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Systematic Review

Antibiotic resistance of biofilm-forming bacteria causing urinary tract infections: A systematic review

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ABSTRACT

Background: Urinary tract infections (UTIs) are a prevalent global health issue and are intensified by the rise of antibiotic resistance and biofilm formation. Analyzing 18 studies published between 2019 and 2024, this review aims to evaluate the antibiotic resistance patterns and biofilm-forming abilities of UTI-causing bacteria, identify the most prevalent species, and discuss contributing prevalence factors to inform future mitigation strategies. The current review found a high prevalence of resistance to commonly used antibiotics, especially penicillin, among Enterobacterales, with *Escherichia coli* and *Proteus vulgaris* exhibiting significant multidrug resistance (MDR). Nitrofurantoin's effectiveness was also reduced in certain biofilm-forming bacteria, with susceptibility rates as low as 15%. Conversely, most isolates in the studies were consistently found to be susceptible to imipenem (89% to 100%) and meropenem (70.3% to 100%). Furthermore, biofilm formation rates ranged from 36.5% to 100%, with a median prevalence of 75.5%. *E. coli* was the most frequently isolated bacteria (66.7%), displaying varying biofilm formation rates influenced by external factors and strain diversity. Other significant biofilm producers, such as *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Staphylococcus saprophyticus*, *Proteus mirabilis*, *P. vulgaris,* and *Klebsiella pneumoniae,* were also noted. 61.11% of the studies revealed a strong association between biofilm formation and MDR. Notably, *P. mirabilis* exhibited the highest proportion of strong biofilm producers and MDR prevalence, which was linked to specific resistance genes. Similarly, *S. aureus*, *K. pneumoniae*, and *E. coli* showed substantial MDR due to biofilm formation, particularly resistance to β-lactams, cephalosporins, and fluoroquinolones. *P. aeruginosa* and *P. vulgaris*, despite lower strong biofilm formation rates, presented significant resistance mechanisms, including efflux pumps and extended spectrum β -lactamase (ESBL) production. These findings emphasize the challenges in treating biofilm-mediated UTIs, highlighting the need for the continuous monitoring of resistance trends and further research on new therapeutic approaches. Future research should investigate the long-term evolution of bacterial resistance and the genetic adaptations of biofilms to inform strategies for mitigating resistance and improving UTI treatment outcomes.

Introduction

Urinary tract infections (UTIs) are one of the most prevalent bacterial infections worldwide, accounting for approximately 40% of nosocomial infections [1]. Every year, more than 400 million people are afflicted with UTIs, causing about 150 million deaths globally [2]. Between 1990 and 2019,

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the prevalence of UTIs has risen by 60% in the general population, suggesting that UTIs are a widespread public health concern that is yet to be eradicated [3].

A critical factor contributing to the high rates of recurrence in UTIs is the ability of most UTI-causing bacteria to form biofilms. Biofilms are structured communities of bacteria that adhere to surfaces, including urinary tract tissues and medical devices, such as catheters. Studies indicate that biofilm-forming bacteria are implicated in approximately 80% of all UTIs, particularly catheter-associated UTIs (CAUTIs) [4]. Encased in a matrix of polysaccharide materials, biofilms are a cluster of microbial cells composed of one or more bacterial species that remain permanently fixed to a surface and enable growth and survival in harsh conditions [5]. These biofilms are known to provide a protective environment that enables bacteria to evade both host immune responses and the effects of antibiotics, leading to persistent infections [6].

Antibiotic resistance has rendered some of the routinely used medications for UTIs ineffective, increasing the risk of more serious disease, hospitalization, and death, while also raising healthcare expenses [2]. UTIs comprise about 15% of all antibiotic prescriptions, highlighting their clinical significance and the necessity for innovative treatment strategies [6]. With the increasing rate of antibiotic resistance, this poses a formidable challenge in managing these drug-resistant infections effectively.

Biofilm formation by UTI-causing bacteria significantly enhances their resistance to commonly used antibiotics, contributing to the escalating persistence and recurrence of infections. It is hypothesized that biofilm-forming bacterial species exhibit more robust resistance mechanisms, thereby diminishing treatment efficacy and posing increased challenges for effective UTI management. With numerous research articles centered on the isolation and analysis of bacteria causing UTIs, there is a need for the further understanding of these studies that each exhibit different results and new information.

To further investigate the antibiotic resistance and biofilm-forming abilities of UTI-causing bacteria, the study seeks to answer this question:

How do biofilm-forming bacteria contribute to antibiotic resistance and the ongoing prevalence of UTIs, and which species are most commonly implicated?

Thus, this systematic review aims to present the antibiotic resistance patterns and biofilm-forming abilities of UTI-causing bacteria, to identify the most prevalent species, and to discuss contributing prevalence factors−to help synthesize evidence needed to mitigate biofilm-mediated UTIs.

METHODS

Eligibility Criteria

The research utilized a qualitative research design that involved an in-depth literature search, selection, and review of studies. An eligibility criterion was applied to ensure suitable and relevant studies were selected.

Inclusion criteria:

- Focused on biofilm-forming pathogenic bacteria of UTIs.
- Used human specimens.
- Specified the biofilm detection method and formation rates.
- Detailed the antibiotic resistance profile of biofilm-forming bacteria.
- Published in the English language.
- Published between 2019 to 2024, to ensure updated information as antibiotic resistance may change within at least two to three years [7].
- Original research articles, case studies, or cohort studies published in peer-reviewed journals or the Scopus database.

Exclusion criteria:

- Studies centered on non-biofilm-forming bacteria associated with UTIs.
- Classified as reviews, editorials, opinion articles, and conference abstracts.
- Vague and inconsistent report on the antibiotic resistance data of biofilm-forming bacteria.

Search Strategy and Quality Assessment

In identifying and gathering potentially relevant studies, four reviewers independently conducted a literature search across PubMed, Scopus, and ScienceDirect. Specific filters such as open access articles published from 2019 to 2024 were applied. The search was further specified by using the keywords “urinary tract infections (UTIs),” “biofilm-forming bacteria,” and “antibiotic

resistance" combined with Boolean operators (AND, OR).

Once generated, the studies were imported to Mendeley, a reference management software, to manage and remove duplicates. Four independent reviewers proceeded to perform the title and abstract screening to confirm eligibility, followed by a full-text screening of the entire article to verify its relevance and comprehensiveness. In the event of a debate on whether to include an article, another author was consulted to reach a consensus. The PRISMA guidelines were applied in documenting the selection of studies. This included a four-phase flow diagram outlining the process of identifying, screening, and assessing the eligibility criteria of reports in a systematic review [8]. The reviewers subjected the selected studies for quality assessment using the Joanna Briggs Institute (JBI) appraisal checklist to assess the relevance of the study, quality of results and eliminate the risk of bias. Supplementary File 1 details the entire search strategy process and presents the complete JBI appraisal checklist results.

Data Extraction

To ensure a synonymous and structured review, four reviewers collected relevant information from the studies and imported it onto a spreadsheet (Google Sheets). The data extracted consisted of general information, such as authors, publication year, study design, and country of the included studies. Extracted data from the methodologies consist of the samples used and their quantity, number of isolates, biofilm detection method, number of biofilm producers, and antibiotics tested. In relation to this current review's objective, the data extracted from the studies were the antibiotic resistance profile, bacteria recovered and their biofilm-formation, treatment challenges, and contributing factors to the prevalence of UTIs.

Ethical Consideration

This review utilized reliable and publicly available journal articles, studies, and literature. Approval from the Far Eastern University (FEU) Center for Learning Enrichment and Research for Students (CLEARS) hereby confirms that ethical guidelines were followed throughout the study, thus strengthening this paper's legitimacy. Proper citation of all data sources and databases used was also ensured.

RESULTS AND DISCUSSION

Study Selection

The initial search generated 889 studies published between 2019 to 2024 across the three databases. After removing 72 duplicates in Mendeley, four reviewers screened 817 studies for their title and abstract. A total of 695 studies were excluded, while 122 studies underwent full-text screening. Excluded studies were not written in English, had no full access, had insufficient data, were out of scope, and used animal isolates. Only 18 studies met the eligibility criteria and were included in the review for data extraction. Figure 1 summarizes the selection process following the PRISMA guidelines.

Study Characteristics

Presented in Figure 2 is the geographical distribution of all 18 articles selected for systematic analysis. South Asia leads with six articles, reflecting a strong research presence that may be potentially relevant to the region. Africa and the Middle East each contribute four articles, indicating a significant scholarly focus in these areas. Europe and South America have a smaller representation, each with only two articles. This distribution highlights global research engagement, suggesting potential regional differences in interest and topical relevance.

The studies collected mostly midstream clean-catch urine specimens, urinary catheters, and other clinical specimens from patients who were either diagnosed or suspected of UTIs. A total of 2,955 bacterial isolates were tested for biofilm production across all studies. Gram-positive bacteria accounted for 27.8% of the studies, whereas Gram-negative bacteria dominated with 88.9%. *Escherichia coli* vastly emerged as the most frequently investigated and most isolated bacteria, as evidenced by its presence and focus in 66.7% of the articles that were part of this review.

With a variety of biofilm detection techniques, the most widely used method was found to be the Microtiter Plate (MTP) method via crystal violet staining, as it is the gold-standard approach [19], comprising ten out of eighteen studies (10/18, 55.6%). Two studies (11.1%) purely employed the Congo Red Agar (CRA) method, whereas three articles (16.7%) used a combination of both MTP and CRA to detect biofilm formation. Meanwhile, two studies (11.1%) utilized the Crystal Violet

Tube-Adherence Method, and only one study (5.6%) applied the Tissue Culture Plate method.

Most of the bacteria isolated were determined to be a part of the Enterobacteriaceae family, which are commonly found in nosocomial infections. Some of the most common isolates obtained across all the studies include uropathogenic *E. coli* (UPEC), *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Proteus spp.*, and *Staphylococcus spp.*, among others.

Antibiotic resistance profile results for each bacterium have been divided into two tables: undifferentiated (Table 1) and confirmed biofilm-producing bacterial isolates (Table 2).

As seen in both tables, most studies highlighted the antibiotic resistance profile of UPEC, proving it to be one of the most resistant bacteria in existence. Providing up-to-date information regarding its resistance profile, as shown in Figure 3, allows humanity to be informed of its current effectiveness against UTIs.

Most isolated bacteria have shown a significantly high susceptibility to imipenem and meropenem, namely *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *and Proteus vulgaris*. Across all studies, susceptibility rates for imipenem ranged from 89% to 100%, while meropenem susceptibility rates ranged from 70.3% to 100%. Among confirmed biofilm producers, imipenem had a consistently high susceptibility rate, ranging from 96% to 100%, with meropenem ranging from 87.4% to 100%.

A different source found imipenem to be a more effective drug than meropenem against *E. coli*, *P. aeruginosa*, *Enterococcus spp.*, *Klebsiella spp.*, and *S. typhi* upon using urine, blood, and pus samples. Meropenem only showed 40.59% sensitivity, whereas imipenem showed a staggering 84.15% sensitivity. Imipenem was also found to be more susceptible to urine specimens and *E. coli* compared to other isolates. Nonetheless, the study still concludes imipenem and meropenem are both equally effective in the treatment of critical illnesses [27].

As one of the most commonly used drugs in treating UTIs, nitrofurantoin was once the most effective drug against Gram-positive and Gram-negative bacteria [28]. However, it was found in this current review that the effectiveness of nitrofurantoin began to decrease as the bacteria started to produce biofilms. The susceptibility of nitrofurantoin went as low as 15% in biofilm-forming *K. pneumoniae* and 24% in biofilm-forming *E. coli* [9] with varying rates of increasing resistance in other studies [19, 23]. Another study discovered that nitrofurantoin had a resistance rate as high as 91.2% against *E. coli* tested for biofilm production [29].

Furthermore, the present study showed a growing pattern of increasing resistance among Enterobacterales to penicillins. Ampicillin proved to be the most frequent antibiotic to have a high resistance rate among both biofilm and non-biofilm producers in UPEC isolates, ranging from 22% to 100%. Amoxicillin also showed fluctuating rates of antibiotic resistance to UPEC, ranging from 8% to 100%. Additionally, results manifested an increasing resistance to trimethoprim/sulfamethoxazole, ciprofloxacin, and amoxicillin/clavulanic acid in *E. coli* and *Klebsiella* spp., aligning with other previous studies [30, 31]. Since ampicillin has a high level of resistance, it should no longer be used to treat UTIs caused by Gram-negative bacteria [32].

Alarmingly, in one included study that identified the presence of biofilm-producing *P. vulgaris*, every antibiotic tested (amikacin, amoxicillin/clavulanic acid, ampicillin, ciprofloxacin, cefixime, ceftriaxone, cephalexin, erythromycin, gentamicin, and trimethoprim/sulfamethoxazole) yielded 100% resistance to the bacteria with the exception of imipenem and meropenem that each produced 100% susceptibility. This shows that the emergence of multidrug-resistant (MDR) *P. vulgaris* has grown to be a threat to even UTI patients. A previous study revealed that MDR *P. vulgaris* exhibited a higher in vitro pathogenicity, as evidenced by enhanced biofilm formation and swimming motility [33]. Based on the included study, *P. vulgaris* was second in producing the most biofilm out of the five bacteria recovered [20].

Variations in the resistance pattern of the bacterial isolates may be due to differences in geographic region, variety of strains, the availability of antibiotics in different countries, variations in antibiotic prescription methods among medical practitioners, the year when the study was conducted, and differing clinical practices.

Results indicate a high prevalence of biofilm formation among isolated bacteria. Table 3 presents the formation rates ranging from 36.5% to

100%, indicating a varied production rate with a significant median prevalence of 75.5%. Samples from confirmed or suspected UTIs had high biofilm production. This suggests biofilm has a key role in the manifestation and recurrence of infection.

This aligns with another study that found biofilm as a leading cause of persistent and recurrent infections [34]. Other studies also showed disparate values yielding 27% to 100% formation rates of bacteria, such as *E. coli* [35, 36].

Bacteria Recovery

E. coli was the predominant pathogen recovered from studies with multiple bacteria profiles as it showed a 24% [9], 47% [24], and 71% [17] recovery rate.

These are backed by studies that found *E. coli* as the most recovered pathogen in catheter-associated UTIs (CAUTIs) at 53% [37] and in overall UTIs at 85% [38]. However, one of the included studies also identified *Pseudomonas aeruginosa* to be the most isolated associated with infection [20]. Hence, the pathogen may differ depending on environmental and geographical factors.

Biofilm formation of recovered bacteria

E. coli produced the most biofilm across studies with multiple bacteria profiles, following 24% [9], 51.5% [24], 70.9% [25], and 100% [17] formation rates. In studies with only *E. coli* isolates, there was disparate biofilm formation rates from 43.2% to 97.2% [11, 12, 14, 16, 19, 21, 22, 24, 25].

Other sources found that while *E. coli* was most recovered, *Enterobacter cloacae, P. aeruginosa,* and *Proteus* spp. had a higher biofilm formation [37, 39]. Formation rates from the included studies were consistent with other sources that had 27% to 99% biofilm formation of *E. coli* [35]. Variability was affected by environmental conditions and differences in strains, which indicates the genetic and adaptive diversity of the bacteria.

Another included study found *P. aeruginosa* to produce more biofilms with 34 out of 38 isolates (89.5%) biofilm formation [20]. This is indicative of its high potency in causing UTIs.

A meta-analysis of *P. aeruginosa* biofilm formation supports these findings with a calculated average rate of 86.5% [40]. While other studies emphasized *E. coli* to have a higher biofilm formation that can reach 100% [36], various sources highlighted the high biofilm formation of *P. aeruginosa* with 92% [41], along with *Proteus* spp. as a major biofilm-forming bacteria [39]. Virulence genes such as bla_{NDM}, bla_{SPM}, $bla_{VIM\text{-}VIM2}$, and bla_{KPC} genes recovered from these bacteria amplify resistance, especially towards carbapenem antibiotics, while *tox*A and *las*B genes are involved in impairing host response [41].

In this review, *Staphylococcus aureus* and *Proteus mirabilis* were both discovered to have 100% biofilm formation [10, 15, 23].

However, other sources indicate that formation rates of *S. aureus* are only as high as 70% and have been determined to cause low percentage and frequency as a UTI pathogen compared to other bacteria [42]. Findings for *P. mirabilis* were corroborated by a study that also recorded 100% biofilm formation of all samples and strains they tested [43]. *P. mirabilis* causes more complicated UTIs due to its ureolytic biomineralization that forms crystals in its biofilm [44].

Biofilm formation within these bacteria served as a protective defense mechanism and hindered successful antibiotic action. Even though certain bacteria, such as *E. coli,* were mostly isolated and had an expansive range of biofilm formation rates, other bacteria can also cause challenging infections due to their virulence factors and biofilm-forming mechanisms.

Intensity of Biofilm Formation Among Biofilm-forming Bacteria

The data extracted from all 18 studies revealed considerable variation in the proportion of bacteria exhibiting strong, moderate, and weak biofilm formation. All 18 studies provided data on biofilm formation intensity, but only 13 provided quantifiable data, making direct comparisons challenging. Across these studies, classification varied slightly, using terms like “obstinate” categorized as strong [9]. Despite these variations, moderate biofilm formation (38.73%) was the most frequently observed phenotype.

A study reported that 134/183 (73.2%) *P. mirabilis* isolates were strong biofilm producers, 47/183 (25.6%) were moderate, and 2/183 (1.1%) were weak [15]. Another study found that among 40 *P. mirabilis* isolates, 30% were strong biofilm producers, 50% were moderate, and 20% were weak [23]. On average, 51.6% of *P. mirabilis* isolates were strong biofilm producers, 37.8% were moderate, and 10.6% were weak. Another study with 60 clinical isolates observed that 35% were

strong biofilm producers, 31.67% were moderate, 30% were weak, and 3.33% were non-biofilm producers [45]. These findings reinforce *P. mirabilis'* role in chronic and recurrent UTIs.

Similarly, *K. pneumoniae* had a significant proportion of strong biofilm producers. One study reported that 56.3% of 154 isolates were strong biofilm producers, 25.7% were moderate, and 10.2% were weak [26]. Another study with 102 isolates found that 19.69% were strong biofilm producers, 33.07% were moderate, and 27.55% were weak [13]. On average, 46.5% of *K. pneumoniae* were strong biofilm producers, 33.3% were moderate, and 20.3% were weak.

E. coli also exhibited variations in biofilm production, with moderate biofilm producers being the most prevalent overall. One study with 211 isolates found that 42% were moderate biofilm producers, 39% weak, and 19% strong [9]. Another study with 168 isolates found moderate biofilm producers comprised 49%, 28% weak, and 23% strong [12]. Other studies reported similar trends, with an average of 20.1% strong biofilm producers, 48.5% moderate, and 31.4% weak [11, 14, 19].

S. aureus also demonstrated high biofilm formation. A study found that 35% of 20 isolates were strong biofilm producers, 55% moderate, and 10% weak [10]. *S. saprophyticus* showed a similar trend, with 35% strong, 32% moderate, and 32% weak biofilm producers [18].

P. aeruginosa and *P. vulgaris* exhibited lower proportions of strong biofilm producers. One included study found that only 17.6% of 34 *P. aeruginosa* isolates were strong biofilm producers, while 26.5% were moderate and 55.9% were weak [20]. Among 21 *P. vulgaris* isolates, 14.3% were strong, 38.1% were moderate, and 47.6% were weak biofilm producers [20]. Despite these findings, another study reported that among twenty *P. vulgaris* isolates, 45% were strong biofilm producers, 55% were moderate, and 0% were weak [43]. These discrepancies may be attributed to differences in clinical sources, environmental conditions, strain variations, and methodologies.

Association of Biofilm-forming Bacteria to Antibiotic Resistance

A strong link between biofilm formation and multidrug resistance (MDR) was found, with 61.11% (11/18) of studies showing a positive correlation.

Many studies found high MDR prevalence in biofilm-forming isolates. One study reported 90.1% MDR among UPEC isolates [14], an increase from 81.1% four years earlier [46]. Another study found 82.5% MDR in biofilm-producing *P. mirabilis*, with strong biofilm producers showing 91.6% [23]. Similarly, MDR rates were higher in biofilm-producing *E. coli* (79.5%) than in non-biofilm producers (62.0%) [25]. MDR was observed in 75.4% of isolates [26], while another study reported MDR rates of 61% and 39% in biofilm-forming and non-biofilm-forming UPEC, respectively [24].

Other studies reinforced these findings, reporting substantial MDR rates among biofilm-forming isolates [13, 18, 21]. MDR was observed in 55% of *S. aureus* strains [10] and 46% of UPEC isolates [11]. Another study found MDR prevalence ranging from 56.6% to 88.9% [22]. Higher antibiotic resistance was confirmed in biofilm-producing *E. coli*, with significant correlations ($p<0.05$) for most antibiotics except amoxicillin and nitrofurantoin [47].

Moreover, several studies also explored bacterial resistance mechanisms. Pan-drug resistant *E. coli* and extensively drug-resistant *Klebsiella spp.* and *Pseudomonas spp.* were identified [9]. Extended spectrum β-lactamase (ESBL)-producing *E. coli* and *K. pneumoniae* showed cephalosporin resistance [17]. High resistance to cephalosporins (53.8%) and fluoroquinolones (61.5%) in UPEC isolates was linked to virulence factor genes [12]. Sulfonamide resistance genes (*sul1, sul2*) were also identified [15]. ESBL production and biofilm-related protein mutations were found to impact antibiotic resistance [16]. MDR-associated resistance genes (bla_{TEM}, $bla_{\text{CTX-M}}$) and integrons (*intI1, intI2*) were identified in *P. mirabilis* [23]. The presence of the bla_{VIM} gene, linked to carbapenem resistance, was also noted [19]. Additionally, 85.5% of ESBL-producing isolates were MDR, with efflux pump and biofilm-associated genes identified [26].

Biofilm resistance mechanisms include reduced antibiotic penetration, enzymatic degradation, genetic adaptation, and resistance gene exchange [20, 21]. MDR was linked to efflux pumps, beta-lactamase production, and outer membrane alterations [14]. In *S. saprophyticus*, MDR was associated with the *mecA* gene [18]. Other studies linked MDR to virulence factors such as hydrophobicity, colicin production, gelatinase

activity, biofilm formation, and siderophore production [22].

Treatment Challenges of Biofilm-Mediated UTIs

Biofilm-forming bacteria possess an enhanced resistance against antibiotics and the immune system of the host [15, 17]. 73.2% of the *P. mirabilis* isolates produce strong biofilm leading to persistent infection and treatment failure [15]. This can further result in chronic UTIs, particularly in individuals who are catheterized or have urinary tract physiological abnormalities. Other studies further confirm this, demonstrating that pneumoniae and coli are hypervirulent pathogens that have become a persistent burden in the medical profession due to their strong biofilm production, which reduces the effectiveness of treatment [12, 13].

A high level of MDR to the treatment associated with biofilm-mediated UTIs plays an extensive role in the treatment challenges. One study showed that in Nepal, Nitrofurantoin is the only oral drug left to treat UTIs as it was once accompanied by ciprofloxacin [25]. Moreover, *K. pneumoniae* is an ESBL-producing bacteria, which allows it to steadily increase in multiple antibiotics, leading to MDR and adding to the complexity of UTI treatment [17]. Methicillin-resistant *S. aureus* (MRSA) resists beta-lactams, macrolides, and tetracyclines complicating the treatment of UTIs [10]. *P. mirabilis* usually colonizes in urinary catheters of patients, forming a crystalline biofilm that worsens treatment, particularly with long-term use [15].

Excessive and inappropriate use of antibiotics leads to difficulty in treatment [20]. This is evident in Uganda where there are no regulations about the use of antibiotics, and patients have access to over-the-counter prescriptions, leading to increased antibiotic exposure and MDR [48].

Factors Affecting the Prevalence of UTIs

E. coli has been constantly recognized as a common causative agent relevant to all ages [9, 25]. The prevalence of *E. coli* has been associated with its ability to form a biofilm, protecting the bacteria that develops an increased antibiotic resistance [25]. Other bacteria that have contributed to the prevalence of UTIs are *K. pneumoniae* and *P. mirabilis* [17].

In hospital settings, the prevalence of pathogens arises from a specific environment. *Pseudomonas* spp. is frequent in the ICU due to long-term use of invasive devices. *Enterococcus* spp. commonly thrives in the ward [9]. *S. aureus* was observed in elderly patients who are catheterized and experiencing bacteremia [10]. Although *S. saprophyticus* does contribute to UTI cases, especially in developing countries, more comprehensive studies on its biofilm formation have yet to be conducted [18].

Women are more likely than men to suffer from a UTI [17, 24, 25]. Females have a 40.3% higher prevalence of UTIs than males who only have a 20% prevalence [9]. Some logical and anatomical reasons for this include the proximity between the anus and the vagina [9, 15]. and the hormonal differences between males and females, especially during pregnancy and the menopausal stage [20].

UTIs are also very common among the elderly population, affecting 29.5% of the population [25]. This is probably due to changes in immune function and the number of comorbidities [49]. Likewise, a high prevalence of UTIs can also be associated with other risk groups, notably infants, pregnant women, catheterized and diabetic patients, and immunocompromised patients as these conditions reduce the defenses of the host, freeing the bacteria to colonize the urinary tract [9, 15, 16].

UTIs can be triggered by family history and a history of UTIs from childhood till the premenopausal period [50]. Immunosuppression, diabetes, and chronic kidney disease are among the underlying conditions that reduce the host's defenses, making it easier for bacteria to colonize the urinary tract [15, 16]. In fact, a study found that UTIs are more common in diabetic patients (42.9%) than in non-diabetic patients (17.4%) [25].

Lifestyle factors such as frequent sexual intercourse, use of contraceptives, and poor hygiene are associated with the prevalence of UTI due to the risk of damaging the normal flora allowing opportunistic bacteria to grow [9].

In healthcare settings, catheterization and other medical devices have been known to act as the surfaces for the growth and colonization of bacteria [16]. Furthermore, most *P. mirabilis* isolates from patients who had catheterization for 10 to 15 days exhibited moderate to strong biofilm formation, whereas isolates from patients who were catheterized for only 7 days exhibited weak biofilm formation [23]. This indicates a correlation between the length of time and the development of biofilm in catheters that raises the risk of UTIs.

Ultimately, the misuse of antibiotics is an unquestionable factor that only worsens the prevalence of UTIs and contributes to the growth of MDR bacteria and strains, further complicating UTI treatment [17, 18].

Antibiotic Activity of UTI-Causing Bacteria

Table 1. Antibiotic resistance profile of bacterial isolates from each study.

Author and Year of the Study	Bacterial Isolates (n)	Susceptibility Rates	Resistance Rates
1. Arafa et al. (2022) [11]	Uropathogenic *Escherichia coli* (UPEC) (n = 50)	-	**Norfloxacin (82%)** Ampicillin (60%) Trimethoprim/Sulfamethoxazole (44%) Cefepime (38%) Ceftazidime (38%) Ciprofloxacin (28%) Gentamicin (12%) Amoxicillin (8%) Nitrofurantoin (8%) Piperacillin/Tazobactam (4%) Amikacin (0%) Ertapenem (0%) Imipenem (0%) Meropenem (0%)
2. Baldiris-Avila et al. (2020) [12]	Uropathogenic *Escherichia coli* (UPEC) (n = 190)	**Doripenem (95.8%)** **Ertapenem (95.8%)** Amikacin (91.6%) Ceftriaxone (91%) Meropenem (90.5%) Cefoxitin (89.5%) Ceftazidime (88.9%) Nitrofurantoin (88.9%) Piperacillin/Tazobactam (86.3%) Gentamicin (72.6%) Tobramycin (62.6%) Cefotaxime (55.8%) Aztreonam (54%) Ciprofloxacin (50.5%) Piperacillin (51.1%) Trimethoprim/Sulfamethoxazole (49.5%) Cefazolin (48.4%) Cefepime (45.8%) Ampicillin/Sulbactam (38.4%) Ampicillin (12.6%)	**Ampicillin (88.4%)** Cefepime (54.2%) Trimethoprim/Sulfamethoxazole (50.5%) Ciprofloxacin (49.5%) Cefazolin (45.8%) Piperacillin (45.2%) Cefotaxime (44.2%) Ampicillin/Sulbactam (42.6%) Aztreonam (33%) Gentamicin (27.4%) Tobramycin (24.2%) Ceftazidime (11.1%) Nitrofurantoin (11.1%) Meropenem (9.5%) Amikacin (8.4%) Cefoxitin (6.3%) Piperacillin/Tazobactam (5.8%) Ceftriaxone (5.3%) Doripenem (4.2%) Ertapenem (4.2%)
3. Ballen et al. (2021) [13]	*Klebsiella pneumoniae* (n = 127)	**Colistin (98%)** Imipenem (89%) Chloramphenicol (87%) Fosfomycin (86%) Gentamicin (83%) Piperacillin/Tazobactam (79%) Cefepime (76%) Aztreonam (71%) Trimethoprim/Sulfamethoxazole (65%) Ceftazidime (63%) Amoxicillin (61%) Ciprofloxacin (59%)	**Ciprofloxacin (41%)** Amoxicillin (39%) Ceftazidime (37%) Trimethoprim/Sulfamethoxazole (35%) Aztreonam (29%) Cefepime (24%) Piperacillin/Tazobactam (21%) Gentamicin (17%) Fosfomycin (14%) Chloramphenicol (13%) Imipenem (11%) Colistin (2%)
4. Gajdacs et al. (2021) [16]	*Escherichia coli* (n = 250)	-	**Ciprofloxacin (43.6%)** Trimethoprim/Sulfamethoxazole (34.4%) Third-generation cephalosporins (19.6%) Fosfomycin (18.8%) Gentamicin (11.6%) Nitrofurantoin (11.2%) Meropenem (0%)
5. Hashem zadeh et al. (2020) [18]	*Staphylococcus saprophyticus* (n = 43)	**Linezolid (100%)** **Nitrofurantoin (100%)** **Quinupristin/Dalfopristin (100%)** **Vancomycin (100%)** Rifampin (95%) Trimethoprim/Sulfamethoxazole (90%) Cefoxitin (74%) Chloramphenicol (74%) Tetracycline (74%)	**Erythromycin (58%)** Clindamycin (46%) Gentamicin (37%) Ciprofloxacin (34%) Cefoxitin (25%) Chloramphenicol (25%) Tetracycline (25%) Trimethoprim/Sulfamethoxazole (9%) Rifampin (4%)

		Ciprofloxacin (65%) Gentamicin (62%) Clindamycin (53%) Erythromycin (41%)	Linezolid (0%) Nitrofurantoin (0%) Quinupristin/Dalfopristin (0%) Vancomycin (0%)
6. Katongole et al. (2020) [21]	Uropathogenic *Escherichia coli* (UPEC) (n = 200)	-	**Amoxicillin (93%)** **Trimethoprim/Sulfamethoxazole (93%)** Gentamicin (87%) Cefuroxime (84%) Nalidixic acid (79%) Amoxicillin/Clavulanic acid (62.5%) Ciprofloxacin (62%) Ceftriaxone (55%) Ceftazidime (54%) Chloramphenicol (28%) Nitrofurantoin (25.5%) Imipenem (0.5%)
7. Kumar et al. (2023) [22]	Uropathogenic *Escherichia coli* (UPEC) (n = 346)	**Chloramphenicol (88.4%)** Meropenem (70.3%)	**Ampicillin (63.4%)** **Nalidixic acid (63.4%)** Cefotaxime (62.1%) Amikacin (N/A) Chloramphenicol (N/A) Ciprofloxacin (N/A) Ceftazidime (N/A) Amoxicillin/Clavulanic acid (N/A) Ceftriaxone (N/A) Cefepime (N/A) Cefuroxime (N/A) Gentamicin (N/A) Kanamycin (N/A) Imipenem (N/A) Meropenem (N/A) Nitrofurantoin (N/A) Norfloxacin (N/A) Trimethoprim (N/A) Trimethoprim/Sulfamethoxazole (N/A) Piperacillin/Tazobactam (N/A)
8. Swedan et al. (2024) [26]	*Klebsiella pneumoniae* (n = 167)	**Ertapenem (85.0%)** Aztreonam (57.5%) Amoxicillin/Clavulanic acid (54.5%) Levofloxacin (53.9%) Cefepime (50.9%) Cefpodoxime (47.3%) Ciprofloxacin (44.9%) Cefotaxime (40.1%) Amikacin (30.5%) Gentamicin (28.7%) Nitrofurantoin (15.0%) Azithromycin (12.6%)	**Azithromycin (87.4%)** Ciprofloxacin (46.1%) Cefepime (44.9%) Aztreonam (35.3%) Amoxicillin/Clavulanic acid (25.7%) Gentamicin (25.1%) Levofloxacin (23.4%) Amikacin (15.6%) Chloramphenicol (15.6%) Ertapenem (13.2%) Imipenem (13.2%)

Bold texts indicate the highest susceptibility and resistance among the tested antibiotics; Studies that only reported the number of susceptible or resistant isolates were converted to percentages.

Table 2. Antibiotic resistance profile of biofilm-producing bacterial isolates from each study.

Author and Year of the Study	Biofilm-forming Bacterial Isolates (n)	Susceptibility Rates	Resistance Rates
1. Almalki & Varghese (2019) [9]	Biofilm-producing Uropathogenic *Escherichia coli* (UPEC) (n = 55/211) *(Produced the most biofilm)*	**Imipenem (96%)** Norfloxacin (89%) Ofloxacin (87%) Ciprofloxacin (82%) Cefuroxime (80%) Ampicillin (78%) Amikacin (71%) Cefepime (71%) Piperacillin (60%) Nalidixic acid (29%) Tetracycline (25%) Nitrofurantoin (24%) Oxacillin (20%) Vancomycin (20%)	**Oxacillin (80%)** **Vancomycin (80%)** Nitrofurantoin (76%) Tetracycline (75%) Nalidixic acid (71%) Piperacillin (40%) Amikacin (29%) Cefepime (29%) Ampicillin (22%) Cefuroxime (20%) Ciprofloxacin (18%) Ofloxacin (13%) Norfloxacin (11%) Imipenem (4%)
	Biofilm-producing *Klebsiella pneumoniae* (n = 40/211) *(Second that produced the most biofilm)*	**Cefepime (100%)** **Ciprofloxacin (100%)** **Imipenem (100%)** Norfloxacin (97.5%) Ampicillin (95%) Amikacin (93%) Cefuroxime (90%) Tetracycline (87.5%) Piperacillin (78%) Nalidixic acid (27.5%) Ofloxacin (18%) Nitrofurantoin (15%) Oxacillin (2.5%) Vancomycin (0%)	**Vancomycin (100%)** Oxacillin (97.5%) Nitrofurantoin (85%) Ofloxacin (83%) Nalidixic acid (72.5%) Piperacillin (23%) Tetracycline (12.5%) Cefuroxime (10%) Amikacin (8%) Ampicillin (5%) Norfloxacin (2.5%) Cefepime (0%) Ciprofloxacin (0%) Imipenem (0%)
2. Aniba et al. (2023) [10]	Biofilm-producing Methicillin-resistant *Staphylococcus aureus* (MRSA) (n = 11/20)	-	**Fusidic Acid (100%)** **Penicillin G (100%)** Erythromycin (72.73%) Fosfomycin (72.73%) Tetracycline (72.73%) Tobramycin (54.55%) Teicoplanin (45.45) Gentamicin (36.36%) Levofloxacin (27.27%) Tigecycline (27.27%) Clindamycin (27.27%) Trimethoprim/Sulfamethoxazole (9.09%) Vancomycin (9.09%) Linezolid (0%)
	Biofilm-producing Methicillin-susceptible *Staphylococcus aureus* (MSSA) (n = 9/20)	-	**Penicillin G (88.89%)** Tetracycline (55.56%) Fusidic Acid (44.44%) Teicoplanin (22.22%) Vancomycin (22.22%) Clindamycin (11.11%) Erythromycin (11.11%) Fosfomycin (11.11%) Gentamicin (0%) Levofloxacin (0%) Linezolid (0%) Tigecycline (0%) Tobramycin (0%) Trimethoprim/Sulfamethoxazole (0%)
3. Dawadi et al. (2022) [14]	Biofilm-producing Uropathogenic *Escherichia coli* (UPEC) (n = 69)	**Meropenem (87.4%)** Nitrofurantoin (78.9%) Gentamicin (76.1%) Amoxicillin/Clavulanic acid (67.6%) Cephalexin (67.6%) Ceftriaxone (67.5%) Cefepime (64.8%) Ciprofloxacin (57.8%) Trimethoprim/Sulfamethoxazole (25.4%) Ampicillin (11.3%)	**Ampicillin (85.9%)** Trimethoprim/Sulfamethoxazole (71.8%) Ciprofloxacin (39.4%) Cefepime (32.4%) Amoxicillin/Clavulanic acid (29.6%) Cephalexin (29.7%) Ceftriaxone (29.7%) Gentamicin (21.1%) Meropenem (9.8%) Nitrofurantoin (18.3%)
4. de Oliveira et al. (2020) [15]	Biofilm-producing *Proteus mirabilis* (n = 183)	**Ertapenem (100%)** **Meropenem (100%)** **Piperacillin/Tazobactam (100%)** Amikacin (99.5%)	-

		Amoxicillin/Clavulanic acid (99.5%) Cephalothin (97.8%) Cefepime (98.4%) Ceftriaxone (98.4%) Cefuroxime (98.4%) Ciprofloxacin (96.7%) Norfloxacin (96.7%) Gentamicin (94.5%) Nalidixic acid (94.5%) Ampicillin (80.3%) Trimethoprim/Sulfamethoxazole (78.1%)	
5. Hasan et al. (2020) [17]	Biofilm-producing Uropathogenic *Escherichia coli* (n = 5/7)	**Amikacin (100%)** **Gentamicin (100%)** **Imipenem (100%)** Amoxicillin/Clavulanic acid (80%) Aztreonam (60%) Cefepime (60%) Trimethoprim/Sulfamethoxazole (60%) Ciprofloxacin (40%) Cefotaxime (40%) Ceftazidime (40%) Ceftriaxone (40%) Amoxicillin (0%)	**Amoxicillin (100%)** Cefotaxime (60%) Ceftriaxone (60%) Aztreonam (40%) Ceftazidime (40%) Ciprofloxacin (40%) Trimethoprim/Sulfamethoxazole (40%) Cefepime (20%) Amikacin (0%) Amoxicillin/Clavulanic acid (0%) Gentamicin (0%) Imipenem (0%)
	Biofilm-producing *Klebsiella pneumoniae* (n = 2/7)	**Amikacin (100%)** **Amoxicillin/Clavulanic acid (100%)** **Ciprofloxacin (100%)** **Gentamicin (100%)** **Imipenem (100%)** Trimethoprim/Sulfamethoxazole (50%) Amoxicillin (0%) Aztreonam (0%) Cefepime (0%) Cefotaxime (0%) Ceftazidime (0%) Ceftriaxone (0%)	**Amoxicillin (100%)** Aztreonam (100%) Cefotaxime (100%) Ceftriaxone (100%) Ceftazidime (100%) Cefepime (50%) Trimethoprim/Sulfamethoxazole (50%) Amoxicillin/Clavulanic acid (0%) Amikacin (0%) Ciprofloxacin (0%) Gentamicin (0%) Imipenem (0%)
6. Hassun a et al. (2024) [19]	Biofilm-producing Uropathogenic *Escherichia coli* ST131 (n = 79)	-	**Cefazolin (100%)** Levofloxacin (87.3%) Ceftazidime (84.2%) Tetracycline (84.2%) Nitrofurantoin (83%) Cefoxitin (64%) Ampicillin/Sulbactam (58.2%) Meropenem (40%)
7. Kar & Devnath (2021) [20]	Biofilm-producing *Pseudomonas aeruginosa* (n = 34/93) *(Produced the most biofilm)*	**Imipenem (100%)** **Meropenem (100%)** Amikacin (61.8%) Gentamicin (41.2%) Ciprofloxacin (32.4%) Amoxicillin/Clavulanic acid (8.8%) Erythromycin (8.8%) Ceftriaxone (8.8%) Trimethoprim/Sulfamethoxazole (0%) Cephalexin (0%) Cefixime (0%) Ampicillin (0%)	**Ampicillin (100%)** **Cefixime (100%)** **Cephalexin (100%)** **Trimethoprim/Sulfamethoxazole (100%)** Ceftriaxone (91.2%) Erythromycin (91.2%) Amoxicillin/Clavulanic acid (91.2%) Ciprofloxacin (67.6%) Gentamicin (58.8%) Amikacin (38.2%) Imipenem (0%) Meropenem (0%)
	Biofilm-producing *Proteus vulgaris* (n = 21/93) *(Second that produced the most biofilm)*	**Imipenem (100%)** **Meropenem (100%)** Amikacin (0%) Amoxicillin/Clavulanic acid (0%) Ampicillin (0%) Ciprofloxacin (0%) Cefixime (0%) Ceftriaxone (0%) Cephalexin (0%) Erythromycin (0%) Gentamicin (0%) Trimethoprim/Sulfamethoxazole (0%)	**Amikacin (100%)** **Amoxicillin/Clavulanic acid (100%)** **Ampicillin (100%)** **Ciprofloxacin (100%)** **Cefixime (100%)** **Ceftriaxone (100%)** **Cephalexin (100%)** **Erythromycin (100%)** **Gentamicin (100%)** **Trimethoprim/Sulfamethoxazole (100%)** Imipenem (0%) Meropenem (0%)
8. Mirzaei et al. (2021) [23]	Biofilm-producing *Proteus mirabilis* (n = 40)	**Ampicillin-sulbactam** (95%)	**Tetracycline (95%)** Nitrofurantoin (92.5%) Trimethoprim/Sulfamethoxazole (75%) Ciprofloxacin (45%) Cefotaxime (42.5%) Ofloxacin (40%)

			Ampicillin (35%) Meropenem (30%) Norfloxacin (25%) Cefixime (22.5%) Amoxicillin/Clavulanic acid (22.5%) Amikacin (15%) Aztreonam (15%) Ceftazidime (7.5%) Ampicillin/Sulbactam (2.5%)
9. Mlugu et al. (2023) [24]	Biofilm-producing Uropathogenic *Escherichia coli* (UPEC) (n = 34)	-	**Ampicillin (79.41%)** **Trimethoprim/Sulfamethoxazole (79.41%)** Amoxicillin/Clavulanic acid (64.71%) Ciprofloxacin (44.12%) Nitrofurantoin (38.24%) Ceftriaxone (35.29%)
10. Raya et al. (2019) [25]	Biofilm-producing Uropathogenic *Escherichia coli* (UPEC) (n = 34)	-	**Amoxicillin (93.2%)** Ciprofloxacin (75.3%) Ceftriaxone (69.9%) Trimethoprim/Sulfamethoxazole (68.5%) Piperacillin/Tazobactam (35.6%) Tetracycline (26.0%) Amikacin (12.3%) Nitrofurantoin (12.3%) Imipenem (9.6%)

Bold texts indicate the highest susceptibility and resistance among the tested antibiotics; Studies that only reported the number of susceptible or resistant isolates were converted to percentages.

Biofilm-forming Bacteria Causing UTIs

Table 3. Biofilm formation of UTI-causing bacteria from each study.

Author and Year of the Study	Number of Isolates	Bacteria Isolated (n, %)	Biofilm Producers (n, %)	Non-biofilm Producers (n, %)	Bacteria Producing the Most Biofilm
1. Almalki & Varghese (2019) [9]	585	*Escherichia coli (24%)* *ESBL Escherichia coli* (2%) *Klebsiella pneumoniae* (19%) *Enterococcus faecalis* (8%) *Staphylococcus aureus* (3%) *Proteus mirabilis* (18%) *Pseudomonas aeruginosa* (17%) *Citrobacter spp.* (9%)	211, 36.06%	374, 63.9%	*Escherichia coli* (24%)
2. Aniba et al. (2023) [10]	20	*Staphylococcus aureus* (100%)	20, 100%	0, 0%	*Staphylococcus aureus* (100%)
3. Arafa et al. (2022) [11]	50	Uropathogenic *Escherichia coli* (UPEC)	22, 44%	28, 56%	UPEC (44%)
4. Baldiris-Avila et al. (2020) [12]	190	Uropathogenic *Escherichia coli* (UPEC)	168, 88%	22, 12%	UPEC (88%)
5. Ballen et al. (2021) [13]	127	*Klebsiella pneumoniae*	102, 80%	25, 20%	*Klebsiella pneumoniae* (80%)
6. Dawadi et al. (2022) [14]	71	Uropathogenic *Escherichia coli* (UPEC)	69, 97.2%	2, 2.8%	UPEC (97.2%)
7. de Oliveira et al. (2020) [15]	183	*Proteus mirabilis*	183, 100%	0, 0%	*Proteus mirabilis* (100%)
8. Gajdacs et al. (2021) [16]	250	*Escherichia coli*	108, 43.2%	142, 56.8%	*Escherichia coli* (43.2%)
9. Hasan et al. (2020) [17]	7	*Escherichia coli* (5, 71%) *Klebsiella pneumoniae* (2, 29%)	7, 100%	0, 0%	-
10. Hashemzadeh et al. (2020) [18]	43	*Staphylococcus saprophyticus*	28, 63%	15, 37%	*Staphylococcus saprophyticus* (63%)

11. Hassuna et al. (2024) [19]	166	*Escherichia coli*	79, 88%	11, 12%	*Escherichia coli* (88%)
12. Kar & Devnath (2021) [20]	131	*Pseudomonas aeruginosa* (38, 29%) *Escherichia coli* (31, 24%) *Proteus vulgaris* (24, 18%) *Klebsiella pneumoniae* (21, 16%) *Staphylococcus aureus* (17, 13%)	93, 71%	38, 29%	*Pseudomonas aeruginosa* (36.5%)
13. Katongole et al. (2020) [21]	200	Uropathogenic *Escherichia coli* (UPEC)	125, 62.5%	75, 37.5%	UPEC (62.5%)
14. Kumar et al. (2023) [22]	232	Uropathogenic *Escherichia coli* (UPEC)	145, 62.5%	-	UPEC (62.5%)
15. Mirzaei et al. (2021) [23]	40	*Proteus mirabilis*	40, 100%	0, 0%	*Proteus mirabilis* (100%)
16. Mlugu et al. (2023) [24]	141	Uropathogenic *Escherichia coli* (UPEC) (47%) *Pseudomonas aeruginosa* (17%) *Proteus mirabilis* (14.2%) *Klebsiella pneumoniae* (11.4%) Non-identified Gram-negative bacilli (9.9%)	UPEC 34/66, 51.5%	UPEC 32/36, 48.5%	UPEC (51.5%)
17. Raya et al. (2019) [25]	238	*Enterobacterales* *Escherichia coli* *Klebsiella spp.* *Enterobacter spp.* *Citrobacter spp.* *Proteus spp.* *Morganella morganii* *Non-Enterobacterales* *Pseudomonas aeruginosa* *Acinetobacter spp.* Gram-positive non-hemolytic *Streptococci* Coagulase-negative *Staphylococcus*	103, 43.3%	135, 56.7%	*Escherichia coli* (70.9%)
18. Sweden et al. (2024)	167	*Klebsiella pneumoniae*	154, 92.2%	-	*Klebsiella pneumoniae* (92.2%)

Figure 1. Study Selection Flowchart

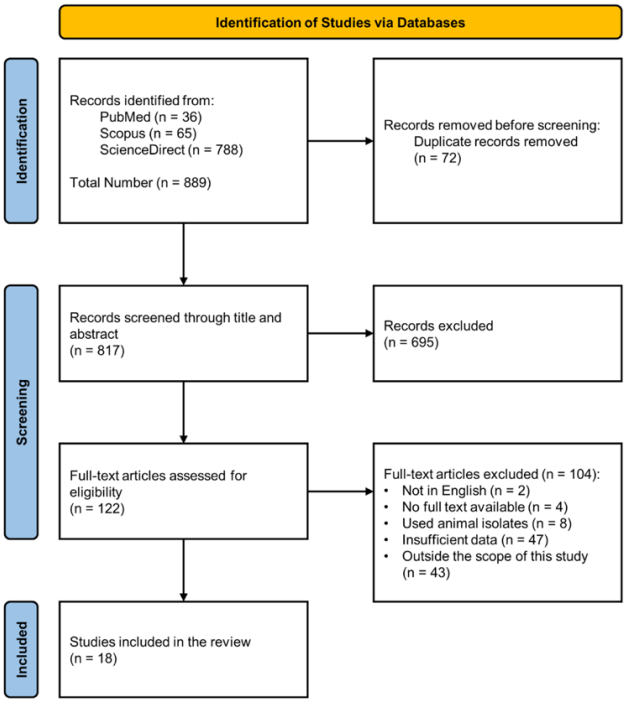


Figure 2. Geography of the 18 chosen articles for systematic review

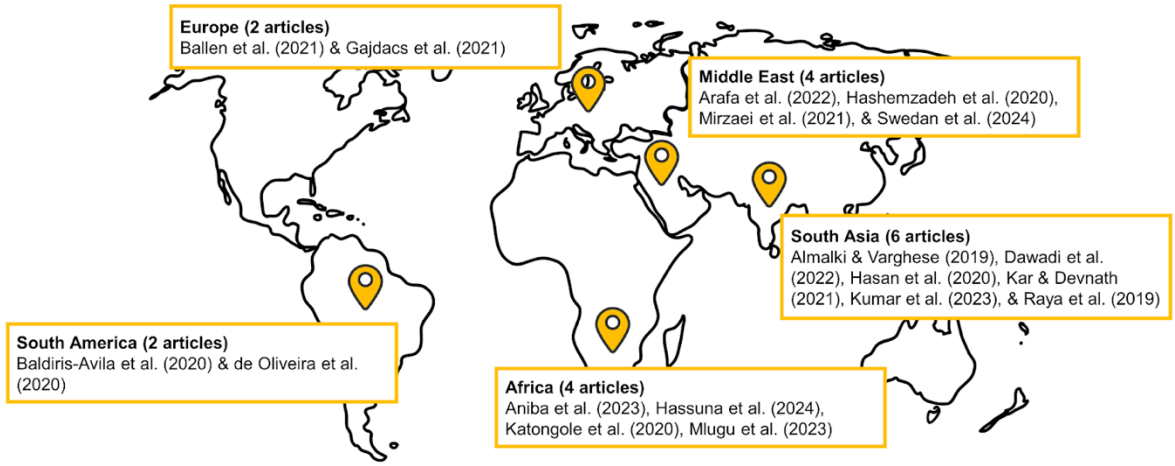


Figure 3. Antibiotic resistance rates of biofilm-producing UPEC across 18 studies

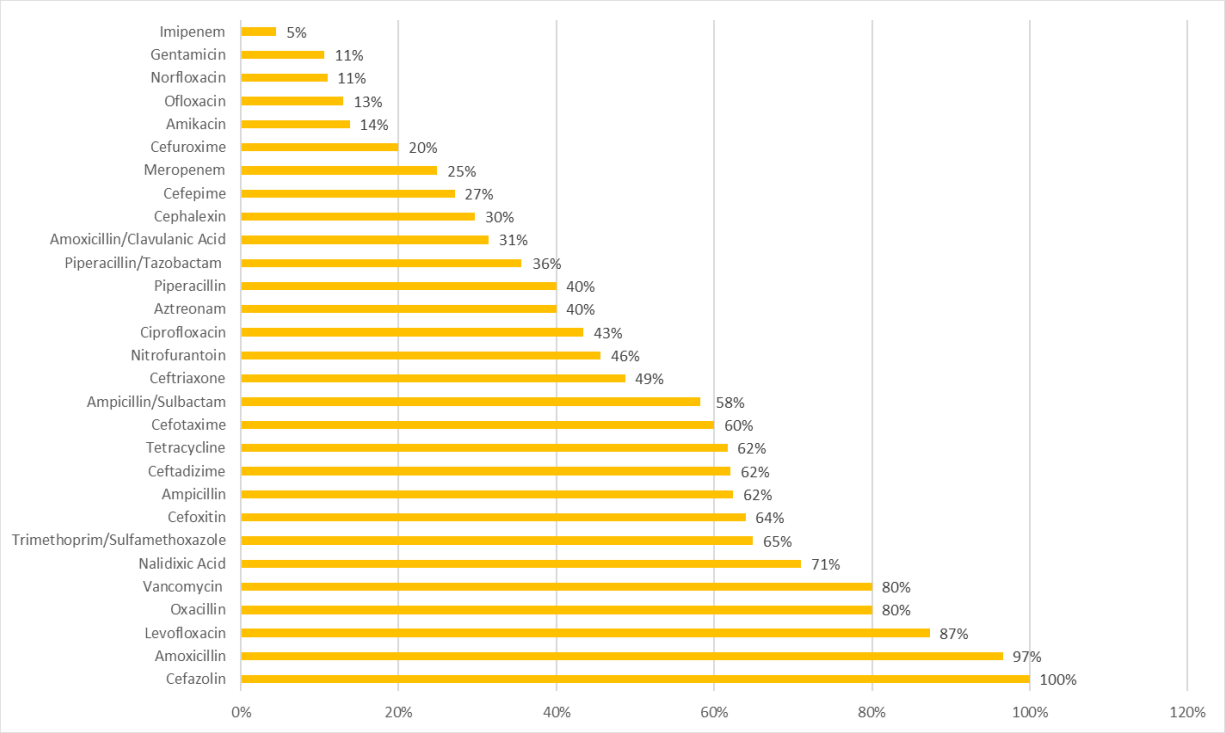
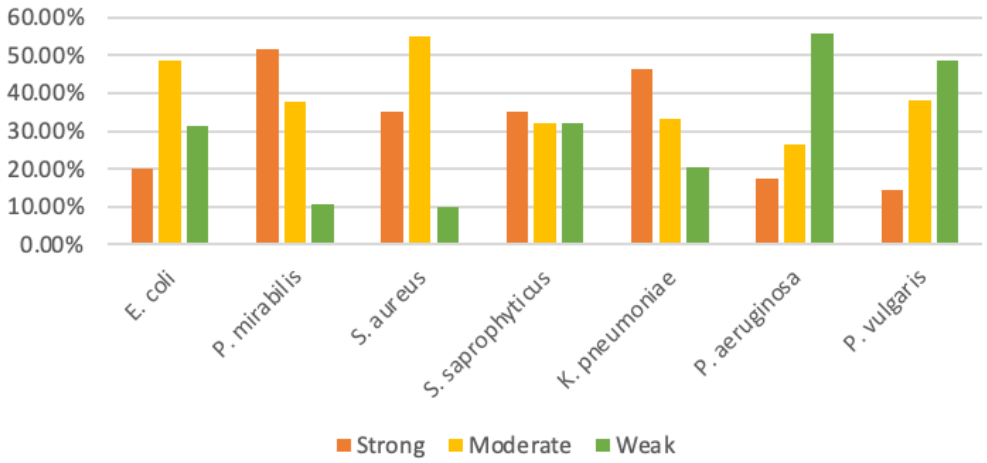


Figure 4. Intensity of biofilm formation among biofilm-forming bacteria



Conclusion

This systematic review highlights the alarming rise of antibiotic-resistant, biofilm-forming bacterial pathogens in UTIs, emphasizing their significant role in persistent and recurrent infections. The findings confirm that uropathogenic *E. coli* (UPEC), *K. pneumoniae*, *P. aeruginosa*, and *P. mirabilis* are among the most prevalent biofilm-forming pathogens, exhibiting high resistance to commonly prescribed antibiotics. Carbapenems, particularly imipenem and meropenem, demonstrated the highest efficacy against these resistant bacteria, though growing resistance trends remain a concern.

The ability of UTI-causing bacteria to form biofilms serves as a critical survival mechanism, enhancing their resistance to antibiotics and host immune responses. Biofilm formation intensity varied across bacterial species, with *P. mirabilis* and *K. pneumoniae* exhibiting strong biofilm-producing capabilities. The association between biofilm formation and MDR further complicates UTI management, necessitating the urgent need for alternative treatment strategies.

Factors such as prolonged catheterization, frequent antibiotic misuse, female anatomy, underlying health conditions, and hospital-acquired infections contribute significantly to the persistence of UTIs. The findings underscore the necessity of stringent antibiotic stewardship programs, improved infection control measures, and the development of innovative therapeutic approaches, including anti-biofilm agents and bacteriophage therapy.

Future research should focus on novel treatment alternatives targeting biofilm disruption, rapid diagnostic methods for early detection of resistant strains, and personalized medicine approaches to optimize UTI treatment. Addressing these challenges is crucial in mitigating the global burden of biofilm-associated UTIs and enhancing patient outcomes.

Disclosure of Potential Conflicts of Interest

Declaration of Interest

The authors declare no competing interest.

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Contributors:

AAF, SD, JCE, JRE, ANSC, DAC, and DME conceptualized and designed the study. EAC guided in the development of the methodology, interpretation of data, and manuscript writing. AAF, SD, JCE, and JRE performed the literature search and extracted the data. AAF, SD, JCE, JRE, ANSC, DAC, and DME wrote the initial draft of the manuscript. AAF, SD, JCE, JRE, and EAC wrote and revised the full paper. All authors have read and agreed to the published version of the manuscript.

References

1. Medina-Polo J, Naber KG, Bjerklund Johansen TE. Healthcare-associated urinary tract infections in urology. GMS Infect Dis. 2021; 9. doi: 10.3205/id000074
2. Mancuso G, Trinchera M, Midiri A, Zummo S, Vitale G, Biondo C. (2024). Novel antimicrobial approaches to combat bacterial biofilms associated with urinary tract infections. Antibiotics. 2024; 13(2): 154. doi: 10.3390/antibiotics13020154
3. Oumer Y, Regasa B, Seid M, Biresaw G, Manilal A. Catheter-associated urinary tract infection: Incidence, associated factors and drug resistance patterns of bacterial isolates in Southern Ethiopia. Infection and Drug Resistance. 2021; 14: 2883–2894. doi: 10.2147/IDR.S311229
4. Agarwal J, Radera, S. Biofilm-mediated urinary tract infections. Biofilms in Human Diseases: Treatment and Control. 2019; 177–213. doi: 10.1007/978-3-030-30757-8_13
5. Rajmane A, Joshi P, Shikhare V, Ramteerthakar M, Kulkarn V. A study of biofilm production and antimicrobial susceptibility pattern among urinary isolates. Indian Journal of Microbiology Research. 2021; 8(4): 268–273. doi: 10.18231/j.ijmr.2021.055
6. Abu Lila A, Rajab A, Abdallah M, Rizvi S, Moin A, Khafagy E, et al. Biofilm lifestyle in recurrent urinary tract infections. Life. 2023; 13(1): 148–148. doi: 10.3390/life13010148
7. Raymond B. Five rules for resistance management in the antibiotic apocalypse, a road map for Integrated Microbial Management. Evolutionary Applications. 2019; (6): 1079–1091. doi:10.1111/eva.12808
8. Selçuk, AA. A guide for systematic reviews: PRISMA. Turk Arch Otorhinolaryngol. 2019; 57(1): 57–58. doi: 10.5152/tao.2019.4058
9. Almalki MA, Varghese R. Prevalence of catheter associated biofilm producing bacteria and their antibiotic sensitivity pattern. Journal of King Saud University – Science. 2019; 32(2): 1427–1433. doi: 10.1016/j.jksus.2019.11.037
10. Aniba R, Dihmane A, Raqraq H, Ressmi A, Nayme K, Timinouni M, et al. Characterization of biofilm formation in uropathogenic Staphylococcus aureus and their association with antibiotic resistance. The Microbe. 2023; 2. doi: 10.1016/j.microb.2023.100029
11. Arafa SH, Alshehri WA, Organji SR, Elbanna K, Obaid NA, Aldosari MS, et al. Antimicrobial resistance, virulence factor-encoding genes, and biofilm-forming ability of community-associated uropathogenic Escherichia coli in Western Saudi Arabia. Polish Journal of Microbiology. 2022; 71(3): 325–339. doi: 10.33073/pjm-2022-029
12. Baldiris-Avila R, Montes-Robledo A, Buelvas-Montes Y. Phylogenetic classification, biofilm-forming capacity, virulence factors, and antimicrobial resistance in uropathogenic Escherichia coli (UPEC). Current Microbiology. 2020; 77(11): 3361–3370. doi: 10.1007/s00284-020-02173-2
13. Ballén V, Gabasa Y, Ratia C, Ortega R, Tejero M, Soto S. Antibiotic resistance and virulence profiles of Klebsiella pneumoniae strains isolated from different clinical sources. Frontiers in Cellular and Infection Microbiology. 2021; 11. doi: 10.3389/fcimb.2021.738223

14. Dawadi P, Khanal S, Joshi TP, Kc S, Tuladhar R, Maharjan BL, et al. Antibiotic resistance, biofilm formation and sub-inhibitory hydrogen peroxide stimulation in uropathogenic Escherichia coli. Microbiology Insights. 2022; 15. doi: 10.1177/11786361221135224

15. de Oliveira WD, Barboza MGL, Faustino G, Inagaki WTY, Sanches MS, Kobayashi RKT, et al. Virulence, resistance and clonality of Proteus mirabilis isolated from patients with community-acquired urinary tract infection (CA-UTI) in Brazil. Microbial Pathogenesis. 2021; 152: 104642. doi: 10.1016/j.micpath.2020.104642

16. Gajdács M, Kárpáti K, Nagy ÁL, Gugolya M, Stájer A, Burián K. Association between biofilm-production and antibiotic resistance in Escherichia coli isolates: A laboratory-based case study and a literature review. Acta microbiologica et immunologica Hungarica. 2021. doi: 10.1556/030.2021.01487

17. Hasan ME, Shahriar A, Shams F, Nath AK, Emran TB. Correlation between biofilm formation and antimicrobial susceptibility pattern toward extended spectrum β-lactamase (ESBL)- and non-ESBL-producing uropathogenic bacteria. Journal of Basic and Clinical Physiology and Pharmacology. 2020; 32(2). doi: 10.1515/jbcpp-2019-0296

18. Hashemzadeh M, Dezfuli AAZ, Nashibi R, Jahangirimehr F, Akbarian ZA. Study of biofilm formation, structure and antibiotic resistance in Staphylococcus saprophyticus strains causing urinary tract infection in women in Ahvaz, Iran. New Microbes and New Infections. 2020; 39: 100831. doi: 10.1016/j.nmni.2020.100831

19. Hassuna NA, Rabea EM, Mahdi WK, Abdelraheem WM. Biofilm Formation and antimicrobial resistance pattern of uropathogenic E. coli ST131 isolated from children with malignant tumors. The Journal of Antibiotics. 2024; 77(5): 324–330. doi: 10.1038/s41429-024-00704-8

20. Kar S, Devnath P. Biofilm formation and antibiotic resistance of urinary catheter associated bacteria from hospitalized patients, Bangladesh. Malaysian Journal of Microbiology. 2021; 17(6): 635–645. doi: 10.21161/mjm.211169

21. Katongole P, Nalubega F, Florence NC, Asiimwe B, Andia I. Biofilm formation, antimicrobial susceptibility and virulence genes of uropathogenic Escherichia coli isolated from clinical isolates in Uganda. BMC Infectious Diseases. 2020; 20(1). doi: 10.1186/s12879-020-05186-1

22. Kumar G, Kumar Y, Kumar G, Tahlan AK. Characterization of uropathogenic E. coli from various geographical locations in India. Journal of Taibah University Medical Sciences. 2023; 18(6): 1527–1535. doi: 10.1016/j.jtumed.2023.07.003

23. Mirzaei A, Esfahani BN, Raz A, Ghanadian M, Moghim S. (2021). From the urinary catheter to the prevalence of three classes of integrons, β-lactamase genes, and differences in antimicrobial susceptibility of Proteus mirabilis and clonal relatedness with Rep-PCR. BioMed Research International. 2021; 2021(1): 1–10. doi: 10.1155/2021/9952769

24. Mlugu EM, Mohamedi JA, Sangeda RZ, Mwambete KD. Prevalence of urinary tract infection and antimicrobial resistance patterns of uropathogens with biofilm forming capacity among outpatients in Morogoro, Tanzania: A cross-sectional study. BMC Infectious

Diseases. 2023; 23(1). doi: 10.1186/s12879-023-08641-x

25. Raya S, Belbase A, Dhakal L, Prajapati KG, Baidya R, Bimali NK. In-vitro biofilm formation and antimicrobial resistance of Escherichia coli in diabetic and nondiabetic patients. BioMed Research International. 2019; 2019: 1–8. doi: 10.1155/2019/1474578
26. Swedan SF, Aldakhily DB. Antimicrobial resistance, biofilm formation, and molecular detection of efflux pump and biofilm genes among Klebsiella pneumoniae clinical isolates from Northern Jordan. Heliyon. 2024; 10(14). doi: 10.1016/j.heliyon.2024.e34370
27. Hunjra NA, Ashraf A, Niamat H. The comparative efficacy of imipenem and meropenem on different bacterial strains obtained from clinical samples. Pakistan Journal of Health Sciences 2022; 3(5): 229–233. doi: 10.54393/pjhs.v3i05.156
28. Calzada FC, Aguilera-Correa JJ, González JC, Moreno JE, Biosca DR, Pérez-Tanoira R. Urinary tract infection and antimicrobial susceptibility of bacterial isolates in Saint Joseph Kitgum Hospital, Kitgum, Uganda. Antibiotics. 2022; 11(4): 504–504. doi: 10.3390/antibiotics11040504
29. Shah TA, Preethishree P, Ashwini, Pai V. Bacterial profile of urinary tract infections: Evaluation of biofilm formation and antibiotic resistance pattern of uropathogenic Escherichia coli. J Pure Appl Microbiol. 2020; 14(4): 2577–2584 doi: 10.22207/jpam.14.4.33
30. Kot B. Antibiotic resistance among uropathogenic Escherichia coli. Polish Journal of Microbiology. 2019; 68(4): 403–415. doi: 10.33073/pjm-2019-048
31. Duicu C, Cozea I, Delean D, Aldea A, Aldea C. Antibiotic resistance patterns of urinary tract pathogens in children from Central Romania. Experimental and Therapeutic Medicine. 2021; 22(1): 748. doi: 10.3892/etm.2021.10180
32. Rosana Y, Billy M, Ocviyanti D. In vitro resistance pattern of urinary tract infections-causing bacteria to ampicillin and ciprofloxacin. Obstetrics & Gynecology International Journal. 2019; 10(5): doi: 10.15406/ogij.2019.10.00469
33. Das BK, Kumar V, Baitha R, Ramteke M, Adhikari A, Bisai K, et al. The emergence of multidrug-resistant Proteus vulgaris infection in cage reared Pangasianodon hypophthalmus: Molecular characterization and host-pathogen response. Microbial Pathogenesis. 2024; 197: 107029. doi: 10.1016/j.micpath.2024.107029
34. Shree P, Singh CK, Sodhi KK, Surya JN, Singh DK. Biofilms: Understanding the structure and contribution towards bacterial resistance in antibiotics. Medicine in Microecology. 2023; 16, 100084. doi: 10.1016/j.medmic.2023.100084
35. Naziri Z, Kilegolan JA, Moezzi MS, Derakhshandeh A. Biofilm formation by uropathogenic Escherichia coli: A complicating factor for treatment and recurrence of urinary tract infections. Journal of Hospital Infection. 2021; 117: 9–16. doi: 10.1016/j.jhin.2021.08.017
36. Castillo FYR, Barrera ALG, Harel J, González FJA, Vogeleer P, Guerra JMA, et al. Biofilm formation by Escherichia coli isolated from urinary tract infections from Aguascalientes, Mexico Microorganisms. 2023; 11(12): 2858. doi: 10.3390/microorganisms11122858

37. Sabir N, Ikram A, Zaman G, Satti L, Gardezi A, Ahmed A, et al. Bacterial biofilm-based catheter-associated urinary tract infections: Causative pathogens and antibiotic resistance. American Journal of Infection Control. 2017; 45(10): 1101–1105. doi: 10.1016/j.ajic.2017.05.009

38. Kaur R, Kaur R. Symptoms, risk factors, diagnosis and treatment of urinary tract infections. Postgraduate Medical Journal. 2020; 97(1154): 803–812. doi: 10.1136/postgradmedj-2020-139090

39. Trinchera M, Midiri A, Mancuso G, Lagrotteria MA, De Ani CA, Biondo C. A four-year study of antibiotic resistance, prevalence and biofilm-forming ability of uropathogens isolated from community- and hospital-acquired urinary tract infections in Southern Italy. Pathogens. 2025; 14(1): 59. doi: 10.3390/pathogens14010059

40. Mirzahosseini HK, Hadadi-Fishani M, Morshedi K, Khaledi A. Meta-analysis of biofilm formation, antibiotic resistance pattern, and biofilm-related genes in Pseudomonas aeruginosa isolated from clinical samples. Microbial Drug Resistance. 2020; 26(7): 815–824. doi: 10.1089/mdr.2019.0274

41. de Sousa T, Hébraud M, Alves O, Costa E, Maltez L, Pereira JE, et al. Study of antimicrobial resistance, biofilm formation, and motility of Pseudomonas aeruginosa derived from urine samples. Microorganisms. 2023; 11(5): 1345. doi: 10.3390/microorganisms11051345

42. Yousefi M, Pourmand MR, Fallah F, Hashemi A, Mashhadi R, Nazari-Alam A. Characterization of Staphylococcus aureus biofilm formation in urinary tract infection. Iranian Journal of Public Health. 2016; 45(4): 485–493. https://pmc.ncbi.nlm.nih.gov/articles/PMC4888176/#:~:text=Overall%2C%2069.2%25%20of%20S.,%2C%20tetracycline%20(57.7%25%20vs.

43. Kwiecinska-Pirog J, Skowron K, Bartczak W, Gospodarek-Komkowska E. The ciprofloxacin impact on biofilm formation by Proteus Mirabilis and P. vulgaris strains. Jundishapur Journal of Microbiology. 2016; 9(4). doi: 10.5812/jjm.32656

44. Wasfi R, Hamed SM, Amer MA, Fahmy LI. Proteus mirabilis biofilm: Development and therapeutic strategies. Frontiers in Cellular and Infection Microbiology. 2020; 10. doi: 10.3389/fcimb.2020.00414

45. Salama LA, Saleh HH, Abdel-Rhman SH, Barwa R, Hassan R. Assessment of typing methods, virulence genes profile and antimicrobial susceptibility for clinical isolates of Proteus mirabilis. Annals of Clinical Microbiology and Antimicrobials. 2025; 24(4). doi: 10.1186/s12941-024-00770-8

46. Mohsenzadeh M, Abtahi-Eivary SH, Pirouzi A, Khaledi A, Rahimi M. A systematic review and meta-analysis of urinary tract infection, frequency of IS elements and MDR isolates retrieved from adult patients. Gene Reports. 2020; 20: 100707. doi: 10.1016/j.genrep.2020.100707

47. Neupane S, Pant ND, Khatiwada S, Chaudhary R, Banjara MR. Correlation between biofilm formation and resistance toward different commonly used antibiotics along with extended spectrum beta lactamase production in uropathogenic Escherichia coli isolated from the patients suspected of urinary tract infections visiting Shree Birendra Hospital, Chhauni, Kathmandu, Nepal. Antimicrobial

Resistance & Infection Control. 2016; 5(1). doi: 10.1186/s13756-016-0104-9

48. Mukonzo JK, Namuwenge PM, Okure G, Mwesige B, Namusisi OK, Mukanga D. Over-the-counter suboptimal dispensing of antibiotics in Uganda. Journal of Multidisciplinary Healthcare. 2013; 6: 303–310 doi:10.2147/jmdh.s49075

49. Rodriguez-Mañas L. Urinary tract infections in the elderly: A review of disease characteristics and current treatment options. Drugs Context. 2020; 9: 1–8. doi:10.7573/dic.2020-4-13

50. Storme O, Saucedo JT, Garcia-Mora A, Dehesa-Dávila M, Naber KG. Risk factors and predisposing conditions for urinary tract infection. Therapeutic Advances in Urology. 2019; 11. doi:10.1177/1756287218814382

51. Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, Currie M, Qureshi R, Mattis P, Lisy K, Mu P-F. Chapter 7: Systematic reviews of etiology and risk. In: Aromataris E, Munn Z (Editors). JBI Manual for Evidence Synthesis. JBI, 2020. Available from https://synthesismanual.jbi.glob

Ferrer AA, Decasa S, Elauria JC, Esguerra JR, Cano EA, Coderos ANS, Cruz DA, Exala DM. Antibiotic resistance of biofilm-forming bacteria causing urinary tract infections: A systematic review. Microbes Infect Dis 2025; 6(3): 6023-6042.