

Recurrent Urinary Tract Infection in Diabetic versus Non-Diabetic Patients in India: A Phenotypic Microbiological Approach

Jaikaran Singh Bakshi¹, Yashdeep Srivastava², Jyoti Trivedi³, Rahul Arora⁴

¹PhD Scholar, Department of Biotechnology, Invertis University, Bareilly, (U.P.)

²Assistant Professor, Department of Biotechnology, Invertis University, Bareilly, (U.P.)

³Assistant Professor, Department of Biochemistry, Autonomous State Medical College, Pilibhit, (U.P.)

⁴Professor (Pharmacology) Department of Pharmacy, Invertis University, Bareilly, (U.P.)

Corresponding Author- Dr Yashdeep Srivastava², Assistant Professor, Department of Biotechnology, Invertis University, Bareilly, (U.P.)

Email: - yashbubiotech@gmail.com

Abstract

Urinary tract infection continues to be one of the most frequently encountered bacterial infections in clinical practice, and patients with diabetes mellitus form a group that is disproportionately affected by it. Altered host defence, incomplete bladder emptying and persistent glycosuria together create an internal environment that is more hospitable to uropathogens, so infections in this group tend to recur more often, respond less predictably to standard antibiotics and involve a wider range of resistant organisms than infections seen in people without diabetes. This review draws together the available literature, with particular attention to work carried out in India over the past decade; to examine how recurrent urinary tract infection behaves differently in diabetic and non-diabetic patients. The epidemiological burden, the immunological basis of increased susceptibility, the range of causative organisms, and the phenotypic laboratory methods used to identify resistance mechanisms such as extended-spectrum beta-lactamase, AmpC beta-lactamase and carbapenemase production are discussed in turn. The contribution of biofilm formation to recurrence, the relationship between glycaemic control and resistance severity, and the practical difficulty of separating relapse from reinfection in routine microbiology laboratories are also considered. Existing risk-prediction approaches for recurrent infection in diabetic patients are reviewed, along with Indian antimicrobial resistance surveillance data that place the problem in a national context. The review closes by identifying gaps that remain in the literature, particularly the relative scarcity of studies from India that combine phenotypic resistance detection, biofilm assessment and glycaemic correlation within a single, adequately powered comparative design, and argues that addressing this gap could meaningfully improve empirical treatment decisions and long-term management of diabetic patients with recurrent infection.

Keywords: recurrent urinary tract infection, diabetes mellitus, antimicrobial resistance, extended-spectrum beta-lactamase, AmpC beta-lactamase, carbapenemase, biofilm, glycated haemoglobin, India

How to cite this article: Jaikaran Singh Bakshi, Yashdeep Srivastava, Jyoti Trivedi, Rahul Arora. Recurrent Urinary Tract Infection in Diabetic versus Non-Diabetic Patients in India: A Phenotypic Microbiological Approach. Int J Drug Deliv Technol. 2026;16(88s):284-296. DOI: 10.25258/ijddt.16.88s.28.

1. Introduction

Urinary tract infection is among the commonest reasons for a patient to present to a general physician, and among the commonest indications for empirical antibiotic prescription in outpatient practice. Its overall burden is well documented, but the picture changes considerably once diabetes mellitus is introduced as a co-existing condition. Diabetes is no longer a disease confined to affluent, older populations; the most recent nationwide ICMR-INDIAB survey estimates that over 101 million adults in India now live with diabetes and a further 136 million with prediabetes, with wide inter-state variation in prevalence [54,55]. Against this backdrop, the International Diabetes Federation similarly projects a continued rise in the global diabetic population over the coming decades, with India remaining among the countries carrying the largest absolute burden [59]. A substantial proportion of this

diabetic population develops one or more urinary infections during the course of their illness. What sets these infections apart from those occurring in the general population is not merely their frequency but their tendency to recur, their broader microbiological spectrum, and their frequent association with organisms that are difficult to treat with first-line antibiotics.

The reasons for this difference are reasonably well worked out at a physiological level. Hyperglycaemia impairs several arms of innate immunity, glycosuria provides an additional carbon source for bacterial growth within the urinary tract, and autonomic neuropathy affecting bladder function leads to incomplete voiding and stasis of urine, all of which favour bacterial persistence. When persistence is compounded by the ability of certain uropathogens to form biofilms on the urothelial surface, the result is an

infection that keeps returning despite courses of antibiotics that would ordinarily be curative in a non-diabetic patient. Recurrence of this kind poses two distinct clinical problems. The first is therapeutic: repeated antibiotic exposure selects for resistant organisms, so that by the time a patient has had several episodes, the causative pathogen is frequently found to be a producer of extended-spectrum beta-lactamase, AmpC beta-lactamase, or in some instances a carbapenemase. The second is diagnostic: distinguishing a true relapse of the original infecting strain from a fresh reinfection with a different organism is not always straightforward using the culture and sensitivity methods available in a routine diagnostic laboratory.

The present review has been undertaken with these problems in mind. Rather than restating the well-known association between diabetes and infection susceptibility in general terms, an attempt has been made to bring together studies that specifically compare diabetic and non-diabetic patients with recurrent urinary tract infection, with emphasis on Indian data wherever it is available, and to examine the phenotypic microbiological methods that remain the mainstay of resistance detection in most Indian laboratories, since molecular and genomic techniques are still confined to a small number of referral and research centres. The review is organised to move from the epidemiological burden of the problem, through its pathophysiological and microbiological basis, into the practical laboratory methods used to characterise resistance and biofilm formation, before considering how glycaemic status, recurrence classification and risk-prediction models fit into the overall clinical picture.

2. Epidemiological Burden of Urinary Tract Infection in Diabetes Mellitus

2.1 The Global Picture

A systematic review and meta-analysis published in 2022 pooling data from multiple countries reported that the prevalence of urinary tract infection among patients with type 2 diabetes mellitus is considerably higher than that reported in the general adult population, with wide variation between individual studies depending on setting, diagnostic criteria and the population studied [1]. A comparable pattern has been reported from the Middle East, where a large cross-sectional study of diabetic patients attending a specialist diabetes institute in Kuwait found that urinary tract infection was substantially more common among patients with poorly controlled glycaemia than among those with well-controlled blood glucose, and that *Escherichia coli* and *Klebsiella pneumoniae* together accounted for the majority of positive cultures in both groups [2].

Reviews focusing specifically on recurrent infection rather than a single episode have reached similar conclusions. A systematic review examining recurrent urinary tract infection in women with type 2 diabetes mellitus concluded that diabetes acts as an independent risk factor for recurrence, and that the pattern of causative organisms and their resistance profile in this population differs sufficiently from that of non-diabetic women to warrant separate consideration in treatment guidelines [6]. Another systematic review that examined the underlying laboratory and animal-model literature on bacterial urinary tract infection in diabetes drew attention to the range of molecular and cellular mechanisms, from impaired neutrophil recruitment to altered urothelial receptor expression, that together explain why the diabetic bladder behaves differently from a non-diabetic one when challenged with the same organism [7]. Region-specific meta-analyses, including one covering diabetic patients across Ethiopia, have similarly reported prevalence figures for urinary tract infection well above what is typically quoted for the general population, along with consistent risk factors such as female sex, longer duration of diabetes and poor glycaemic control [9].

2.2 The Indian Perspective

India's diabetic population is large enough that even modest infection rates translate into a considerable clinical burden, and several hospital-based Indian studies have looked specifically at how urinary tract infection presents differently in diabetic patients compared with non-diabetics. A prospective comparative study conducted in a tertiary care hospital in the National Capital Territory of Delhi, which enrolled equal numbers of diabetic and non-diabetic adults with culture-proven urinary tract infection, found that while the causative organisms overlapped considerably between the two groups, diabetic patients presented more often with atypical symptoms such as vomiting and incontinence rather than the classical triad of fever, dysuria and frequency, and were significantly more likely to develop pyelonephritis [3]. A separate hospital-based study of bacteriuria in diabetic patients reported that nearly half of the patients screened had significant bacteriuria, with poor glycaemic control and diabetic complications such as neuropathy and foot disease showing a clear association with the presence of infection [4].

Studies that have followed diabetic patients over time rather than simply documenting a single episode provide a somewhat more concerning picture. An Indian study examining risk factors specifically for recurrence in type 2 diabetic patients followed a cohort for six months after an initial episode and found that a substantial minority developed a further infection during that period, with poor renal function and

elevated glycated haemoglobin (HbA1c) emerging as significant predictors of recurrence on multivariate analysis in men, while renal calculi, cystopathy and poor glycaemic control were associated with recurrence in women [5]. Taken as a whole, the Indian literature supports the broader international picture: diabetic patients do not merely acquire urinary tract infection more often, they also experience a more complicated and recurrence-prone course once infection sets in, which in turn is what drives the interest in phenotypic microbiological characterisation of the organisms responsible.

Asymptomatic bacteriuria, defined as significant bacterial growth in urine in the absence of symptoms, deserves separate mention because it is considerably more common in diabetic patients and is thought to precede a proportion of symptomatic episodes. A global meta-analysis pooling data across several countries estimated the incidence of asymptomatic bacteriuria in type 2 diabetic patients at close to a quarter of the population studied, with age, female sex, duration of diabetes, HbA1c, hypertension and proteinuria identified as consistent risk factors [51]. A Greek case-control study reported a comparable prevalence and additionally found that vitamin B12 status was inversely associated with the presence of asymptomatic bacteriuria, an association that has not yet been explored in Indian cohorts [52]. Indian data on this question, though more limited in sample size, point in the same direction: a prospective study from Kolkata found that long-standing diabetes was the principal risk factor for asymptomatic bacteriuria, and that patients with poor baseline glycaemic control were more likely to progress to symptomatic infection during follow-up [40], while a separate case-control study from Srinagar and a hospital-based study from Punjab reported similar prevalence figures along with an association between renal function and the presence of bacteriuria [41,53]. Frailty has also been identified as an independent contributor to urinary tract infection risk in diabetic patients with chronic kidney disease in a very large Taiwanese cohort, suggesting that the accumulation of comorbidity, rather than diabetes alone, may be what ultimately drives the highest-risk subgroup [44].

3. Pathophysiological Basis of Increased Susceptibility

The heightened susceptibility of diabetic patients to urinary tract infection cannot be explained by a single mechanism, and the literature on diabetes-associated immune dysfunction describes a combination of metabolic, neurological and immunological changes acting together. At the level of innate immunity, chronic hyperglycaemia has been shown to impair neutrophil chemotaxis, phagocytic activity and the generation of reactive oxygen species required for

intracellular killing of bacteria, so that even when neutrophils are recruited to the site of infection in adequate numbers, their bactericidal efficiency is reduced [7]. Reviews of immune dysregulation in type 2 diabetes mellitus have extended this picture further, describing alterations in macrophage function, natural killer cell activity and cytokine signalling, including toll-like receptor pathways, all of which contribute to a state in which the diabetic host mounts a less effective and sometimes a paradoxically more inflammatory response to bacterial invasion.

Beyond the purely immunological changes, several anatomical and physiological factors specific to diabetes contribute to urinary stasis and bacterial persistence. Autonomic neuropathy, a common long-term complication of poorly controlled diabetes, affects the nerve supply to the detrusor muscle and can result in incomplete bladder emptying, sometimes progressing to a frankly neurogenic bladder. Residual urine left behind after voiding acts as a reservoir in which bacteria can multiply undisturbed, and this mechanism has been proposed by several Indian authors as a partial explanation for the higher rate of asymptomatic bacteriuria observed in diabetic patients, particularly those with a longer duration of disease [4]. Glycosuria adds a further layer to this problem: urine that contains excess glucose provides a readily available carbon source for uropathogens, and laboratory work using diabetic animal models of urinary tract infection has demonstrated that elevated glucose concentrations in the bladder environment can directly enhance bacterial growth and, in some organisms, promote the expression of virulence factors relevant to colonisation of the urothelium [7].

Taken together, these mechanisms help explain not only why diabetic patients acquire urinary tract infection more readily but also why, once infection is established, it is harder to clear completely and more likely to recur. This has direct implications for the microbiology laboratory, since organisms that persist under these conditions are also those most likely to be repeatedly exposed to antibiotics, setting the stage for the emergence of resistance mechanisms discussed later in this review.

4. Microbiological Spectrum of Uropathogens: Diabetic versus Non-Diabetic Patients

Across nearly every study reviewed, *Escherichia coli* emerges as the single most common uropathogen in both diabetic and non-diabetic patients, generally accounting for somewhere between fifty and eighty per cent of culture-positive samples depending on the setting. What differs between the two groups is less the identity of the dominant organism and more the relative proportion of less common organisms and the resistance behaviour of the dominant one. A comparative Nepalese study of biofilm formation in

Escherichia coli isolated from diabetic and non-diabetic patients found that while *Escherichia coli* remained the leading isolate in both groups, the overall rate of urinary tract infection was considerably higher among diabetics, and isolates from diabetic patients showed a distinctly higher resistance rate to several commonly used antibiotic classes compared with isolates from non-diabetic patients [16].

Klebsiella pneumoniae is consistently reported as the second most frequent isolate in Indian and South Asian series, and several authors have noted that its relative contribution tends to rise as the proportion of diabetic and hospitalised patients in a study population increases [3,24]. *Proteus* species, *Pseudomonas aeruginosa* and *Enterococcus faecalis* make up smaller but clinically important proportions of the isolates, particularly in patients with a history of catheterisation, recurrent hospitalisation or structural abnormality of the urinary tract. The North Indian etiological study comparing diabetic and non-diabetic patients specifically noted a higher representation of *Proteus* and *Pseudomonas* species among diabetics compared with non-diabetics, even though the overall antimicrobial sensitivity pattern of the two groups did not differ dramatically at the level of the whole cohort [3]. This observation is a useful reminder that microbiological spectrum and resistance pattern, while related, are not the same thing, and both need to be examined separately when comparing diabetic and non-diabetic populations.

Gram-positive organisms, principally *Staphylococcus saprophyticus* and *Enterococcus* species, form a smaller but non-negligible share of isolates in most series, and their presence tends to be somewhat more frequent in outpatient, community-acquired infections than in hospital-based cohorts. A ten-year European analysis found that the relative contribution of Gram-positive cocci to urinary isolates has been rising steadily, a trend attributed partly to an ageing, more comorbid patient population that includes a growing proportion of diabetics [49], and a recent narrative review of enterococcal urinary tract infection similarly noted that *Enterococcus faecalis* and *Enterococcus faecium* are increasingly recognised as agents of complicated infection, particularly in patients with indwelling catheters or structural urinary tract abnormality [50]. Indian data are broadly consistent with this picture: a Karnataka series found *Enterococcus faecalis* in roughly two-thirds of enterococcal urinary isolates, with close to a third of isolates classified as multidrug resistant [25], while an earlier north Indian study of community-acquired enterococcal infection reported comparable species distribution along with a meaningful proportion of vancomycin-resistant isolates even outside the hospital setting [26]. A separate tertiary-care series

from India reported a broadly similar antimicrobial susceptibility pattern among enterococcal isolates from mixed clinical specimens [27], and methicillin-resistant *Staphylococcus aureus*, though still an uncommon urinary isolate overall, has been documented with increasing frequency in a recent comprehensive review incorporating a north Indian cohort [48].

Yeasts, chiefly *Candida* species, are occasionally reported, more so in patients who have received repeated courses of broad-spectrum antibiotics or who have indwelling urinary catheters, though most bacteriology-focused studies restrict their analysis to bacterial isolates and exclude candiduria unless it is judged to be clinically significant. A recent Indian cross-sectional study of candiduria specifically among diabetic patients found that non-albicans *Candida* species, including *Candida krusei*, *Candida tropicalis* and *Candida glabrata*, together outnumbered *Candida albicans* among urinary isolates, a distribution with direct implications for empirical antifungal choice given the variable azole susceptibility of non-albicans species [42]; comparable shifts towards non-albicans species among hospitalised patients, including those with diabetes as an underlying risk factor, have been reported from intensive care settings as well [43]. For the purposes of a review focused on phenotypic resistance detection, the practical point that emerges from this section is that Enterobacterales, and *Escherichia coli* and *Klebsiella pneumoniae* in particular, remain the organisms against which phenotypic tests for extended-spectrum beta-lactamase, AmpC beta-lactamase and carbapenemase production are most frequently and most usefully applied, even though Gram-positive and fungal uropathogens should not be overlooked when designing a comparative diabetic versus non-diabetic study.

5. Antimicrobial Resistance: Mechanisms and Phenotypic Detection

The rise of antimicrobial resistance among uropathogens has been documented extensively in the Indian literature over the past decade, and diabetic patients, by virtue of their more frequent and more prolonged antibiotic exposure, are disproportionately represented among patients from whom resistant organisms are isolated. Three resistance mechanisms are of particular importance in Enterobacterales causing urinary tract infection: production of extended-spectrum beta-lactamase, production of AmpC beta-lactamase, and production of carbapenemase. Since molecular confirmation of these mechanisms through polymerase chain reaction or sequencing remains confined to a limited number of centres in India, phenotypic detection continues to be the backbone of routine diagnostic practice, and a

number of Indian studies have specifically evaluated the performance of these phenotypic methods in local settings.

5.1 Extended-Spectrum Beta-Lactamase (ESBL)

Extended-spectrum beta-lactamase producing organisms hydrolyse extended-spectrum cephalosporins and monobactams, rendering many of the antibiotics traditionally relied upon for empirical treatment of urinary tract infection ineffective. Detection in most Indian laboratories relies on the double-disc synergy test or the combined disc test, in which a marked increase in the zone of inhibition around a cephalosporin disc placed near a disc containing clavulanic acid is taken as evidence of extended-spectrum beta-lactamase production. A prospective study from north India that specifically examined *Escherichia coli* isolated from urine samples found that roughly a third of multidrug-resistant isolates were confirmed as extended-spectrum beta-lactamase producers using these phenotypic methods, with a further proportion showing co-production of extended-spectrum beta-lactamase together with AmpC beta-lactamase [19]. A separate molecular characterisation study from north India, which combined phenotypic screening with genotypic confirmation in patients with healthcare-associated urinary tract infection, similarly reported a high proportion of extended-spectrum beta-lactamase producing *Escherichia coli* and *Klebsiella pneumoniae* isolates, underlining that this resistance mechanism is now firmly established rather than an occasional finding [21].

5.2 AmpC Beta-Lactamase

AmpC beta-lactamases confer resistance to cephamycins in addition to the extended-spectrum cephalosporins affected by extended-spectrum beta-lactamase, and their phenotypic detection is somewhat less straightforward, since the double-disc synergy test used for extended-spectrum beta-lactamase does not reliably identify AmpC producers. The AmpC disc test, in which a disc soaked in AmpC-inducing substrate is placed adjacent to a cefoxitin disc and a flattening or indentation of the inhibition zone is looked for, along with the cefoxitin-cloxacillin double-disc method, are the two phenotypic approaches most commonly used in Indian laboratories for this purpose. A study conducted in a tertiary care hospital in Sikkim that examined four hundred non-repetitive Enterobacteriaceae isolates using a battery of phenotypic tests found that AmpC production, either alone or in combination with extended-spectrum beta-lactamase or metallo-beta-lactamase production, was present in a meaningful proportion of multidrug-resistant isolates, and that co-occurrence of more than one resistance mechanism in the same isolate was not uncommon [18]. The north

Indian prospective study on urinary *Escherichia coli* isolates referred to above reported an even higher proportion of AmpC production than extended-spectrum beta-lactamase production among its multidrug-resistant isolates, which is a pattern seen in several other Indian series and is thought to reflect the widespread use of cephalosporins in both community and hospital settings [19].

5.3 Carbapenemase Production

Carbapenemase production represents the most clinically alarming of the three mechanisms, since carbapenems are frequently reserved as last-line agents for infections caused by organisms already resistant to cephalosporins and fluoroquinolones. A decade-long retrospective analysis of *Klebsiella pneumoniae* isolated from urine samples at a tertiary care centre in Mysuru, South India, illustrates how rapidly this problem has evolved: carbapenem resistance among urinary *Klebsiella pneumoniae* isolates rose from under four per cent in 2014 to over sixty-six per cent by 2021, before declining somewhat to just below forty per cent by 2023, a trajectory that the authors attributed partly to changes in antibiotic stewardship practice introduced during the intervening years [24]. Phenotypic detection of carbapenemase production in Indian laboratories relies principally on the modified Hodge test and, increasingly, on the modified carbapenem inactivation method, which has largely superseded the modified Hodge test because of its improved sensitivity and specificity. Work from Nepal examining *Klebsiella* species isolated at a national reference laboratory demonstrated that combining phenotypic detection of extended-spectrum beta-lactamase, metallo-beta-lactamase, carbapenemase and AmpC production within a single testing algorithm was both feasible and informative in a resource-limited setting, and that isolates capable of biofilm formation were disproportionately represented among those carrying multiple resistance mechanisms simultaneously [17], a finding of direct relevance to the biofilm discussion later in this review.

5.4 Practical Considerations for Phenotypic Testing in Resource-Limited Settings

A recurring theme across the Indian and South Asian literature on phenotypic resistance detection is that these methods, while less definitive than molecular confirmation, remain entirely appropriate for routine diagnostic use provided they are performed and interpreted according to Clinical and Laboratory Standards Institute guidelines [56]. Kirby-Bauer disc diffusion continues to serve as the foundation for initial antimicrobial susceptibility testing, upon which the more specific confirmatory tests for extended-spectrum beta-lactamase, AmpC beta-lactamase and carbapenemase production are then built. Several authors have pointed out that screening criteria based

on reduced susceptibility to indicator antibiotics, such as ceftazidime, cefotaxime, cefoxitin or imipenem, allow laboratories to identify which isolates merit further confirmatory testing without having to apply the full battery of tests to every isolate, an approach that keeps the additional workload and cost manageable even in smaller diagnostic laboratories [19,20]. This stepwise approach, moving from disc diffusion screening to targeted phenotypic confirmation, is the model that most current Indian studies, including several of those cited in this review, have adopted, and it is also the approach that underlies the classical microbiological methodology proposed for characterising recurrent uropathogens in diabetic and non-diabetic patients within India.

5.5 Empirical Treatment Options in the Setting of Rising Resistance

Rising resistance to cephalosporins and fluoroquinolones has renewed clinical interest in older, narrow-spectrum agents such as fosfomycin and nitrofurantoin for uncomplicated cystitis, and a considerable number of recent Indian studies have specifically evaluated their in vitro activity against uropathogens. A study from western India testing fosfomycin against multidrug-resistant and extended-spectrum beta-lactamase producing *Escherichia coli* found susceptibility rates in excess of ninety per cent, supporting its continued role as an oral option even against resistant strains [28], and comparable findings have been reported from Uttarakhand, where fosfomycin retained high activity against uropathogens isolated from a day-care outpatient population [30]. A more recent cross-sectional study from a north Indian tertiary centre similarly found excellent fosfomycin susceptibility among *Escherichia coli* isolates, although *Klebsiella pneumoniae* showed markedly higher resistance, a distinction the authors argued should discourage empirical fosfomycin use whenever *Klebsiella* is the suspected pathogen [29]. Nitrofurantoin has shown a broadly similar pattern of preserved activity against *Escherichia coli* in Indian series examining urinary isolates specifically with reference to these two agents [31], and a recent narrative review of Indian antibiotic resistance trends in uropathogens concluded that fosfomycin and nitrofurantoin remain reasonable first-line empirical choices for uncomplicated community-acquired cystitis, while cautioning that fluoroquinolones and, increasingly, oral cephalosporins can no longer be relied upon for empirical use in most regions of the country [39]. A retrospective five-year Indian analysis of resistance trends reached a similar conclusion, noting a steady erosion of susceptibility to commonly prescribed oral agents over the study period [38], and a study of outpatient prescribing practices in India found that

inappropriate empirical antibiotic selection, including use of agents without confirmed local susceptibility data, was itself an independent contributor to the resistance detected on subsequent culture [46]. Comparable resistance trends have also been documented in neighbouring South Asian settings, reinforcing that this is a regional rather than a purely Indian phenomenon [47]. International treatment guidelines for urological infection continue to recommend narrow-spectrum, culture-guided therapy wherever possible, a principle that is particularly relevant for diabetic patients who are more likely to have been exposed to multiple antibiotic courses before the current episode [58].

6. Biofilm Formation and Its Role in Recurrence

Biofilm formation has increasingly been recognised as a mechanism that links antimicrobial resistance with clinical recurrence, since organisms embedded within a biofilm matrix are considerably less accessible to both host defences and antibiotics than their free-floating, planktonic counterparts. The crystal violet microtiter plate assay remains the most widely used laboratory method for quantifying in vitro biofilm-forming capacity, owing to its simplicity, low cost and reasonable reproducibility, even though it is acknowledged to have certain limitations, including batch-to-batch variability arising from differences in washing and re-solubilisation steps during the procedure.

A Nepalese cross-sectional study that compared biofilm formation among *Escherichia coli* isolated from diabetic and non-diabetic patients found that a substantial proportion of isolates from both groups were positive for biofilm production using the microtiter plate method, and that biofilm-producing isolates were significantly more likely to be multidrug resistant than non-biofilm producers, with quinolones, cotrimoxazole and third-generation cephalosporins showing markedly higher resistance rates among biofilm producers [16]. This association between biofilm production and multidrug resistance has been echoed in subsequent work on *Klebsiella* species, where phenotypic detection of extended-spectrum beta-lactamase, metallo-beta-lactamase, carbapenemase and AmpC production was combined with biofilm assessment in the same set of isolates, and organisms carrying multiple resistance determinants were again found to be enriched among the biofilm-forming subgroup [17].

The specific contribution of hyperglycaemia to biofilm formation has also received attention outside the purely clinical literature. Experimental work using a diabetic animal model of recurrent urinary tract infection demonstrated that elevated glucose concentrations directly enhanced biofilm biomass formed by uropathogenic *Escherichia coli* in vitro, and

that this glucose-driven increase in biofilm mass was associated with reduced antibiotic efficacy against the same isolates, providing a plausible biological explanation for why diabetic patients with poor glycaemic control appear to experience more biofilm-associated, treatment-resistant infections than diabetic patients whose blood glucose is better controlled [18]. From a purely laboratory standpoint, this body of work supports the inclusion of a biofilm assay alongside conventional antimicrobial susceptibility testing whenever recurrent urinary tract infection in a diabetic patient is being investigated, since a positive biofilm result carries implications both for expected treatment response and for the likelihood of further recurrence.

7. Glycaemic Status and Its Correlation with Resistance and Clinical Severity

Glycated haemoglobin, generally abbreviated as HbA1c, provides a retrospective measure of average blood glucose control over the preceding two to three months and has been used by several authors as the principal variable against which resistance patterns and clinical severity of urinary tract infection are compared in diabetic patients. The Kuwaiti study of diabetic patients referred to earlier in this review divided its cohort into those with controlled and uncontrolled glycaemia on the basis of HbA1c values and found that the frequency of urinary tract infection was substantially higher in the uncontrolled group, although the specific organisms isolated and their antibiotic resistance pattern did not differ greatly between the two glycaemic categories in that particular cohort [2]. Other studies, however, have found a more direct relationship between poor glycaemic control and resistance severity, and the difference may partly reflect variation in how uncontrolled glycaemia is defined and how large a difference in mean HbA1c separates the study groups being compared.

The Indian cohort study examining recurrence specifically in type 2 diabetic patients found that patients who went on to develop recurrent urinary tract infection during six months of follow-up had a significantly higher HbA1c at the time of their follow-up assessment compared with patients who remained free of recurrence, and identified elevated HbA1c as an independent predictor of recurrence on multivariate analysis in male patients [5]. This finding is broadly consistent with subsequent nomogram-based prediction models developed in China, one of which incorporated an HbA1c threshold of 6.5 per cent as one of several independent predictors of urinary tract infection in elderly patients with type 2 diabetes mellitus, alongside variables such as age, duration of diabetes, fasting plasma glucose, indwelling urinary catheterisation and concomitant obstructive disease [14,15]. Taken together, the available evidence

suggests that while glycaemic control does not always change which organism is isolated, it does appear to influence both the likelihood of infection occurring in the first place and the probability that an established infection will recur, which is precisely the relationship that a comparative phenotypic study examining resistance profile against HbA1c category is best placed to clarify further.

A further dimension to the glycaemic control question has emerged with the widespread adoption of sodium-glucose cotransporter-2 (SGLT2) inhibitors as first- or second-line therapy for type 2 diabetes mellitus, since these agents work by deliberately increasing urinary glucose excretion and might therefore be expected to worsen, rather than improve, the urinary environment described earlier in this review. A recent narrative review examining this question concluded that although SGLT2 inhibitors clearly increase glycosuria, the balance of clinical trial and real-world evidence does not support a large or consistent increase in symptomatic urinary tract infection, and that genital mycotic infection appears to be the more clinically significant adverse effect of this drug class [32]. A real-world observational study from Thailand similarly found that the incidence of urinary tract infection among patients started on SGLT2 inhibitors was not markedly higher than would be expected in a comparable diabetic population not on this therapy, although the authors noted that pre-existing poor glycaemic control and a prior history of urinary tract infection remained more important predictors of recurrence than SGLT2 inhibitor use itself [33]. For a study conducted in the Indian setting, where SGLT2 inhibitor prescribing has increased considerably over the past several years, recording current diabetes medication alongside HbA1c would allow this question to be examined directly rather than assumed, and would add a contemporary dimension that most of the older Indian literature on this subject does not address.

8. Recurrent Urinary Tract Infection: Relapse versus Reinfection

Recurrent urinary tract infection is conventionally defined as two or more symptomatic episodes within six months, or three or more episodes within twelve months, following apparent clinical resolution of a preceding infection. Within this broad definition, however, lies an important distinction that has direct treatment implications: whether a given recurrence represents relapse, meaning persistence of the original infecting organism that was never fully eradicated, or reinfection, meaning a genuinely new infection, often but not always caused by a different organism, arising after the initial infection had been successfully cleared. Relapse is conventionally considered likely when a further episode occurs within one to two weeks of

completing treatment and the same organism is recovered, whereas reinfection is more often diagnosed when the interval since the previous episode exceeds two weeks, when a documented sterile culture intervened between episodes, or when the organism recovered differs from the one identified previously. In practice, distinguishing the two on the basis of organism identification and antibiogram alone, without resorting to molecular strain typing, carries a degree of uncertainty that has been acknowledged even in studies that have had access to advanced typing methods. Cohort studies of women with recurrent cystitis that have combined antibiotic susceptibility testing with genetic typing have found that isolates recovered from successive episodes are genetically identical in a substantial minority of cases, consistent with relapse or persistence, while the remainder represent reinfection with a genetically distinct strain, and that antibiotic susceptibility profile alone correctly predicts clonal relationship in the majority, though not all, of the isolate pairs examined. For a diabetic population in particular, where impaired bladder emptying and intracellular bacterial persistence within the urothelium are both plausible mechanisms of relapse, and where community exposure to uropathogenic strains via periurethral or gastrointestinal reservoirs continues throughout the period of poor glycaemic control, both relapse and reinfection are likely to occur, sometimes within the same patient across different episodes.

For a phenotypic microbiology-based study, the most feasible approach to this classification problem, in the absence of access to whole genome sequencing or pulsed-field gel electrophoresis, is to combine the time interval between episodes with organism identification down to species level and, where resources allow, comparison of the antibiogram pattern between the index isolate and the recurrent isolate. A recurrence occurring within two weeks of completed treatment, involving an organism of the same species with an identical or near-identical resistance pattern, is reasonably classified as probable relapse, whereas a recurrence occurring after a longer interval, particularly one involving a different organism or a markedly different resistance pattern, is more appropriately classified as probable reinfection. While this approach cannot achieve the certainty offered by molecular typing, it remains a practical and defensible method for classifying recurrence in settings where genomic tools are not routinely available, and is the approach most consistent with the classical, phenotypic orientation of the microbiological methodology under consideration in this review.

9. Risk Prediction Models for Recurrent Urinary Tract Infection in Diabetic Patients

Interest in developing a formal risk-prediction tool for urinary tract infection in diabetic patients is not new, but the sophistication of the models proposed has increased considerably over the years reviewed here. Earlier work relied on relatively simple scoring systems built from a small number of clinical variables identified through multivariate logistic regression, whereas more recent studies, particularly those originating from China, have applied nomogram-based approaches that combine several independently significant predictors into a single visual scoring tool with a calculated area under the receiver operating characteristic curve to express predictive performance. One such nomogram, developed from a cohort of over four hundred patients with type 2 diabetes mellitus, incorporated glycated haemoglobin above 6.5 per cent, age above sixty-five years, duration of diabetes exceeding ten years, fasting plasma glucose, presence of an indwelling urinary catheter and co-existing obstructive urological disease as independent predictors, and achieved a concordance index in excess of 0.85 in its development cohort, indicating good discriminatory ability [14]. A separate, independently developed nomogram focusing specifically on older patients with type 2 diabetes mellitus reported a somewhat more modest but still respectable area under the curve of around 0.76 to 0.78 in its training and validation cohorts, using pathogen distribution data and a comparable set of clinical predictors [15]. Indian data contributing to this line of work remain comparatively sparse, and the cohort study on recurrence in type 2 diabetic patients conducted in India, while not developing a formal nomogram, did identify a set of statistically significant predictors, including renal function, glycated haemoglobin, renal calculi and cystopathy, that could plausibly be incorporated into an Indian risk-prediction model if a sufficiently large cohort were assembled for that purpose [5].

From the perspective of a phenotypic microbiological study of the kind under discussion in this review, the value of these risk-prediction efforts lies less in their statistical sophistication and more in the consistency of the clinical variables they repeatedly identify as significant, namely glycaemic control, duration of diabetes, renal function and structural or functional urinary tract abnormality. A study that systematically records these same variables alongside its microbiological findings, even without attempting to construct a formal predictive score, would be well positioned to contribute meaningfully to this developing area of the literature and, in time, to the eventual development of a validated, India-specific clinico-microbiological risk score for recurrent urinary tract infection in diabetic patients.

10. The Indian Scenario: National Antimicrobial Resistance Surveillance Data

Placing hospital-based and single-centre Indian studies in a wider national context is made possible by the surveillance data published annually by the Indian Council of Medical Research through its Antimicrobial Resistance Surveillance Network. The network's 2023 annual report, drawing on tens of thousands of culture-positive isolates contributed by more than twenty regional centres across the country, confirmed that *Escherichia coli* and *Klebsiella pneumoniae* remain the most commonly isolated organisms from urine samples in Indian hospitals, and documented a continuing decline in susceptibility of these organisms to several commonly used antibiotic classes over the years for which comparable data are available, while also noting that fosfomycin and nitrofurantoin retained comparatively favourable susceptibility rates for uncomplicated cystitis caused by *Escherichia coli*, particularly among outpatients [23].

This national picture is broadly consistent with what has been reported from individual Indian centres cited earlier in this review, including the marked rise in carbapenem resistance among urinary *Klebsiella pneumoniae* isolates documented over a ten-year period in Mysuru [24], and the substantial proportion of extended-spectrum beta-lactamase and AmpC beta-lactamase producing *Escherichia coli* reported from north Indian tertiary care centres [19,21]. The picture emerging from India is also consistent with the global surveillance data published by the World Health Organization through its Global Antimicrobial Resistance and Use Surveillance System, which similarly documents declining susceptibility of *Escherichia coli* and *Klebsiella pneumoniae* to third-generation cephalosporins and fluoroquinolones across most reporting regions, with South-East Asia among the regions showing the steepest declines [57]. A retrospective multi-year analysis of regional urinary tract infection burden and resistance patterns outside India has reported a broadly similar trajectory, reinforcing that the trend documented in Indian surveillance is part of a wider international pattern rather than a phenomenon unique to the country [60]. What the national and global surveillance data add to individual hospital reports is a sense of scale and trend: the resistance patterns observed in single hospital studies are not isolated local phenomena but form part of a broader, sustained trajectory towards declining susceptibility among the two organisms most responsible for urinary tract infection in India. For a study specifically comparing diabetic and non-diabetic patients, this background is important because it establishes that even the baseline, non-diabetic resistance rate against which any diabetes-specific

increase would need to be compared is itself already elevated relative to a decade ago, and any interpretation of study findings needs to take this rising baseline into account.

11. Gaps in the Current Literature

Despite the substantial body of work reviewed above, several gaps remain that are directly relevant to the design of further phenotypic microbiological research on recurrent urinary tract infection in diabetic patients in India. First, while individual components of the problem, namely resistance pattern, biofilm formation and glycaemic correlation, have each been studied reasonably extensively, comparatively few Indian studies have combined all three within a single, adequately powered comparative design that enrolls matched diabetic and non-diabetic groups and follows them prospectively for recurrence, as opposed to documenting a single cross-sectional episode.

Second, most Indian phenotypic resistance studies, including several cited in this review, have been conducted in single tertiary care centres with sample sizes that, while adequate for descriptive purposes, are not always large enough to support confident subgroup analysis by diabetic status, glycaemic category or duration of diabetes. Third, classification of recurrence as relapse versus reinfection has generally been either omitted altogether or addressed only superficially in Indian studies, in contrast to the more detailed molecular classification attempted in some non-Indian cohorts, largely because the phenotypic classification approach outlined earlier in this review, based on time interval, species identity and antibiogram comparison, has not yet been applied systematically within an Indian diabetic population. Fourth, although risk-prediction nomograms for urinary tract infection in diabetic patients have now been developed and validated in Chinese cohorts, no comparable, India-specific clinico-microbiological risk score currently exists, despite the fact that several of the same predictor variables have already been shown to be significant in Indian data.

Addressing these gaps does not require molecular or genomic infrastructure beyond what is already available in most Indian teaching hospital microbiology departments. A study design that combines classical culture and identification, Kirby-Bauer susceptibility testing, phenotypic confirmation of extended-spectrum beta-lactamase, AmpC beta-lactamase and carbapenemase production through combined disc tests, crystal violet biofilm assay, and structured recording of HbA1c and recurrence pattern over a defined follow-up period would be well placed to address each of the gaps identified above using methodology that is already well validated in the literature reviewed here, without requiring reliance on

molecular or next-generation sequencing techniques that remain inaccessible to most Indian centres.

12. Conclusion

Recurrent urinary tract infection in diabetic patients is not simply a more frequent version of the infection seen in non-diabetic individuals; it is, in important respects, a distinct clinical and microbiological entity shaped by impaired host defence, urinary stasis, glycosuria-driven bacterial growth, and an increased propensity for both antimicrobial resistance and biofilm formation. The Indian literature reviewed here, though not as extensive as that available from some other regions, consistently supports each element of this picture and, taken together with national surveillance data, paints a clear trajectory of rising resistance among the organisms most responsible for these infections. Phenotypic microbiological methods, properly performed according to established laboratory standards, remain fully capable of characterising this resistance and of identifying biofilm-forming isolates, even in the absence of molecular confirmation, and continue to offer the most realistic and widely applicable approach for Indian centres seeking to study this problem in greater depth. A well-designed comparative study built around these classical methods, combined with careful attention to glycaemic status and a structured approach to classifying recurrence, stands to make a genuine and practically useful contribution to the management of this common and clinically significant condition.

References

1. Salari N, Karami MM, Bokaei S, Chalesghar M, Shohaimi S, Akbari H, et al. The prevalence of urinary tract infections in type 2 diabetic patients: a systematic review and meta-analysis. *Eur J Med Res.* 2022;27:20.
2. Sewify M, Nair S, Warsame S, Murad M, Alhubail A, Behbehani K, Al-Refaei F, Tiss A. Prevalence of urinary tract infection and antimicrobial susceptibility among diabetic patients with controlled and uncontrolled glycemia in Kuwait. *J Diabetes Res.* 2016;2016:6573215.
3. Jagadeesan S, Tripathi BK, Patel P, Muthathal S. Urinary tract infection and Diabetes Mellitus—Etiological profile and antibiogram: A North Indian perspective. *J Family Med Prim Care.* 2022;11(5):1902-1906.
4. Biswas D, Pawar N, Patro SK, Krishna NS, Parida D, Bhagatana PK. Clinical profile and spectrum of bacteriuria in patients with diabetes: An analytical study. *J Family Med Prim Care.* 2022;11(6):3190-3195.
5. Nabi T. Clinical profile and risk factors of recurrent urinary tract infection in patients with type 2 diabetes. *Int J Acad Med.* 2020;6(4):304-309.
6. Papp SB, Zimmern PE. Recurrent urinary tract infections and type 2 diabetes mellitus: a systematic review predominantly in women. *Front Urol.* 2023;3:1275334.
7. Paudel S, John PP, Poorbaghi SL, Randis TM, Kulkarni R. Systematic review of literature examining bacterial urinary tract infections in diabetes. *J Diabetes Res.* 2022;2022:3588297.
8. Girma A, Aemiro A, Workineh D, Tamir D. Magnitude, associated risk factors, and trend comparisons of urinary tract infection among pregnant women and diabetic patients: a systematic review and meta-analysis. *J Pregnancy.* 2023;2023:8365867.
9. Tegegne KD, Wagaw GB, Gebeyehu NA, Yirdaw LT, Shewangashaw NE, Kassaw MW. Prevalence of urinary tract infections and risk factors among diabetic patients in Ethiopia: a systematic review and meta-analysis. *PLoS One.* 2023;18(1):e0278028.
10. Ahmed AE, Abdelkarim S, Zenida M, Baiti MAH, Alhazmi AAY, Alfaifi BAH, et al. Prevalence and associated risk factors of urinary tract infection among diabetic patients: a cross-sectional study. *Healthcare (Basel).* 2023;11(6):861.
11. Gosa F, Gebresilasie A, Manilal A, et al. Prevalence and associated factors of urinary tract infections among diabetic patients in Arba Minch Hospital, Arba Minch province, South Ethiopia. *Turk J Urol.* 2019;45(Suppl 1):S56-S62.
12. Shah MA, Kassab YW, Anwar MF, Al dahoul HK, Menon S, Kaur HJ, Ifzaal M, Muthanna FMS, Searan WM. Prevalence and associated factors of urinary tract infections among diabetic patients. *Health Sci J.* 2019;13(2):646.
13. Wajid H, Manzoor H, Manzoor M, Mirza S, Khan HS, Hassan S, Ali B. Recurrent urinary tract infection in diabetics: a retrospective analysis. *Cureus.* 2025;17(7):e87816.
14. Li Y, Li L, He L. Establishment and validation of a risk prediction model for urinary tract infection in elderly patients with type 2 diabetes mellitus. *Front Endocrinol.* 2025;16:1557185.
15. Yang L, Yin J, Yang Z, Liu J. Development and validation of a prediction model for urinary tract infection in older patients with type 2 diabetes mellitus. *Front Endocrinol.* 2026;17:1706338.
16. Raya S, Belbase A, Dhakal L, Govinda Prajapati K, Baidya R, Kishor Bimali N. In-vitro biofilm formation and antimicrobial resistance of *Escherichia coli* in diabetic and nondiabetic patients. *Biomed Res Int.* 2019;2019:1474578.
17. Kuinkel S, Acharya J, Dhungel B, Adhikari S, Adhikari N, Thapa Shrestha U, Banjara MR, Rijal KR, Ghimire P. Biofilm formation and phenotypic detection of ESBL, MBL, KPC and

- AmpC enzymes and their coexistence in *Klebsiella* spp. isolated at the National Reference Laboratory, Kathmandu, Nepal. *Microbiol Res (Pavia)*. 2021;12(3):683-697.
18. Rodrigues IC, Ribeiro-Almeida M, Campos J, Silveira L, Leite-Martins L, Ribeiro J, Martins da Costa P, Prata JC, Pista Â, Martins da Costa P. Uropathogenic *Escherichia coli* in a diabetic dog with recurrent UTIs: genomic insights and the impact of glucose and antibiotics on biofilm formation. *Microorganisms*. 2025;13(8):1946.
 19. Salvia T, Dolma KG, Dhakal OP, Khandelwal B, Singh LS. Phenotypic detection of ESBL, AmpC, MBL, and their co-occurrence among MDR Enterobacteriaceae isolates in a tertiary care hospital in Sikkim, India. *J Lab Physicians*. 2022;14(3):329-335.
 20. Das D, Vohra P, Mane P, Shaozai CK. Extended spectrum, AmpC & metallo beta-lactamases producing *Escherichia coli* in urinary isolates: a prospective study in north India. *Indian J Med Res*. 2025;161(2):167-175.
 21. Verma S, Kalyan RK, Gupta P, Khan MD, Venkatesh V. Molecular characterization of extended spectrum beta-lactamase producing *Escherichia coli* and *Klebsiella pneumoniae* isolates and their antibiotic resistance profile in health care-associated urinary tract infections in North India. *J Lab Physicians*. 2023;15(2):194-201.
 22. Hamdan A, AbuHaweeleh MN, Al-Qassem L, Kashkoul A, Alremawi I, Hussain U, Khan S, ElBadway MMS, Chivese T, Farooqui HH, Zughaier SM. Prevalence of antimicrobial resistance among the WHO's AWaRe classified antibiotics used to treat urinary tract infections in diabetic women. *Antibiotics (Basel)*. 2024;13(12):1218.
 23. Antimicrobial Resistance Surveillance Network. Annual Report 2023. New Delhi: Indian Council of Medical Research; 2023.
 24. Sumana MN, Maheshwarappa YD, Kalyani G, Mahale RP, Sowmya GS, Rao MR, et al. A retrospective study of the antimicrobial susceptibility patterns of *Klebsiella pneumoniae* isolated from urine samples over a decade in South India. *Front Microbiol*. 2025;16:1553943.
 25. Bhat S, Gunawardana DU, Boparai DK, Bamunusinghe TK, Krishanth K, Premakrishna A, Narasimhaswamy N. Antibigram pattern of *Enterococcus* species among urinary tract-infected patients visiting a tertiary care hospital in Karnataka, India. *Antimicrob Steward Healthc Epidemiol*. 2024;4(1):e419.
 26. Goel V, Kumar D, Kumar R, Mathur P, Singh S. Community acquired enterococcal urinary tract infections and antibiotic resistance profile in North India. *J Lab Physicians*. 2016;8(1):50-54.
 27. Khan S, Bansal H, Gandham N, Mirza S, Vyawahare C, Patil R, Mukhida S, Das NK. Antimicrobial susceptibility pattern of enterococci isolated from various clinical samples in a tertiary care hospital in India. *IMC J Med Sci*. 2023;17(2):1-6.
 28. Jain R, Pal N, Hooja S. Fosfomycin susceptibility among multidrug resistant and extended spectrum beta-lactamase producing uropathogenic *Escherichia coli* isolates at a tertiary care hospital of Western India. *CHRISMED J Health Res*. 2022;9(2):125-129.
 29. Badoni G, Singh V, Rohilla R, Sharma T, Panwar VK, Omar BJ, Gupta P. Fosfomycin susceptibility patterns among uropathogens and clinical predictors of resistance: a cross-sectional study at a tertiary care centre in northern India. *Cureus*. 2026;18(5):e108724.
 30. Sharma S, Verma PK, Rawat V, Umesh, Negi V. Fosfomycin sensitivity pattern among uropathogens isolated from patients visiting the day care facility of Sushila Tiwari Hospital in the Kumaun region, Uttarakhand, India. *J Clin Diagn Res*. 2021;15(6):DC30-DC33.
 31. Vyas A, Tripathi P, Advani M. Antibiotic susceptibility pattern of urinary isolates of *Escherichia coli* with focus on fosfomycin and nitrofurantoin. *J Pure Appl Microbiol*. 2026;20(1):429-436.
 32. Pishdad R, Auwaerter PG, Kalyani RR. Diabetes, SGLT-2 inhibitors, and urinary tract infection: a review. *Curr Diab Rep*. 2024;24(9):405-414.
 33. Uitrakul S, Aksonnam K, Srivichai P, Wicheannarat S, Incomenoy S. The incidence and risk factors of urinary tract infection in patients with type 2 diabetes mellitus using SGLT2 inhibitors: a real-world observational study. *Medicines (Basel)*. 2022;9(12):59.
 34. Kande S, Patro S, Panigrahi A, Khora PK, Pattnaik D. Prevalence of uropathogens and their antimicrobial resistance pattern among adult diabetic patients. *Indian J Public Health*. 2021;65(3):280-286.
 35. Patil SR, Karande GS, Shinde RV, Pawar SK. Gram-negative uropathogens in diabetic patients: a study of ampicillinase, cephalosporinase, extended-spectrum beta-lactamase, and metallo beta-lactamase producing phenotypes. *J Pharm Bioallied Sci*. 2025;17(Suppl 3):S2569-S2571.
 36. Vaishnav B, Wadivkar A, Pailla R, Mondkar S. Clinical and microbiological profile of gram-negative infections in critically ill diabetic patients. *Cureus*. 2024;16(8):e65955.

37. Alemu M, Belete MA, Gebreselassie S, Belay A, Gebretsadik D. Bacterial profiles and their associated factors of urinary tract infection and detection of extended spectrum beta-lactamase producing gram-negative uropathogens among patients with diabetes mellitus at Dessie Referral Hospital, Northeastern Ethiopia. *Diabetes Metab Syndr Obes.* 2020;13:2935-2948.
38. Singh B, Patel A, Agrawal RP, Jain SK. Trends in antibiotics resistance for urinary tract infections - a five-year retrospective study in India. *Bioinformation.* 2025;21(9):1010-1015.
39. Jayasree KM, Vignesh NV, Sathyapriyan, Vignesh GV. A review on current antibiotic resistance trends of uropathogens in India: a survey from the urology department, 2020-2025. *Int J Pharm Sci.* 2025;3(9):3025-3034.
40. Banerjee M, Majumdar M, Kundu PK, Maisnam I, Mukherjee AK. Clinical profile of asymptomatic bacteriuria in type 2 diabetes mellitus: an eastern India perspective. *Indian J Endocrinol Metab.* 2019;23(3):293-297.
41. Laway BA, Nabi T, Bhat MH, Fomda BA. Prevalence, clinical profile and follow up of asymptomatic bacteriuria in patients with type 2 diabetes - a prospective case control study in Srinagar, India. *Diabetes Metab Syndr.* 2021;15(2):455-459.
42. Patil VD, Mane PM, Patil SR. Emergence of non-albicans *Candida* species in candiduria among diabetic patients: a cross-sectional study. *Cureus.* 2026;18(5):e108577.
43. Kaur R, Dhakad MS, Goyal R, Kumar R. Emergence of non-albicans *Candida* species and antifungal resistance in intensive care unit patients. *Asian Pac J Trop Biomed.* 2016;6(5):455-460.
44. Chao CT, Lee SY, Wang J, Chien KL, Huang JW. Frailty increases the risk for developing urinary tract infection among 79,887 patients with diabetes mellitus and chronic kidney disease. *BMC Geriatr.* 2021;21:349.
45. Confederat LG, Condurache MI, Alexa RE, Dragostin OM. Particularities of urinary tract infections in diabetic patients: a concise review. *Medicina (Kaunas).* 2023;59(10):1747.
46. Sampathkumar R, Saranya R, Gnanasekaran D, Thakran V, Aslam H, Pascal S. Antibiotic resistance in urinary tract infections: a study on trends and contributing factors in outpatient care among Indian patients. *Bioinformation.* 2024;20(12):1908-1912.
47. Rahimi BA, Afghan JK, Sirat R, Kakar KA, Lali WM, Rahimy N, Farooqi K. Antibiotic resistance among patients with urinary tract infections in Kandahar, Afghanistan. *Indian J Community Med.* 2023;48(6):867-872.
48. Kumar G, Shukla S, Agarwal S, Shukla D, Soni SR, Verma RK, Singh V, Kumar A, Kumar D. Methicillin-resistant *Staphylococcus aureus* in urinary tract infections: a comprehensive review with insights from a north Indian cohort. *Cureus.* 2025;17(12):e99015.
49. Gajdács M, Ábrók M, Lázár A, Burián K. Increasing relevance of Gram-positive cocci in urinary tract infections: a 10-year analysis of their prevalence and resistance trends. *Sci Rep.* 2020;10:17658.
50. Codelia-Anjum A, Lerner LB, Elterman D, Zorn KC, Bhojani N, Chughtai B. Enterococcal urinary tract infections: a review of the pathogenicity, epidemiology, and treatment. *Antibiotics (Basel).* 2023;12(4):778.
51. Dai M, Hua S, Yang J, Geng D, Li W, Hu S, Chen H, Liao X. Incidence and risk factors of asymptomatic bacteriuria in patients with type 2 diabetes mellitus: a meta-analysis. *Endocrine.* 2023;82(2):263-281.
52. Matthiopolou G, Ioannou P, Mathioudaki A, Papadakis JA, Daraki VN, Pappas A, Souris S, Maraki S, Stathopoulou C, Kofteridis DP. Asymptomatic bacteriuria in patients with type 2 diabetes mellitus. *Infect Dis Rep.* 2023;15(1):43-54.
53. Bharti A, Chawla SS, Kumar S, Kaur S, Soin D, Jindal N, Garg R. Asymptomatic bacteriuria among the patients of type 2 diabetes mellitus. *J Family Med Prim Care.* 2019;8(2):539-543.
54. Anjana RM, Unnikrishnan R, Deepa M, Pradeepa R, Tandon N, Das AK, et al, for the ICMR-INDIAB Collaborative Study Group. Metabolic non-communicable disease health report of India: the ICMR-INDIAB national cross-sectional study (ICMR-INDIAB-17). *Lancet Diabetes Endocrinol.* 2023;11(7):474-489.
55. Anjana RM, Deepa M, Pradeepa R, Mahanta J, Narain K, Das HK, et al. Prevalence of diabetes and prediabetes in 15 states of India: results from the ICMR-INDIAB population-based cross-sectional study. *Lancet Diabetes Endocrinol.* 2017;5(8):585-596.
56. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing. CLSI Supplement M100. 34th ed. Wayne, PA: CLSI; 2024.
57. World Health Organization. Global Antimicrobial Resistance and Use Surveillance System (GLASS) Report 2022. Geneva: World Health Organization; 2022.

58. European Association of Urology. EAU Guidelines on Urological Infections. Arnhem: EAU Guidelines Office; 2023.
59. International Diabetes Federation. IDF Diabetes Atlas. 10th ed. Brussels: International Diabetes Federation; 2021.
60. Wireko S, Ngmaakan G, Dwomoh D, Hansen C, Nartey S, Senu E. Regional burden of urinary tract infection, its aetiologies, and antibiotic resistance patterns, 2020-2023: a retrospective study. *Health Sci Rep.* 2025;8(11):e71503.