli* is UTI, the strain responsible for which is UPEC (Zhou *et al*., 2023). Unlike commensal strains, UPEC has virulence determinants that enable colonization, adhesion to the urinary tract epithelium, and the ability to withstand host defense mechanisms (Bunduki *et al*., 2021). These characteristics make UPEC a major cause of UTI in cats, with clinical manifestations that can vary from mild to severe (Kidsley *et al*., 2020). UTI is one of the most common urogenital diseases in cats, with a significant impact on morbidity and the potential for recurrent clinical complications (Weese *et al*., 2019). According to Johansen *et al*. (2011), clinically, UTIs are divided into two main categories: uncomplicated UTIs and complicated UTIs. Uncomplicated UTIs are generally caused by UPEC and occur in individuals with good health status, normal anatomy and urinary tract function, and without systemic comorbidities that can increase susceptibility to infection (Sujith *et al*., 2024). Conversely, complicated UTIs usually occur in patients with structural or functional abnormalities of the urinary tract, obstruction, or immunosuppression conditions that play a role in increasing the risk of bacterial colonization and disease progression (Baimakhanova *et al*., 2025). In line with research conducted by Freitag *et al*. (2006), cats suffering from chronic diseases have a higher tendency to experience UTIs. With virulence characteristics that distinguish UPEC from commensal strains, this bacterium plays an important role in the etiology of UTIs in cats, which can further be observed through epidemiological and prevalence data from various studies in various countries.

Prevalence of UTI in cats

According to a study conducted by Hernando *et al*. (2021), the prevalence and characterization of urinary tract infections in cats in Spain showed that the most frequently isolated bacterial genus was *Escherichia* spp., with a proportion of 42.7% of the entire cat population studied. According to Garcês *et al*. (2022) a study conducted in Portugal on cats, the dominant bacteria identified included *Escherichia* spp. 44.5%. The prevalence in Korea showed the incidence of UTI due to *E. coli* was 17.5% (Weese *et al*., 2022). Research conducted by Chan *et al*. (2022) in Hong Kong showed that the most dominant bacteria isolated from feline patients was *E. coli* with a percentage of 46.5% in cat urine samples. Research in the United States showed that 43% of *E. coli* was found in cat urine samples (KuKanich *et al*., 2020). Based on various studies in several countries, it can be concluded that *E. coli* is the most dominant bacteria causing UTIs in cats, with prevalence varying between 17.5% and 46.5%. This finding underscores the importance of recognizing *E. coli* as the primary pathogen in feline UTIs.

Clinical symptoms of UTI in cats

Urinary Tract Infection can occur in cats of all ages, although previous studies have emphasized a higher prevalence in older cats due to aging-related immune function decline (Bailiff *et al*., 2008). According to Martinez-Ruzafa *et al*. (2012), the distribution of UTIs is relatively even in young, middle-aged, and older cats, possibly influenced by the inclusion of cats undergoing transurethral procedures or urogenital surgery. Clinical symptoms of UTIs in cats vary. Most cats show lower urinary tract signs, such as dysuria, pollakiuria, hematuria, stranguria, or urinary retention, but approximately one-third of cases may be asymptomatic (Olin and Bartges, 2022). According to Olin and Bartges (2015), UTIs in cats can be classified into two main categories: uncomplicated UTIs and complicated UTIs. Uncomplicated UTIs generally occur in cats with good health status, as well as normal urinary tract anatomy and function (Dorsch *et al*., 2019). These infections are usually sporadic, non-recurrent, and responsive to standard therapy. In contrast, complicated UTIs occur in cats with comorbidities, or conditions that affect the structure or function of the urinary tract (Thassakorn *et al*., 2025). Predisposing factors that increase the risk of persistent infection, recurrent infection, or treatment failure include endocrine diseases such as diabetes mellitus, hyperadrenocorticism, or hyperthyroidism, and chronic kidney disease (Mayer-Roenne *et al*., 2007; Sykes and Westropp, 2014). Additionally, anatomical abnormalities of the urinary or reproductive tract, immune disorders, neurogenic bladder, and pregnancy are also risk factors for complicated UTIs (Dorsch *et al*., 2019; Weese *et al*., 2019; Johnson, 2017). These conditions create an environment that facilitates bacterial colonization, prolongs the duration of infection, and decreases response to treatment.

Urinary Tract Infection is closely related to an increase in abnormal urination frequency, structural abnormalities in the urinary tract, and changes in the urothelial layer that plays a role in maintaining the integrity of the mucosal defense (Hasan and Ajeel, 2024). This disorder can be experienced by both male and female cats, with clinical symptoms varying from mild to severe, such as dysuria characterized by difficulty urinating, hematuria due to bleeding in the urinary tract, pollakiuria indicated by increased urination frequency but with small volumes, periuria or urinating behavior outside the litter box, urethral obstruction that can cause emergency conditions, stranguria in the form of pain during urination, to urinary retention that has the potential to cause serious complications in the upper urinary tract (Dorsch *et al*., 2019; Hernandez *et al*., 2014; Eggertsdóttir *et al*., 2007).

UTI isolate resistance in *E. coli* cases

Antimicrobial resistance (AMR) and multidrug resistance (MDR) in *E. coli*, the cause of UTIs in cats, show significant regional variation. Table 1 presents AMR and MDR data for *E. coli* isolated from feline UTI cases in several countries. The results indicate varying resistance patterns across regions, with some antibiotics exhibiting very high levels of resistance.

In Saudi Arabia, UTI-causing *E. coli* showed complete resistance (100%) to amoxicillin/clavulanic acid, followed by tetracycline (55.5%), vancomycin (44.4%), ceftazidime (33.3%), cefepime (22.2%), and ciprofloxacin (11%) (Ataya *et al*., 2023). These findings indicate a significant prevalence of resistance to beta-lactam antibiotics and tetracyclines in cat isolates in the region.

In Germany, a study by Aurich *et al*. (2022) reported high resistance to amoxicillin/clavulanic acid (93.4%), trimethoprim-sulfamethoxazole (87.6%), and ampicillin (76.1%), suggesting that commonly used first-line antibiotics are experiencing declining effectiveness.

In Italy, Bellato *et al*. (2024) found more variable resistance, with aminopenicillins with β-lactamase inhibitors having 50.1% resistance, while those without inhibitors reached 40.0%. Additionally, quinolones (36.1%), aminoglycosides (32.7%), first- and second-generation cephalosporins (31.9%) and third- and fourth-generation cephalosporins (29.7%), tetra-

Table 1. AMR and MDR data for *E. coli* UTI cases in cats.

Country	Other antibiotics and their percentages	Reference
Arab	Amoxicillin/Clavulanic Acid (100%) Tetracycline (55.5%) Vancomycin (44.4%) Ceftazidime (33.3%) Cefepime (22.2%) Ciprofloxacin (11%)	(Ataya *et al*., 2023)
German	Amoxicillin/clavulanic acid (93.4%) Trimethoprim-sulfamethoxazole (87.6%) Ampicillin (76.1%)	(Aurich *et al*., 2022)
Italy	Aminopenicillins • With β-lactamase inhibitors (50.1%) • Without inhibitors (40.0%) Quinolones (36.1%) Aminoglycosides (32.7%) First- and second-generation cephalosporins (31.9%) third- and fourth-generation cephalosporins (29.7%) Tetracyclines (25.3%) Sulfonamides + folate reductase inhibitors (24.3%) Nitrofuran derivatives (8.5%) Amphenicols (8.2%) Carbapenems (2.9%)	(Bellato *et al*., 2024)
Poland	Ampicillin/Sulbactam (54%) Amikacin (39%) Aztreonam (32%) Chloramphenicol (37%) Trimethoprim/Sulfamethoxazole (17%) Colistin (10%) Gentamicin (10%)	(Jańczak *et al*., 2024)
Korea	Ampicillin (65.7%) Ciprofloxacin (41.8%) Gentamicin (37.3%) Cefazolin (35.8%) Cefaclor (35.8%) Cefixime (35.8%) Trimethoprim-sulfamethoxazole (35.8%) Cefotaxime (34.3%) Amoxicillin/clavulanic acid (26.9%) Doxycycline (19.4%) Cefoxitin (17.9%) Cefepime (13.4%)	(Oh and Park, 2025)

cyclines (25.3%), sulfonamides with folate reductase inhibitors (24.3%), nitrofuran derivatives (8.5%), amphenicols (8.2%), and carbapenems (2.9%) were also reported, indicating multilineage resistance to various antibiotic classes.

In Poland, Jańczak *et al.* (2024) reported resistance to ampicillin/sulbactam (54%), amikacin (39%), chloramphenicol (37%), aztreonam (32%), trimethoprim-sulfamethoxazole (17%), colistin (10%), and gentamicin (10%). This pattern suggests varying degrees of resistance to beta-lactam antibiotics and aminoglycosides.

In Korea, Oh and Park (2025) found that *E. coli* UTI isolates had the highest resistance to ampicillin (65.7%), followed by ciprofloxacin (41.8%), gentamicin (37.3%), and several cephalosporin-generation antibiotics such as cefazolin, cefaclor, cefixime (35.8% each), as well as trimethoprim-sulfamethoxazole (35.8%) and cefotaxime (34.3%). Amoxicillin/clavulanic acid (26.9%), doxycycline (19.4%), cefoxitin (17.9%), and cefepime (13.4%) showed lower resistance, but still indicated a decreased treatment risk.

The role of virulence genes in upec pathogenesis

Bacterial virulence and adaptability play a crucial role in the colonization and pathogenesis of urinary tract infections. According to Abdul-Ghaffar and Abu-Risha (2017), the severity of UTIs caused by *E. coli* is influenced by the expression of various virulence factors. These virulence factors not only influence the severity of urinary infections but also determine the specific location of infection. Molecularly, virulence genes are concentrated in pathogenicity islands that can be transferred horizontally between bacterial populations, thus expanding the spread of pathogenicity (Dorsch *et al*., 2019). In UPEC, the expression of adhesins such as type 1 and P fimbriae, as well as iron uptake systems and the production of exotoxins including hemolysins, enhance the bacteria's ability to adhere to and invade the urothelial epithelium (Whelan *et al*., 2023). This invasion often triggers cellular apoptosis and mucosal desquamation, while some isolates are able to penetrate deeper into tissues, persist intracellularly, and form biofilms, reducing the effectiveness of antimicrobial therapy and complicating isolation from urine. These characteristics make UPEC a pathogen with a high risk of causing recurrent infections (Vejborg *et al*., 2011). According to Huang *et al.* (2020), a combination of virulence factors increases UPEC's ability to migrate to the upper urinary tract, invade the bladder, progress to the kidneys (pyelonephritis), and even enter the bloodstream, causing bacteremia.

Symptomatic infections in cats are strongly influenced by UPEC genetic factors, including adhesins, invasion proteins, toxins, and other factors that play a role in extraintestinal pathogenesis (Bunduki *et al*., 2021). The presence of virulence genes along with antibiotic resistance factors increases the risk of persistent and difficult-to-treat infections (Schroeder *et al*., 2017). Although the genetic profile of UPEC is nearly identical to that of commensal *E. coli*, the key difference lies in their pathogenic properties (Eberly *et al*., 2020). This high genetic similarity makes UPEC identification challenging, so the presence of *E. coli* in urine samples of patients with clinical symptoms is often sufficient to indicate the presence of a uropathogenic strain (Zagaglia *et al*., 2022). UPEC strains must be able to overcome various physiological barriers, such as continuous urine flow, pH variations, low oxygen levels, and the presence of urea (Whelan *et al*., 2023). After successful entry, the bacteria attach, invade, and replicate within the bladder epithelial cells, forming intracellular bacterial communities (IBCs) (Justice *et al*., 2006). Furthermore, UPEC can form quiescent intracellular reservoirs (QIRs), which are intracellular reservoirs containing dormant bacteria (Kwak *et al*., 2024). These reservoirs can be reactivated through desquamation of superficial epithelial cells, releasing the bacteria back into the bladder lumen and triggering recurrent infections.

The virulence mechanism of UPEC involves the coordinated regulation of multiple genes encoding virulence factors. These factors include adhesive structures such as flagella, pili, non-pilus adhesives, outer membrane vesicles, and a polysaccharide capsule (Terlizzi *et al*., 2017). Outer membrane proteins, lipopolysaccharides, and various toxins, including α-hemolysin, cytotoxic necrotizing factor 1 (*Cnf*1), and autotransporter cytotoxins that induce vacuolation, also play a role in host colonization (Whelan *et al*., 2023). UPEC's ability to maintain iron supply in the iron-poor urinary tract environment also enhances its virulence (Mann *et al*., 2017). This mechanism involves the use of siderophores, iron transporters, and outer membrane receptors to bind heme. Furthermore, biofilm formation is a crucial virulence factor that protects the bacteria from antimicrobial effects and helps evade detection by the host immune system (Sharma *et al*., 2023). In urinary tract infections, biofilms can form on catheter surfaces, the bladder wall, and within epithelial cells, contributing to both acute and persistent infections (Zagaglia *et al*., 2022).

Types of virulence genes in UPEC cat

Uropathogenic *E. coli* in cats has various virulence genes that play an important role in colonization, persistence, and pathogenesis of urinary tract infections. According to Shah *et al.* (2019), virulence factors in UPEC that play a role in the occurrence of UTI are classified into two groups, namely virulence factors related to the bacterial surface structure (type 1 fimbriae, P fimbriae, S fimbriae, and afimbrial adhesins), and virulence factors that are produced and excreted to the target site of action, such as α-Hemolysin (*hly*A), Cytotoxic Necrotizing Factor-1 (*cnf*1), and various siderophores such as yersiniabactin (*fyu*A) and aerobactin (*iut*A). The genes *fim*1 (type 1 fimbriae), *pap*C (P fimbriae), afa (afimbrial adhesin), and *sfa* (S fimbriae) have been identified as key factors involved in UPEC

pathogenesis, particularly in the early stages of adhesion during urinary tract infection (Khaleque *et al*., 2017).

Adhesion genes such as type 1 fimbriae (*fim*A) and curli fimbriae (*csg*A) are involved in the mechanisms by which bacteria adhere to urothelial epithelial cells, facilitate biofilm formation, and maintain their position in the bladder despite continuous urine flow (Zhou *et al*., 2023). Type 1 fimbriae play a role in initial colonization, while flagella support motility and invasion into the distal epithelium, and curli play a role in stable attachment and stimulate a local inflammatory response (Wojciuk *et al*., 2022). UPEC also has the ability to acquire iron, which is very limited in urine, through siderophore genes, such as enterobactin (ent/fep/fes), yersiniabactin (*irp/fyu*A), salmochelin (iroBCDE/N), and aerobactin (iuc/*iut*A) (Subashchandrabose and Mobley, 2015). This system allows the bacteria to obtain essential nutrients for their survival, with enterobactin and salmochelin being highly prevalent, while aerobactin is only found in a small proportion of isolates (Whelan *et al*., 2023).

Table 2 presents the types of virulence genes possessed by UPEC in cats, along with their primary functions and pathogenic mechanisms. According to Kadry *et al*. (2020), fimbrial virulence genes are heteropolymer protein structures whose ends are composed of adhesin subunits. They function to recognize and bind to specific receptors, enabling UPEC to attach to and invade the urothelium. The *fim*A gene is most frequently found in cat urine isolates (Tramuta *et al*., 2011). Type-1 fimbriae (*fim*A) are the prototype form of the fimbrial family that plays an important role in colonization of the urinary bladder, by recognizing the uroplakin receptor that is anosylated on the superficial umbrella cell layer of the bladder urothelium (Spaulding and Hultgren, 2016). Fimbrial adhesion is an extracellular protein structure that allows UPEC to adhere to bladder cells and prevent expulsion from the urinary system through urine flow. The most defined and most common fimbrial adhesion is type 1 fimbriae. According to Le Bouguénec (2005), that type 1 fimbriae, which play a role in increasing adhesion ability to host epithelial cells, are known to have an important role in the early stages of the biofilm formation process. According to Zamani and Salehzadeh (2018) genomic analysis of the UPEC population *fim*A gene has a prevalence of 86–100%.

The curli fimbriae gene, encoded by the *csg*A gene, has an affinity for the extracellular matrix and the ability to bind to laminin and fibronectin. This property makes it a crucial component in biofilm formation (Chahales and Thanassi, 2017). According to Golpasand *et al*. (2024), *Csg*A amyloid functions as the main subunit of curli fimbriae and is part of the extracellular matrix, contributing to increased bacterial cell resistance to antibiotics within biofilms (Cordeiro *et al*., 2016; Dueholm *et al*., 2012). Curli fimbriae formed through the Curli pathway contribute to various forms of urinary tract infections. In a study by Golpasand *et al*. (2024), the prevalence of the *csg*A gene was recorded at 90.4%. According to Whelan *et al*. (2023), the *Csg*A protein is the main subunit of curli, playing a crucial role in the polymerization of curli fibers on the surface of bacterial cells. In addition to adhesion, UPEC's persistence is supported by the MalX and *Omp*A genes (Yazdanpour *et al*., 2020). MalX, which is part of the pathogenicity island, functions in glucose and maltose transport, thus supporting bacterial metabolism in the urinary bladder (März *et al*., 2024). The outer membrane protein *Omp*A helps UPEC survive in the dynamic urinary tract environment, including the bladder, while reducing the effectiveness of host defense mechanisms (Rodrigues *et al*.,

Table 2. Types and mechanisms of virulence genes of UPEC in cats.

Virulence gene type	Main function	Virulence mechanisms	Reference
*fim*A (Type 1 fimbriae)	Initial adhesion and colonization	Encodes an adhesin protein that binds to the mannose receptor uroplakin in the urothelium; plays a role in initial colonization and biofilm formation	(Spaulding and Hultgren, 2016; Le Bouguénec, 2005)
*pap*C / *pap*G (P fimbriae)	Adhesion to the renal epithelium	Encodes pili that bind to the glycosphingolipid Gal-α(1–4)-Gal in renal epithelium; triggers inflammatory responses and supports pyelonephritis	(Lane and Mobley, 2007; Du *et al*., 2021)
sfa (S fimbriae)	Adhesion to the upper urinary tract epithelium	Encodes a mannose-resistant adhesin that binds to α-sialyl-2,3-α-galactose residues in uroepithelial glycoprotein; also plays a role in neonatal meningitis	(Antão *et al*., 2009; Rahdar *et al*., 2015)
afa (Afimbrial adhesin)	Non-fimbrial attachment	Encodes a surface adhesin that allows binding to epithelial cells without fimbrial structures; enhances tissue invasion	(Khaleque *et al*., 2017)
*csg*A (Curli fimbriae)	Biofilm formation	The major subunit of curli binds to laminin and fibronectin in the extracellular matrix; strengthening biofilms and antibiotic resistance	(Chahales and Thanassi, 2017; Golpasand *et al*., 2024)
*hly*A (α-Hemolysin)	Hemolytic toxin	Encodes a pore-forming toxin that causes host cell lysis, damages tissue, and triggers apoptosis through disruption of PKB/ACLY	(Stanley *et al*., 1998; Zhang *et al*., 2021)
*cnf*1 (Cytotoxic Necrotizing Factor 1)	Cytotoxic toxins	Modifies the host cell cytoskeleton through deamidase activity; causes vacuolization, cell cycle inhibition, and facilitates intracellular invasion	(Landraud *et al*., 2000; Khalaf and Flayyih, 2022)
*iut*A/iucA (Aerobactin system)	Iron acquisition	Encodes the siderophore receptor aerobactin to take up Fe^{3+} in iron-poor urine; supports UPEC growth and virulence	(Calhau *et al*., 2015; Bunduki *et al*., 2021)
*fyu*A/*irp*2 (Yersiniabactin system)	Iron transport and oxidative stress	Encodes the siderophore yersiniabactin which neutralizes the toxic effects of heavy metals and aids colonization	(Kudinha *et al*., 2012)
*iro*N/*iro*BCDE (Salmochelin system)	Lipocalin-resistant iron acquisition	Encodes the siderophore salmochelin that can avoid binding to host lipocalin-2; supports survival in the urine	(Bunduki *et al*., 2021)
ent/fep/fes (Enterobactin system)	Classical siderophore system	Produces enterobactin with high affinity for Fe^{3+}, allowing growth in iron-deficient urinary environments	(Wojciuk *et al*., 2022)
*omp*A (Outer membrane protein A)	Resistance and persistence	Outer membrane protein that protects against phagocytosis and maintains cell integrity in the urinary environment	(Rodrigues *et al*., 2022; Yazdanpour *et al*., 2020)
malX (Pathogenicity island marker)	Metabolism and virulence	Involved in maltose/glucose transport and a marker for the presence of pathogenicity islands (PAIs); supports metabolism during infection	(Tramuta *et al*., 2011)
USP (Uropathogenic Specific Protein)	Uropathogen specific proteins	Plays a role in increasing colonization capacity and infectivity; is associated with cases of urinary tract bacteremia.	(Kurazono *et al*., 2003)
*fim*H	Fimbrial adhesion gene (Fimbriae type 1 adhesin)	The *fim*H gene encodes an adhesin protein at the tip of type 1 fimbriae, which plays a crucial role in the adhesion of *Escherichia coli* to urinary tract epithelial cells via mannosylated receptors on the host cell surface. The *Fim*H adhesin enables the bacteria to adhere firmly to the urinary mucosa, preventing urine flow, and triggering initial colonization that leads to urinary tract infection. This gene is a key virulence factor in UPEC and contributes to biofilm formation and enhances the bacteria's ability to withstand host immune responses	(Putri *et al*., 2026; Schwartz *et al*., 2013)

2022). Virulence factors, including adhesins and siderophore systems, can be integrated into the pathogenicity island, moved via transposons, and transferred horizontally via plasmids (Schmidt and Hensel, 2004). These genetic transfer mechanisms provide adaptive advantages for UPEC, allowing the bacteria to respond quickly to environmental stresses and accelerate the evolutionary process.

Toxin genes such as hemolysin (*hly*) and cytotoxic necrotizing factor 1 (*cnf*1) play a role in damaging host tissue, triggering cell lysis, apoptosis, and vacuolization, which support intracellular invasion and persistent infection (Kendek *et al*., 2024). This combination of adhesion, persistence, siderophore, and toxin genes allows UPEC to adhere, survive, obtain essential nutrients, and damage host tissue, resulting in recurrent, persistent, and difficult-to-treat urinary tract infections in cats (Garcia *et al*., 2013). This genetic profile confirms the isolate's status as UPEC, similar to ExPEC strains in humans and other animals.

Uropathogenic *E. coli* is a major agent of urinary tract infections in companion animals, including cats, and feline UPEC isolates exhibit a high prevalence of several classic virulence genes. According to research conducted by Kurazono *et al*. (2003), the usp (uropathogenic specific protein) gene was found in 60% of cat urine isolates, while other adhesin and toxin genes were also frequently found: pil (type 1 pilus) in 85.3%, *pap* (P-pili) in 57.1%, *sfa* (S fimbriae) in 62.9%, *hly* (hemolysin) in 60.0%, and *cnf*1 (cytotoxic necrotizing factor 1) in 62.9% of cat urine isolates. The function of the UPEC virulence gene in cats, namely, Aspepil (type 1 pilus / type-1 fimbriae) functions to encode an adhesive structure that facilitates initial attachment to the bladder urothelium; this attachment is a crucial step for colonization and the formation of intracellular communities or biofilms (Martinez *et al*., 2000). Pills are also frequently present in fecal isolates and are therefore not always specific for the uropathogenic phenotype, but are very common in UTI isolates (Zhang *et al*., 2000).

The *Pap* gene (P fimbriae) encodes P-pili, which attach to epithelial glycolipids and are associated with a tropism for kidney tissue (pyelonephritis) (Lane and Mobley, 2007). In addition to adhesion, P-pili ligation can trigger a local inflammatory response that supports tissue damage (Spaulding and Hultgren, 2016). P fimbriae are pili or fimbriae structures that function as the main adhesion factor for UPEC in colonizing the urinary tract (Melican *et al*., 2011). These fimbriae are encoded by the *pap*BAHCDJKEFG operon, which is generally located on pathogenicity islands (PAIs) such as PAI-CFT073-pheV (Snyder *et al*., 2005). According to Du *et al*. (2021), *Pap*C functions as an accommodator protein, *Pap*D as a chaperone, and *Pap*G as an adhesive. The distal portion of P fimbriae is equipped with the *Pap*G adhesin protein, which binds specifically to glycosphingolipids containing Gal-α-(1,4)-Gal residues on the surface of uroepithelial cells. Based on their binding specificity, there are three *Pap*G allelic variants: *Pap*GI, *Pap*GII, and *Pap*GIII (García-García *et al*., 2025). P fimbriae (*pap*G allele III) also function as a specific adhesin for the urethra and kidneys, increasing the risk of pyelonephritis in cats (Lane and Mobley, 2007).

The *Sfa* gene (S fimbriae) is an additional adhesive determinant that contributes to the ability to adhere to uroepithelial surfaces and extraintestinal tissues (Antão *et al*., 2009). S fimbriae are mannose-resistant adhesins encoded by the *sfa* operon (Rahdar *et al*., 2015). This operon consists of nine genes, with the *Sfa*A protein acting as the major subunit, while *Sfa*G, *Sfa*H, and *Sfa*S function as minor subunits (Whelan *et al*., 2023; Werneburg and Thanassi, 2018). The *Sfa*F protein plays a role in the assembly and translocation process of the outer membrane (Whelan *et al*., 2023). Regulation of fimbriae expression is controlled by the *Sfa*B and *Sfa*C proteins, with a regulatory mechanism through phase variations influenced by environmental factors, such as temperature, osmolarity, glucose concentration, and other external conditions (Blomfield and van der Woude, 2007). S fimbriae have a specific affinity for alpha-sialyl-2,3-alpha-galactose residues found in urothelial tissue glycoproteins, especially in the bladder and kidneys (Werneburg and Thanassi, 2018). In addition to its role in the pathogenesis of urinary tract infections, the presence of fimbriae is also associated with neonatal meningitis, presumably through its adhesive ability to sialoglycoproteins, which are also expressed on brain microvascular endothelial cells (Iwahi *et al*., 1983). Molecular studies have reported a prevalence of the *sfa* operon in *E. coli* ranging from 42–87% (Nasrollahian *et al*., 2024).

The *hly* (hemolysin) gene is a secreted toxin that damages host cell membranes, increasing tissue permeability and facilitating bacterial invasion or spread (Stanley *et al*., 1998). In cat isolates, *hly* is found in substantial proportions, suggesting a role in pathogenesis. α-Hemolysin (*Hly*A) is a pore-forming toxin and a virulence factor produced by many strains of UPEC, with hemolysin production prevalence reported to range from 21–47% of isolates in various studies (Karam *et al*., 2018; Shah *et al*., 2019). The gene encoding *Hly*A is located in the *hly*CABD operon, which consists of four genes (Stanley *et al*., 1998). *Hly*A can trigger apoptosis in host cells by modulating cell death pathways and disrupting the regulation of cellular processes (Dhakal and Mulvey, 2012). For example, *Hly*A inhibits protein kinase B (PBK), which plays a role in preventing apoptosis and stimulating immune responses in bladder epithelial cells (Wiles *et al*., 2008). Furthermore, *Hly*A decreases the activity of the ACLY enzyme, resulting in decreased acetyl-CoA levels and affecting histone acetylation, resulting in suboptimal expression of proinflammatory cytokine and chemokine genes (Zhang *et al*., 2021). During infection, *Hly*A also stimulates increased granulocyte-macrophage colony-stimulating factor (GM-CSF), leading to macrophage accumulation and kidney damage in cases of acute pyelonephritis (Wang *et al*., 2020). In vitro studies have shown that UPEC isolates that form stronger biofilms tend to have higher hemolysin activity, reinforcing the role of *Hly*A in the virulence and pathogenesis of urinary tract infections (Nhu *et al*., 2019).

The cytotoxic necrotizing factor 1 (*cnf*1) gene, a toxin that modulates the host cell cytoskeleton, triggers cellular changes such as vacuolization or apoptosis that can facilitate intracellular invasion and persistence (Stenske *et al*., 2009). According to Babacan and İzgür (2021), *cnf*1 functions to increase virulence and inflammatory responses. According to Landraud *et al*. (2000), *cnf*1 plays a role in facilitating bacterial attachment and colonization of urinary tract epithelial cells. According to Khalaf and Flayyih (2022), *cnf*1 is a type AB toxin group produced by UPEC strains. This toxin plays a role in modifying the host cell cytoskeleton, thereby inhibiting the cell cycle in the G2 phase and triggering bacterial macropinocytosis (Fabbri *et al*., 2010). This mechanism supports *E. coli* colonization while reducing epithelial cell turnover. *cnf*1 is known to play a role in urinary tract infections. The *cnf*1 molecule is a single chain with a molecular weight of approximately 115 kDa, consisting of a receptor-binding domain at the N-terminal and a catalytic region at the C-terminal that exhibits deamidase activity (Yun *et al*., 2014).

The siderophore system, controlled by the *iut*A, ireA, *fyu*A, iroN, and aer genes, is associated with the onset and severity of UTIs (Kudinha *et al*., 2012). Siderophore molecules play a crucial role in helping *E. coli* obtain iron from the host, which is necessary for colonization and survival (Kuznetsova *et al*., 2025). Siderophores also provide protection against the potential toxic effects of these metals (Bunduki *et al*., 2021). According to Calhau *et al*. (2015), the high prevalence of the *iut*A gene supports bacterial growth in urine, a low-iron environment, making iron acquisition crucial for UTI development. Furthermore, this gene is thought to be more frequently found in antibiotic-resistant strains, as it is typically located on the ColV plasmid, known to carry antimicrobial resistance determinants.

uropathogenic specific protein (usp): a gene identified as part of a pathogenicity island (PI), is more frequently found in cat urine isolates than in fecal isolates from healthy dogs/cats, suggesting a link to the uropathogenic phenotype (García and Fox, 2021). The usp gene has been found in UPEC strains in studies by Kurazono *et al*. (2003) and Yamamoto (2007), and is reported as a virulence factor that increases the bacteria's infectious capacity. In humans, usp is more frequently found in UPEC isolates than in fecal *E. coli* isolates. Several studies have also shown that this

gene plays a role in the pathogenesis of urinary tract infections in various UTI syndromes and different patient groups. Babacan and İzgür (2021) found a significant correlation between USP and urinary tract bacteremia, suggesting a role for UPEC in the transition of infection from the urogenital tract to the bloodstream. Other findings revealed that the prevalence of USP was relatively similar in isolates from cystitis, pyelonephritis, and prostatitis cases, and was often associated with various common UPEC serotypes.

The *fim*H gene encodes the *Fim*H adhesin protein, which is the tip of the fimbriae or type 1 pili expressed by UPEC (Putri *et al*., 2026). *Fim*H plays a key role in the early stages of urinary tract infection by enabling bacteria to adhere to urothelial cells of the bladder or urethra through interaction with mannose residue (D-mannose) receptors or mannose-containing glycoprotein structures on the host cell surface (Schwartz *et al*., 2013). This adhesion mechanism is important because urine flow physiologically tends to push bacteria out of the bladder (Feenstra *et al*., 2017). By attaching with *Fim*H and type 1 fimbriae, UPEC bacteria can maintain colonization and initiate the formation of bacterial cell communities (e.g., biofilms or intracellular communities) (Terlizzi *et al*., 2017). For example, studies have found a *fim*H prevalence ranging from 87.5% to over 90% in human UPEC isolates (Hojati *et al*., 2015). In addition to its basic adhesion function, *fim*H gene variants (SNPs) have also been associated with the ability to form biofilms and adapt to changing urine flow and urinary tract environments, strengthening its clinical role as a potential target for vaccines or adhesion blockade therapies.

UPEC Zoonosis Urgency

Understanding the distribution of virulence genes is crucial for explaining infection dynamics and for developing strategies for the prevention, diagnosis, and treatment of UTIs caused by UPEC in cats. UPEC infections in cats not only impact animal health but also pose a potential zoonotic risk due to close interaction with humans (Bubpamala *et al*., 2018; Flament-Simon *et al*., 2020). The presence of UPEC in cats is not only important for animal health but also has a direct impact on human health (Hakim *et al*., 2024). According to Koontz *et al*. (2023), cats with urinary tract infections have the potential to serve as reservoirs for this bacterium. Through close contact between pets and their owners, the potential for transmission of the bacteria or their virulence genes to humans is a matter of concern. This situation is increasingly relevant considering the modern lifestyle, where many cats are companion animals in the home, so intense interaction can open up transmission routes (Foreman-Worsley *et al*., 2021). UPEC found in cats often carries antimicrobial resistance. If these resistant strains are transferred to humans, they pose a greater problem because they can limit therapeutic options, increase the risk of treatment failure, and prolong the duration of illness (Putra *et al*., 2019; Widodo *et al*., 2023). From a One Health perspective, this issue cannot be viewed separately from animal and human health, as both are closely interconnected with the surrounding environment (Ansharieta *et al*., 2021). Therefore, identifying the genetic factors of UPEC in cats is urgent, not only to understand the mechanisms of infection in animals but also to anticipate the potential for zoonotic spread to humans.

Conclusion

Uropathogenic *E. coli* is a major pathogen causing UTIs in cats, with a high prevalence globally. The success of UPEC in causing infection is closely related to the expression of various virulence genes that support colonization, persistence, and tissue damage. The presence of adhesion factors, siderophores, outer membrane proteins, and toxins allow UPEC to adapt to the hostile urinary tract environment and cause a complex clinical course. The genetic profile of UPEC in cats is similar to that of human isolates, thus enhancing its zoonotic potential. Genetic characterization of UPEC is not only important for understanding the pathogenesis of UTIs in cats but is also relevant in the context of One Health, particularly in efforts to prevent, diagnose, and control infections effectively.

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Conflict of interest

The authors declare that there is no conflict of interest.

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