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STUDY ON ANTIMICROBIAL PRESCRIBING PATTERN AND MICROBIOLOGICAL PROFILE IN URINARY TRACT INFECTIONS: DIABETIC VERSUS NON-DIABETIC PATIENTS

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ABSTRACT

Urinary tract infections(UTI) are among the commonest bacterial infections seen across the community and hospital practice, whose frequency, bacteriological profile and the response to therapy is seen to be altered by the presence of diabetes mellitus. This review draws literature mentioning about the epidemiological, microbiological and prescribing pattern comparing diabetic and non-diabetic patients with UTI. The literatures drawn from settings ranging across Asian and South-Asian countries have shown that diabetic patients exhibit a consistently higher pattern of culture positive UTI, dominated by *Escherichia coli*, followed by *Klebsiella pneumonia*, *Enterococcus* and other atypical micro-organisms, and antibiograms that tend to run toward greater resistance to commonly prescribed agents such as ampicillin, cotrimoxazole and other fluoroquinolones. Prescribing surveys from Ecuador, Bangladesh and elsewhere describe strong gaps between guideline recommended first line agents and the actual dispensing scenario, with underuse of nitrofurantoin and fosfomycin. Taken together, the literature argues for diabetes aware antimicrobial stewardship, routine culture guided prescribing in this population, and further comparative research from tertiary care settings.

KEYWORDS: urinary tract infection; diabetes mellitus; antimicrobial resistance; uropathogens; antibiogram; prescribing pattern.

INTRODUCTION

Urinary tract infection remains one of the most often diagnosed bacterial infections worldwide, cutting across age groups, sexes and non-subjective settings, and accounting for a considerable share of both outpatients consultations and prescriptions (1). It is broadly accepted that women caries a disproportionate share of this burden throughout their lifetime, yet the growing researches in the field have shown how general disease, and diabetes mellitus in particular, reshapes both the likelihood of infection and its non-subjective course (1,2). Diabetes is now one of the near general non communicable diseases globally, and its coexistence with UTI have changed the course of it. Hyperglycemia promotes glycosuria, and a urine output in glucose provides a favourable medium for bacterial multiplication. Superimposed on this is a degree of immune-compromised health, described across the literature as impaired neutrophil chemotaxis, phagocytosis and intracellular killing, that leaves ill patients less able to clear an existing infection quickly (3).

The consequence, reported with moderate consistency across different healthcare systems, is that ill patients experience UTI more oftenly and are prone to complex presentations which appear to carry a bacterial and resistance profile that differs subtly from that of their non-diabetic counterparts (3,4,5). This has realistic implications that extend considerably beyond the microbiology laboratory. If diabetic patients are more likely to harbor resistant organisms then the empirical therapy initiated before the culture reports are done is more likely to fail in this subgroup (6,7). Antimicrobial resistance is not a static problem observed only in intensive

hospital settings but arguably becoming a more wide spread reality in outpatient clinics by virtue of recurrent infection and repeated antibiotic exposure (8,9).

This review brings together accessible literature examining the microbiological spectrum of uropathogens, the antimicrobial resistance patterns observed and the antibiotic prescribing behaviour observed in diabetic patients compared with non-diabetic patients with UTI. The intention is not only to catalogue isolated organism frequencies from separate centres, but to look for the recurring threads that run through studies conducted in the Middle East, Africa, South Asia, Latin America and elsewhere, and to consider what these threads mean for intelligent healthful utilization in a population that is increasing worldwide.

EPIDEMIOLOGICAL BURDEN OF UTI IN DIABETIC AND NON-DIABETIC POPULATIONS

The scale of the problem is excellently appreciated through pooled estimates rather than single-center studies. A systematic review and meta-analysis of Ethiopian data covering fourteen eligible studies and nearly 3,800 diabetic participants placed the pooled prevalence of UTI at approximately 16 percent, with considerable regional variation and higher figures reported from studies conducted after 2018. It suggests that the burden may not be static but is drifting upward. Female sex, illiteracy and a prior history of UTI emerged as self-reliant predictors of infection in that pooled analysis, findings that echo through much of the individual study literature as well (2).

Separate comparative studies that directly enrolled both diabetic and non-diabetic patients tend to confirm this excess risk in further concrete terms. A Saudi study drawing 1,100 patients with symptoms indicative of UTI found clinically significant bacteriuria in 32.8 percent of diabetic patients against 19.2 percent of non-diabetics. This gap is widely sufficient to be clinically meaningful and not just merely a statistical expression (4). A more recent study, pairing again both the groups of broadly similar size, reported UTI frequencies of 43.33 percent among diabetics compared with 28.46 percent among non-diabetics, with the difference reaching statistical significance and being further pronounced among patients older than forty-five years and among women within the diabetic subgroup (5). Al-Asoufi et al. did a similar work from Jordan, examining over a hundred urine samples similarly describing the unequal distribution of infecting organisms between diabetic and non-diabetic participants, with several species essentially confined to one group or the other. It suggests that diabetes does not simply raise the absolute risk of infection but also reshapes which organisms are likely to be responsible (1).

Age and sex continue to interact with diabetic status in ways that matter for clinical practice. Recurrent UTI in older adults, where diabetes is common, has been studies through large retrospective cohorts. One such analysis done by Ahmed H et al. followed almost 20,000 adults aged sixty-five and above with recurrent UTI and found that long term antibiotic prophylaxis was related with a meaningfully reduced risk of further clinical recurrence and hospitalization, particularly among men (8). Diabetic status was not the exclusive variable driving these outcomes, but the overlap between advancing age, diabetes and the recurrence of infection is not to be ignored and it reinforces why age stratified and comorbidity stratified analysis matters when interpreting UTI epidemiology rather than treating diabetic and non-diabetic patients as a single undifferentiated population.

Work from Saudi primary health care centers examining prevalence and predictors of UTI specifically among patients with Type 2 Diabetes, and a parallel European study identifying prognostic factors for UTI in Type 2 Diabetes both points toward the same direction. Glycemic control, disease duration and the presence of microvascular complications tend to track with infection risk, suggesting that UTI in diabetic [patients is not just an isolated infection case but is often bound up with the broader trajectory of glycemic and metabolic control (9,10). Even relatively newer classes of anti-diabetic therapy have entered this conversation, with data on SGLT2 inhibitors describing an association between this drug class and genitourinary infection, a reminder that the epidemiology of UTI in diabetes is not fixed but continues to be reshaped by the process of diabetes (11).

MICROBIOLOGICAL SPECTRUM OF UROPATHOGENS

Despite the geographical spread of the studies referred here, from Jordan and Saudi Arabia through Ethiopia, Sudan, Bangladesh and the Indian subcontinent, there has been a striking consistency in one finding: *Escherichia coli* remains the most common isolated pathogen in both diabetic and non-diabetic patients (1,3,12,13,14,15,16). The difference between the two groups is very less in the identity of leading organism

but more the shape of remaining distribution. Several Ethiopian studies examining bacterial profile and antimicrobial susceptibility specifically among diabetic patients describe a spectrum in which *Klebsiella* species, *Staphylococcus aureus*, *Proteus* species and, less commonly, *Pseudomonas* and *Enterococcus* species fill out the remainder of isolates, with the relational proportions shifting somewhat from one hospital population to another (3,12,14,16). Gena M.E. et al. worked from Blue Hora University Teaching Hospital in Southern Ethiopia, focusing only on a diabetic cohort of just 250 patients, situates itself within this broader pattern, framing impaired immune function and prolonged hyper-glycemia as the mechanistic backdrop against which this organism mix arises (3).

A comparative work that has enrolled diabetic and non-diabetic arms together offers a more direct view of how the spectrum shifts with diabetic status. Al-Asoufi et al. study from Jordan found inequality in the bacterial species isolated between the two groups, with several species, including *Enterobacter aerogenes*, *Enterobacter cloacae*, *Citrobacter freundii*, *Acinetobacter Baumannii* and *Bacillus subtilis*, basically absent from diabetic samples while still appearing among non-diabetics, even as *E. coli* retained its position as the dominant isolate overall. The authors further noted that dependable infections tended to be further common, and at times more severe in diabetic patients than in their non-diabetic counter parts; a distinction that speaks to clinical severity as much as to organism identity (1).

A Bangladeshi data drawn from an institution based retrospective study done by Shill MC et al. on 800 patients approached the same question from the angle of susceptibility rather than pure organism frequency, and concluded that microbial sensitivity of the common uropathogens was declining in diabetic patients relative to non-diabetics, implying that even where the same organism is responsible for infection in both the groups, the diabetic isolate is statistically further likely to prove less convincible to standard first line agents (6). This distinction, between which organism causes infection and how convincible that organism turns out to be, is one that recurs throughout the literature and arguably matters further for prescribing decisions than organism identity alone. A Sudanese study looking at prevalence, susceptibility and related factors in ill patients and a similar Arba Minch, Ethiopia study investigating prevalence and related factors for UTI and Diabetics both confirm the overall East African scene of E.coli predominance with a possibly smaller tail of Klebsiella and other Enterobacteriacae. (15,16).

ANTIMICROBIAL RESISTANCE PATTERNS: DIABETIC VERSUS NON-DIABETIC COMPARISONS

While the organism spectrum in diabetic and non-diabetic UTI is only slightly different, the resistance data tells a more consistent and clinically urgent story. In a recent multicenter study, patients were stratified into simple UTI, complex UTI without diabetes, and complex UTI with diabetes. E. coli isolates from the two complex groups were resistant to a broader range of antibiotics and antibiotic classes than isolates from patients with simple infection, with a higher proportion of non *E. coli* organisms in these groups (17). This gradient, from uncomplicated to complicated to complicated with diabetes, is useful way of thinking about the resistance literature as a whole: diabetes appears to function less as an isolated risk factor and more as one contributors, alongside recurrence, prior antibiotic exposure and structural urinal abnormality, to a broader complicated UTI phenotype that carries elevated resistance risk (17,18).

Studies done in South Asian countries examining antimicrobial resistance describe elevated resistance to commonly available first line agents, including ampicillin and co-trimoxazole, among diabetic isolates consistent with the Jordanian finding that cephalothin performed poorly across both patient groups while agents such as chloramphenicol, ciprofloxacin and vancomycin retained comparatively better activity (1,19,20).

A comparative tertiary care study looking specifically at resistance to multiple antibiotics in diabetic versus non diabetic UTI patients adds further weight to this pattern, describing multidrug resistance as disproportionately concentrated in the diabetic arm of the comparison (18). The mechanistic explanation offered across this literature converges on a humble number of interacting factors: diabetic patients undergo further steady urine culture and antibiotic exposure by virtue of further steady symptomatic and symptomless infection, they are further promising to have had prior hospitalization or catheterization, and impaired topical host defence may itself create selective pressure favouring the persistence of less susceptible organisms once colonization occurs. None of this suggests that diabetic patients require unconditionally different antibiotic classes, but it argues that existential choices in this population should be made with infernal threshold for

obtaining culture and sensitivity testing, and with near attention to topical antibiogram data particular to diabetic patient cohorts than to hospital wide averages.

ANTIMICROBIAL PRESCRIBING PATTERNS AND RATIONAL USE

In parallel to the microbiological literature, there is a body of work looking at what clinicians significantly prescribe for UTI, and how much that practice aligns with guideline recommendations, culture results and increasingly rational stewardship principles. Sanchez X et al. conducted a cross sectional study with outpatient and second level hospital encounters. They found an appropriate antibiotic prescription rate of just over 56 percent, with nitrofurantoin and fosfomycin, both recommended first line agents in most current guidelines, particularly underused relative to broader spectrum alternatives (7).A comparable study done in Bangladesh by Khatun SA et al. examining prescribing patterns of antimicrobials among outpatients with UTI, and a study done by Shrestha L et al. in Nepal describing prescription patterns benchmarked against antimicrobial susceptibility testing at a tertiary care hospital, both describe a synonymous tension between what is prescribed empirically and what culture data would significantly support (21,22).

Emergency department prescribing has come under specific scrutiny. A study done by Chardavoyne PC et al. at United States evaluating the appropriateness of antibiotic prescriptions issued for UTI in the emergency setting found a substantial room for improvement. It suggests that inappropriate empirical prescribing for UTI is not confined to resource limited settings but is a recurring feature of acute, time pressured clinical encounters more generally, careless of health system (23). A broader analysis of antibiotic prescribing patterns together with post treatment follow up in UTI patients extends this line of inquiry beyond the initial prescription itself, examining whether patients who receive antibiotics for UTI are adequately followed up and whether treatment failure or recurrence is being systematically captured, an area that the review literature suggests remains comparatively under studied relative to prescribing appropriateness (24).

This adds another layer of complexity with renal and hospital based prescribing. A study by Dhodi DK et al., on the prescribing patterns of antibiotics in UTI patients with coexisting nephritic disorders in a tertiary care hospital, highlighted the extra care needed in the selection and dosing of antimicrobials in patients with compromised nephritic function, which has a considerable overlap with the diabetic population due to the common occurrence of diabetic nephropathy (25). A larger drug utilisation study evaluating physician adherence to treatment guidelines in patients with UTI also demonstrated the gap between what is recommended and what is actually prescribed, further supporting the idea that prescribing in accordance with guidelines for UTI is still more of a goal than a solid achievement in many hospital systems.(26).

A separate evaluation of diagnosis and antibiotic prescription patterns among hospitalized UTI patients adds a further dimension by questioning not only the choice of antibiotic but the symptomatic threshold used to initiate treatment in first place. This is an issue that becomes pertinent in diabetic patients where symptomless bacteriuria is general and where treating it is now generally discouraged by current guidelines (27).

RISK FACTORS, PREDICTORS AND SPECIAL POPULATIONS

Beyond the presence of diabetes itself, several recurring predictors surface across this literature. Female sex is repeatedly identified as a risk factor for UTI in both diabetic and non-diabetic population. Though several studies suggest the strength of this association may differ by diabetic status, but it is more pronounced or statistically significant exclusively within the diabetic subgroup in some analysis (2,5). Advancing age, poor glycemic control, long duration of diabetes, prior catheterization and a history of previous UTI are among the different predictors that appear about regularity irrespective of what country the study is conducted (2,9,10). Illiteracy and limited health literacy also to some extent have also emerged as self-reliant predictor in the pooled Ethiopian analysis done by Tegegne KD et al. (2).

Substantially older adults represent a peculiarly pivotal subgroup given the steady coexistence of diabetes, continual UTI and polypharmacy in this age band. The cohort evidence on antibiotic prophylaxis in aged patients with continual UTI, while not restricted to diabetics, offers a template for how comorbidity stratified prevention strategies might eventually be tailored more specifically to older adults. It is seen for particularly men in that cohort, historically an under studied group in UTI research generally, appeared to derive a clear benefit from prophylaxis in terms of reduced clinical recurrence and hospitalization (8). Newer pharmacologic considerations are also entering this space, with SGLT2 inhibitor use among Type 2 Diabetics progressively

recognized as its own contributor to genitourinary infection risk, a factor that clinicians managing diabetic UTI must now weigh alongside the more traditional considerations of glycemic control and neuropathic bladder dysfunction (11).

DISCUSSION

Read together, this literature converges on a reasonably coherent narrative, even though it originates from health systems as different as those of Jordan, Ethiopia, Bangladesh, Saudi Arabia, Equador and the Indian subcontinent. Diabetic patients experience UTI further often compared to their non-diabetic counterparts. The most profound causative organism is *E. coli* but the surrounding spectrum and the resistance profile of that spectrum tends to be less favourable in diabetic patients and the prescribing practice for UTI in general, keeping diabetic status aside, continues to fall short of guideline concordance in a meaningful proportion of encounters across very different practice settings (1,2,3,4,5,6,7,17).

The practical implications for prescribers are notably short even if the underlying evidence base is heterogeneous. First, existential antibiotic selection for suspected UTI in diabetic patients plausibly warrants a somewhat infernal threshold for sending a urine culture before, or very presently after starting therapy, given the systematically reported gap is susceptibility between the diabetic and non-diabetic isolates (6,17,18). Second, topically generated antibiograms, rather than published resistance data from different regions, should guide existential choice wherever they are available, since the resistance patterns across different countries differ sufficient in magnitude while loosely concordant in direction. Third, the continual under-use of nitrofurantoin and fosfomycin relative to broader spectrum agents, documented most clearly in the Ecuadorian data but varied elsewhere, suggests that stewardship interventions targeted specifically at first line agent selection rather than at antibiotic use in general, may offer a relatively efficient point of intervention (7). Finally, symptomless bacteriuria in diabetic patients continues to be treated further often than current evidence supports, and correcting this pattern of over treatment may do as much for resistance containment in this population as tightening the choice of agent for genuinely symptomatic infection (27,28).

CONCLUSION

The comparative review article on UTI in diabetic versus non-diabetic patients, spanning microbiology, resistance surveillance and prescribing behaviour, points towards a population that is not radically different from the general UTI population in terms of which organism is most often responsible, but is meaningfully different in how readily that organism resist standard therapy. *E. coli* remains the main organism across almost every setting that is reviewed here, yet the diabetic patients appear to carry a bacterial and resistance burden that tilts consistently towards greater difficulty. Antimicrobial prescribing for UTI continues to diverge from guideline recommendations in both diabetic and non-diabetic patients across widely different health systems, with under use of preferred first line agents and a persistent tendency towards existential broad spectrum therapy. Bringing these threads together argues for diabetes aware prescribing protocols, wider acceptance of culture guided therapy in this subgroup, and continued institution level research that can generate the locally relevant antibiogram and prescribing data on which genuinely rational antimicrobial use ultimately depends.

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