

Management of Urinary Tract Infections: a retrospective review in the local Urology Unit

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Background: Urinary Tract Infections (UTIs) affect an estimated 150 million people per annum worldwide and can be classified into simple and complicated as well as upper and lower. The primary method of diagnosing a UTI is via an adequate and timely sample of urine for culture and sensitivity. The main aims of this retrospective audit were to determine the type of UTIs admitted to the Urology unit at Mater Dei Hospital, the rate of utilization and timing of urine and blood cultures, the empirical antimicrobials prescribed and the rate of resistance to these antimicrobials, especially the rate of Fluoroquinolone resistance.

Method: In this retrospective audit, patients admitted with a UTI to the Urology Department during a 4-week period were included in the study.

Results: The majority of patients included in this study were diagnosed with a complicated UTI. A urine sample for culture and sensitivity was taken on the first day of admission in most cases, with *Escherichia coli* being the commonest cultured organism. Resistance to Fluoroquinolones was exhibited in 36% of cases. Piperacillin/Tazobactam was the empirical antibiotic of choice in 59.4% of the patients with the majority showing sensitivity to it. Most patients were discharged with an outpatient follow-up however, only 35% of patients had further imaging studies.

Conclusion: International guidelines regarding diagnosing and treating UTIs are adhered to at large. However, local guidelines are required to improve empirical antimicrobial choice and prescription according to the local prevalent organisms and their sensitivities.

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Urinary tract infections (UTIs) are among the commonest presenting complaints to the Accident and Emergency (A&E) department, affecting an estimate of 150 million people per annum worldwide.¹ Infections affecting the lower urinary tract, that is, the bladder, prostate and urethra, generally present with dysuria, urgency and frequency while those involving the kidney (pyelonephritis) present with flank pain, fever and constitutional symptoms.²

UTIs are classified into simple and complicated with the latter being defined as infections that present in males, pregnant females, patients with anatomical and/or functional aberrations of the renal tract, patients with indwelling urinary catheters and immunocompromised patients.³ Risk factors associated with UTI include regular sexual intercourse, postmenopausal females and history of UTIs during pre-menopause or childhood, family history, incomplete voiding and patients with neurogenic lower urinary tract symptoms (LUTS).⁴ Possible complications of UTIs include persistent LUTS, abscess formation, renal failure and stone formation.⁵

Escherichia coli is the most common causative organism followed by *Klebsiella pneumoniae*, *Enterococcus* spp and *Proteus mirabilis*.⁶ Identification of the causative organism is essential in suspected complicated UTIs and in uncomplicated UTIs which recur within four weeks, do not respond to empirical antibiotics or those with an atypical presentation. The current gold standard for this is via a urine sample for microscopy, culture and sensitivity, ideally taken prior to any antimicrobial administration. Significant bacteriuria that is suggestive of UTI is characterised by 100,000 or more colony forming units (CFU) per millilitre of urine.⁷

The main roles of radiological imaging in patients presenting with UTIs are to identify possible underlying causes including obstruction and/or anatomical aberrations.⁸ Indeed, the European Association of Urology (EAU) recommends an ultrasound (US) examination of the upper urinary tracts in patients presenting with a UTI on a background of previous urolithiasis, deranged renal function and/or high urinary pH. Patients who remain febrile 72 hours after treatment initiation and those with clinical deterioration require further assessment

with a contrast-enhanced computed tomography (CT) scan. In pregnant females, an US or Magnetic Resonance Imaging (MRI) is preferred.²

Treatment of UTIs generally involves antimicrobials and symptomatic relief. The choice of antimicrobials should be determined by the sensitivity of the causative organism, efficacy of the drug as well as side effect profile, cost and availability. Aminopenicillins and fluoroquinolones are contraindicated as empirical treatment of uncomplicated UTIs in view of resistance.² In 2019, the European Medicines Authority (EMA) restricted the use of empirical Fluoroquinolones in all European Union (EU) member states on account of their long lasting, severe and potentially irreversible adverse effects.⁹

Urine culture should be repeated one week after treatment cessation in order to assess the efficacy of treatment. US imaging of the renal tract is advised in males after their first UTI and in females with more than two UTIs every 6 months. A CT intravenous urography (IVU) is recommended in patients with a slow response to antimicrobials, in cases of recurrent UTIs and in patients with a high risk for papillary necrosis. Additionally, urodynamic studies should be performed in patients with unexplained abnormal bladder emptying¹⁰

AIMS

The primary objectives of this retrospective audit are to determine the classification of UTIs to the local Urology unit as well as to evaluate the frequency at which urine and blood culture and sensitivity samples are collected. Additionally, this audit aims to identify the types and classes of empirical antibiotics prescribed to patients admitted with UTIs and to assess the rate of resistance to these antimicrobials. Secondary objectives include examining the type and indications of imaging modalities utilised in the diagnosis and management of UTIs, as well as evaluating the follow-up of UTI patients through outpatient visits, imaging studies, and flexible cystoscopies.

MATERIALS AND METHODS

Data regarding patients admitted with a UTI to the Urology Unit at Mater Dei Hospital was gathered retrospectively over a 4-week period in June 2023. All

data was obtained from iCM Clinical Manager and Patient Dashboard. Permission was obtained from the data protection officer at Mater Dei Hospital, and all data was anonymised in a spreadsheet.

Demographics, including age, gender, diabetic status, and whether they were on Empagliflozin prior to admission, were recorded. UTIs were then classified as either simple or complicated using the aforementioned criteria, and by anatomical site (i.e., lower versus upper UTI). Data regarding whether urine and blood samples for culture and sensitivity were taken, the timing of sample collection, the organism cultured, and the resistance pattern to Fluoroquinolones was noted. The type, route, dose, and duration of empirical antibiotics prescribed were recorded for each patient, as well as the sensitivity of the cultured organism to the initial antibiotic prescribed and whether the antimicrobials were altered according to the culture and sensitivity results. Furthermore, the patient's total length of hospital stay, any follow-up imaging and the imaging modality performed, as well as follow-up flexible cystoscopy and outpatient appointments, were recorded.

Patients admitted to Mater Dei Hospital with a UTI during June 2023 who were not under the care of a Urology firm and those under the age of 18 years were excluded from the study.

RESULTS

A total of 37 patients were included in this study with 33 being male and 4 female. The average age of the patients was 58.24 years. 13 out of 37 patients were diagnosed with diabetes mellitus prior to the admission and none of these patients were on Empagliflozin. A total of 6 patients out of 37 had a recent HbA1c over the last 6 months with the average recording being 6.8%.

94.5% (n=35) of patients were investigated with a urine culture and sensitivity, 80% of which were taken on the first day of admission with the remainder being taken on day 2. A complicated UTI was diagnosed in 36 out of 37 patients (97.2%). The commonest anatomical site was epididymo-orchitis in 17 (45.9%) of the patients followed closely by cystitis in 16 (43.2%) of the patients. The average length of the hospital stay was 6.14 days.

Escherichia coli was the commonest organism cultured (25.7%) and a total of 9 patients had a negative urine culture and sensitivity result. Amongst the positive urine cultures, 22.2% (n=12) were resistant to Ciprofloxacin, 33.3% (n=8) were sensitive and the remainder showed intermediate sensitivity.

Blood cultures were taken from a total of 15 patients (40.5%), 10 (66.6%) of which came back negative, 2 cultured *Serratia marcescens*, 1 with *Staphylococcus hominis*, 1 *Staphylococcus aureus* and 1 *Enterococcus faecalis*.

Piperacillin-tazobactam was the empirical antibiotic of choice in 22 of the patients, 4 patients were administered empirical Co-amoxiclav and 4 others were prescribed Levofloxacin empirically. 1 of the patients received Gentamicin, another patient received Ceftriaxone as an empirical antibiotic, 1 other patient was given Ciprofloxacin and another received a combination of Ceftazidime and Doxycycline.

Sensitivity to empirical antibiotics was seen in 18 of the patients, 1 patient was resistant and the other had intermediate sensitivity. No data was available for the rest of the patients.

Upon discharge, only 13 of the patients were followed up with imaging whilst no image follow-up was recorded for the other patients. US Kidneys was the commonest imaging modality used in 4 patients, followed by US testes in 3 patients and CT IVU in 2 patients. 62.1 % (n=23) of patients from the total cohort were discharged with a surgical outpatient follow-up whilst 29.7% (n=11) had no documented follow-ups and 8.1% (n=3) had no data recorded. Follow-up cystoscopy was only carried out in 14.2% (n=5) of patients,

DISCUSSION

UTIs are described as microbial infections of the urinary tract leading to inflammation of the affected structures.¹¹ Diagnosis of a UTI depends on the clinical history and the presence of risk factors. Uncomplicated cystitis in a female with no risk factors can be diagnosed on a history of lower urinary tract symptoms in the absence of vaginal discharge.¹² Urine cultures for uncomplicated cystitis are only indicated if suspecting acute pyelonephritis,

persistent symptoms, symptoms which recur within 4 weeks from treatment completion and females with atypical symptoms.¹³ All complicated UTIs merit a urine culture and sensitivity, as previously mentioned. The majority of patients in this cohort had a urine culture and sensitivity sample taken at presentation, in accordance with EAU guidelines.

Most patients with a UTI can be managed safely in the community with short courses of antimicrobials. To date, there are no scoring systems which help Emergency physicians decide which patients presenting with a febrile UTI are at risk of poor outcomes and thus require a hospital admission. Therefore, physicians tend to rely on the patient's clinical presentation, parameters, comorbidities and blood results to aid their decision-making.¹⁴

The absolute majority of the patients included in this study were classified as a complicated UTI. This might be because most patients with simple UTIs are either managed in the community by General Practitioners or discharged from A&E with a community follow-up. Another contributing factor is that patients with a simple UTI that require admission for any reason are admitted under a General Medicine Specialist rather than a Urology Consultant.

Complicated UTIs can be caused by a wider spectrum of microbial pathogens than simple UTIs. The commonest causative organisms in complicated UTIs are *E. coli*, *Proteus* spp, *Klebsiella* spp, *Pseudomonas* spp, *Serratia* spp and *Enterococcus* spp.¹ With *E. coli* being the commonest organism cultivated from our patients, this audit can be considered as a representative sample of the patients presenting with a complicated UTI.

The EAU recommends for all patients admitted with a complicated UTI to be prescribed intravenous antimicrobials according to local guidelines, resistance patterns and past urine culture and sensitivity results.³ According to our results, Piperacillin/Tazobactam is the most commonly prescribed empirical antimicrobial amongst patients admitted with UTIs. This is likely due to the high local resistance to Fluoroquinolones, as demonstrated in our patient cohort. Indeed, this is in concordance with the EAU guidelines which only advise the use of Fluoroquinolones if resistance rates are under 10%.³

First line antimicrobials recommended by the EAU include second or third generation Cephalosporins, Aminoglycosides with or without Amoxicillin or a broad-spectrum Penicillin with or without an Aminoglycoside.³ Piperacillin/Tazobactam is a very potent broad-spectrum β -lactamase inhibitor with activity against Gram positive, Gram negative, aerobic and anaerobic bacteria.¹⁵ The main problem with its empirical use is the increasing resistance throughout the last few years, especially in relation to *E. coli* and *Klebsiella pneumoniae*.¹⁶

A recent study conducted by Abolghasemi et al found that there is no difference in terms of efficacy and side-effect profile between Piperacillin/Tazobactam and intravenous Amoxicillin/ Clavulanic acid in patients admitted with complicated UTIs.¹⁷ This indicates that Piperacillin/ Tazobactam should be reserved for more severe infections, including those caused by extended spectrum β -lactamase (ESBL) producing Enterobacteriaceae and *Pseudomonas* spp.¹⁸

One of the six Ds that characterise antimicrobial stewardship is de-escalation. The others are correct diagnosis, drug, dose, duration and debridement and/or drainage.¹⁹ De-escalation is lacking among this cohort as most patients are switched from Piperacillin/Tazobactam to Amoxicillin/ Clavulanic acid and both are classified as broad-spectrum antibiotics. Proper follow-up of urine culture and sensitivity results as well as input from Microbiologists and Pharmacists can both improve this aspect of UTI management.

Regarding follow-up of adult patients admitted with complicated UTIs, there is very limited research and data available internationally in relation to clinical follow-ups, imaging and flexible cystoscopies. The only available guidelines advise all males with a documented UTI and females with recurrent UTIs to have either an US or CT IVU performed looking for any underlying anatomical abnormality as well assessment of bladder emptying and prostate size in males.¹⁰ However, these guidelines are not clear about the ideal timing and modality of choice for different patient cohorts. This ambiguity is likely why a large portion of our patients did not receive any outpatient follow-up. Additionally, the lack of protocols available can result in patients being lost to follow-up, especially those managed solely in the

community by family or emergency physicians. An interesting addition to this audit would have been to assess the percentage of patients diagnosed with a UTI who required admission after being initially discharged from A&E.

The main limitations of this audit are the limited sample size, short duration and method of data collection. As previously mentioned, only patients admitted to the Urology unit were included in the audit, further limiting the sample size and increasing the likelihood of the sample not being representative. Some data regarding urine culture and sensitivity results and follow-ups was not obtainable from ICM or Patient Dashboard, thus introducing bias in the results and their interpretation.

CONCLUSION

UTIs are amongst the commonest Urology admissions and therefore proper diagnosis and management are essential in accordance with antimicrobial stewardship principles. Proper urine sampling for culture and sensitivity prior to antimicrobial initiation is important for more targeted treatment. In our opinion, local departmental guidelines on the classification of UTIs and ideal empirical antimicrobials should be set up in accordance with the local prevalent microorganisms and their sensitivities. Further research is needed to develop an international clinical score to identify patients at higher risk of complications from UTIs, who would therefore benefit from admission. Additionally, more comprehensive protocols are necessary to provide primary care and emergency physicians with clear criteria for determining which patients require further diagnostic investigations and referral to Urology services.

Abbreviations

UTIs:	Urinary tract infections
A&E:	Accident and Emergency
LUTS:	Lower urinary tract symptoms
CFU:	Colony forming units
EAU:	European association of urology
US:	Ultrasound
CT:	Computed Tomography
MRI:	Magnetic resonance imaging
EMA:	European Medicines Authority
EU:	European Union
IVU:	Intravenous urography
ESBL:	Extended spectrum Beta-lactamase

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