Original Article

Pitfalls in diagnosis and management of suspected urinary tract infection in an urban tropical primary care setting

Alison A Jackson[1], Pauline Siew Mei Lai[1], Aqtab Mazhar Alias[1], Nadia Atiya[2], Siti Nurkamilla Ramdzan[1], Tun Firzara Abdul Malik[1], Fadzilah Hanum Mohd Mydin[1], Haireen Abd Hadi[1], Sajaratulnisah Othman[1]

[1] Department of Primary Care Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia
[2] Department of Medical Microbiology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Abstract

Introduction: Diagnosis and management of urinary tract infection (UTI) are complex, and do not always follow guidelines. The aim of this study was to determine adherence to the 2014 Malaysian Ministry of Health guidelines for managing suspected UTI in a Malaysian primary care setting.

Methodology: We retrospectively reviewed computerized medical records of adults with suspected UTI between July-December 2016. Excluded were consultations misclassified by the search engine, duplicated records of the same patient, consultations for follow-up of suspected UTI, patients who were pregnant, catheterised, or who had a renal transplant. Records were reviewed by two primary care physicians and a clinical microbiologist.

Results: From 852 records, 366 consultations were a fresh episode of possible UTI. Most subjects were female (78.2%) with median age of 61.5 years. The major co-morbidities were hypertension (37.1%), prostatic enlargement in males (35.5%) and impaired renal function (31.1%). Symptoms were reported in 349 (95.4%) consultations. Antibiotics were prescribed in 307 (83.9%) consultations, which was appropriate in 227/307 (73.9%), where the subject had at least one symptom, and leucocytes were raised in urine full examination and microscopic examination (UFEME). In 73 (23.8%) consultations antibiotics were prescribed inappropriately, as the subjects were asymptomatic (14,4.6%), urine was clear (17,5.5%), or UFEME did not show raised leucocytes (42,13.7%). In 7 (2.3%) consultations appropriateness of antibiotics could not be determined as UFEME was not available.

Conclusion: Several pitfalls contributed to suboptimal adherence to guidelines for diagnosis and management of suspected UTI. This illustrates the complexity of managing suspected UTI in older subjects with multiple co-morbidities.

Key words: antibiotic stewardship; asymptomatic bacteriuria; diagnosis; Malaysia; primary care; urinary tract infection.

Introduction

Audit of management of suspected urinary tract infection (UTI) addresses either the diagnostic process [1], or the choice of antibiotics [2], or both [3,4]. Auditing antibiotic choice is straightforward, and studies reported that primary care doctors perform poorly with respect to guidelines [2-4]. In Malaysia a morbidity survey in primary care showed that only 26/60 (43.3%) of prescriptions for UTI were antibiotics recommended by guidelines [5]. Adherence to prescribing advice can be improved, e.g., using audit reports and reminders integrated into patient management software [6].

Auditing the diagnostic process is more complicated as it requires review of symptoms recorded and investigations requested. Diagnosis of UTI is difficult as classic symptoms, (e.g., dysuria, urgency and frequency), can have other causes such as sexually-transmitted infections (STI), atrophic vaginitis or bladder calculus. Uncertainty is greater in the elderly who may have chronic genito-urinary symptoms or incontinence [7]. Studies come from western, temperate countries [1, 4], and it is unclear which are the important differential diagnoses in the tropics. For example, as incidence of urinary calculus is high in Malaysia [8], this may be a more frequent differential than in cooler countries.

To assist diagnosis many studies [9-12] have attempted to derive decision rules or algorithms, by comparing reported symptoms and results of point-of-care-tests with urine culture. One interpretation is that dipstick negative for both nitrites and leucocytes rules out UTI, but it is less clear whether UTI can be diagnosed with positive results for one or both of nitrites and leucocytes [13].

The pathophysiology of UTI is that bacteria multiplying in the bladder trigger an inflammatory response, and many leucocytes enter the bladder [14]. Thus pyuria (presence of leucocytes in the urine) makes the diagnosis of UTI much more likely [14], and some definitions of UTI require pyuria [7]. Nitrites result from bacteria breaking down nitrates in the urine, which requires contact time. Nitrites are specific for bacteria, but not very sensitive, as they may be flushed out if urine is passed frequently [14]. Thus the finding of nitrite negative but leucocyte positive may occur in UTI. If only nitrites are positive, not leucocytes, bacteria are confirmed in the urine, but they may be commensals or contaminants [7,14].

Recently asymptomatic bacteriuria (ABU) has been highlighted [7,15,16]. It occurs when urine is colonised temporarily or long-term by commensal bacteria, without causing inflammation or symptoms. Found in all age-groups, the incidence rises from 1-5% in healthy pre-menopausal women, to 4-19% in otherwise healthy elderly men and women, and 15-50% in institutionalised elderly patients [15]. According to current guidelines antibiotics should only be prescribed for ABU in two situations: pregnancy, and before urological procedures where mucosal bleeding is anticipated. In other patients, e.g., non-pregnant women, ABU has been shown to protect against symptomatic UTI [17]. In diabetic patients ABU is more common (0.7-27%), but antibiotics are not helpful and not recommended [18]. Inappropriate antibiotic prescribing for ABU in developed countries has been reviewed [19]; most studies involved hospital inpatients.

Since diagnosis in suspected UTI is often uncertain, studies have assessed management strategies other than immediate antibiotics. Delaying antibiotics by 48 hours reduces their use and achieves similar, i.e., non-inferior, symptom control to immediate antibiotics [20]. Trials of ibuprofen [21] or diclofenac [22] instead of antibiotics showed these were inferior to antibiotics. However, symptomatic treatment combined with delayed antibiotics may suit some patients, using shared decision-making [22,23]. NICE guidance on antimicrobial stewardship endorses delayed antibiotics [24], and current British advice [25] includes this option in UTI.

The present study attempted to assess both the diagnostic process and antibiotic choice in an urban primary care clinic in Malaysia. Antibiotic choice was compared with national guidelines [26] which use antibiotic resistance data from national surveys [27], and local guidelines [28], which use the hospital's own antibiotic resistance data.

Methodology

Study design, setting and period

A retrospective study was conducted by reviewing electronic medical records (EMR) of all patients aged 18 years and above, who attended the primary care clinic with suspected UTI between July-December 2016. The clinic is attached to the teaching hospital of a public university in Kuala Lumpur, Malaysia. Patients attending this clinic were seen by non-specialist medical doctors, Masters of Family Medicine trainees or Family Medicine Specialists. The clinic uses a rapid laboratory service providing an automated urine dipstick reading and a microscopy report (UFEME).

Selection of subjects

Consultations where UTI was suspected were identified by searching the following keywords recorded under a provisional or confirmed diagnosis: 'urinary tract infection', 'UTI', 'cystitis', 'pyelonephritis', 'urosepsis' or 'bacteriuria'. We excluded consultations which were misclassified by the search engine: e.g. (i) misidentification of terms such as 'chole**cystitis**' as cystitis or 'ro**uti**ne' as UTI; (ii) duplicated records of the same patient at the same consultation where the doctor entered both 'provisional' and 'confirmed' diagnoses. We also excluded consultations for follow-up of suspected UTI. We excluded patients who were pregnant, catheterized, or who had a renal transplant, as guidelines for treatment are different.

Instrument used

A case report form was developed to obtain relevant information including: patient demographics, co-morbidities, previous UTI, immunosuppressive medication, conditions causing disability, use of antibiotics within four weeks before index consultation; patients' relevant symptoms and signs of UTI; request for investigations and the results (e.g., UFEME, culture and sensitivity (C&S)); and management (antibiotic prescription, other medication and advice).

Guidelines used

We compared the practice in our setting with the 2014 Malaysia Ministry of Health (MMOH) [29] guideline, (Figure 1). In addition to the points illustrated, this guideline recommends that doctors note: sexual history, use of spermicide, recurrent UTI, structural defects, and vaginal discharge in women as

its presence makes UTI less likely. The choice of antibiotics was compared with the national and local guidelines pertaining at the time [26,28]. These recommended nitrofurantoin, cefuroxime or co-amoxiclav. Ciprofloxacin was only advised in pyelonephritis. Recommended duration of antibiotics was three-seven days in women, and at least seven days in men.

Operational definition

In this clinic, doctors did not perform dipstick because of the rapid access to UFEME, which was used almost universally in suspected UTI. UFEME was also requested routinely in the follow-up of patients with diabetes and hypertension, primarily to detect proteinuria. The UFEME laboratory report includes an automated photometric dipstick readout of nitrite, leucocyte esterase, and haemoglobin. Unless these are all negative, microscopy is performed. The report includes erythrocytes (raised if $> 1/\mu L$ in males, $> 3/\mu L$ in females), leucocytes (raised if $> 3/\mu L$ in males, $> 10/\mu L$ in females), and presence of bacteria.

The diagnostic process was compared with the guideline suggested by the MMOH [29]. This guideline, which resembles British guidance [25], includes a diagnostic algorithm recommending empiric antibiotic treatment in patients under 65 years with at least three typical symptoms, such as dysuria, frequency, and urgency. When there are fewer symptoms, it advises urinalysis by dipstick, whereby positive nitrite and leucocytes, or positive nitrite alone, could be treated with antibiotics without further investigation. If only leucocytes are positive, UTI is possible. If nitrites and leucocytes are both negative, UTI is very unlikely. We simplified the MMOH guideline to a decision rule, or operational definition, that antibiotic prescribing for suspected UTI was deemed appropriate if there was at least one relevant symptom, and raised leucocytes on microscopy.

Figure 1. Guideline for management of urinary tract infection (UTI) in men and women (Malaysian Ministry of Health 2014 [29], adapted).
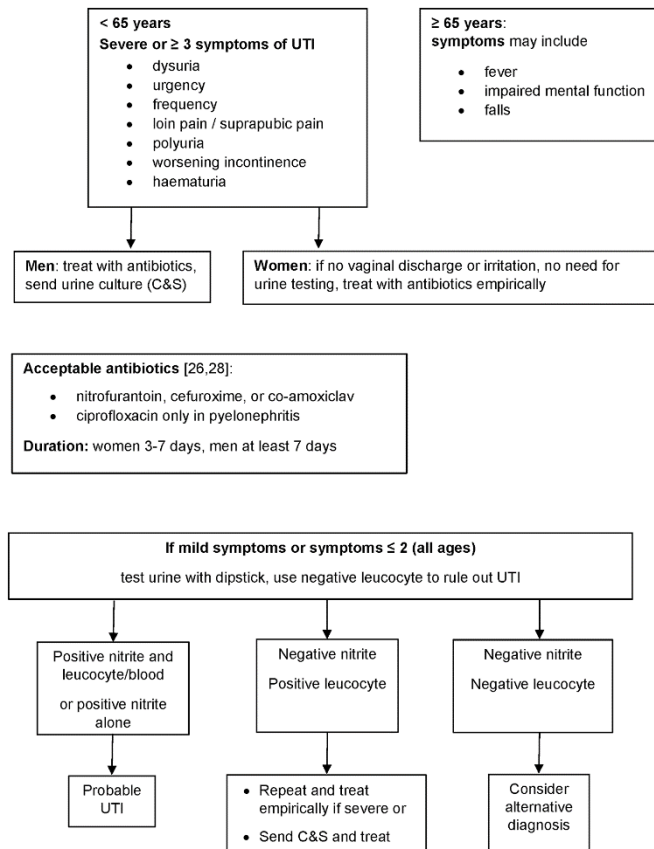

Table 1. Demographic characteristics of subjects with suspected urinary tract infection, in urban primary care in Malaysia, July-December 2016.

N = 348	n (%)
Female	272 (78.2)
Age, years	61.5 (42.2-70.9)
Median age (IQR) years	
18-34	59 (17.0)
35-49	50 (14.4)
50-64	88 (25.3)
≥ 65	151 (43.4)
Ethnicity	
Malay	116 (33.3)
Chinese	105 (30.2)
Indian	99 (28.4)
Others*	28 (8.0)
Recorded allergy to antibiotics	17 (4.9)
Recorded co-morbidities and complicating factors	
Hypertension	129 (37.1)
Prostatic enlargement (males = 76)	27 (35.5)
Impaired renal function (eGFR ≤ 90 mL/min)	109 (31.3)
Diabetes mellitus	101 (29.0)
Previous UTI	96 (27.6)
Mobility impairment likely to interfere with toileting	41 (11.8)
Antibiotics in last 4/52	33 (9.5)
Urinary incontinence	32 (9.2)
Renal, ureteric or bladder calculus	28 (8.0)
Major psychiatric disorder	19 (5.5)
Anatomical abnormalities of the urinary tract	14 (4.0)
Urogenital prolapse (females = 272)	10 (3.7)

*Others: Malaysian but ethnicity not specified 6, Indonesian 4, Bangladeshi 4, Filipino 2, Nepalese 2, Pakistani 2, Nigerian 2, Bidayuh (east Malaysian tribe) 1, Indian national 1, Chinese national 1, Sri Lankan 1, Thai 1, Vietnamese 1. The non-Malaysians comprised 21 (6.0%) of subjects, and of these 11 were male.

Procedure

Having identified consultations where UTI was suspected, we extracted data about that consultation, the index consultation, including symptoms, signs, investigations and management. We noted UFEME findings, and whether symptoms and UFEME result supported use of antibiotics. We noted whether urine culture was requested. Data on co-morbidities were extracted from the index consultation, the follow-up within eight weeks, and from consultations and investigations of the previous twelve months. Descriptive statistics were prepared using SPSS 25. The study received ethical approval from the University of Malaya Medical Centre Medical Ethics Committee.

Results

In total 852 consultations were retrieved, of which 366 were included (Figure 2). Most subjects were female (78.2%), with a median age of 61.5 years. The

Table 2. Symptoms recorded during consultations for suspected urinary tract infection, in urban primary care in Malaysia, July-December 2016.

N = 366	n %
Dysuria	216 (59.0)
Frequency	187 (51.1)
Suprapubic pain	100 (27.3)
Incomplete voiding	43 (11.7)
Fever	42 (11.5)
Haematuria	36 (9.8)
Nocturia	35 (9.6)
Flank or loin pain	35 (9.6)
Urgency	34 (9.3)
Abnormal flow or output*	28 (7.7)
Back pain	19 (5.2)
Cloudy urine	17 (4.6)
Inadequate fluid intake	17 (4.6)
Nausea	16 (4.4)
Incontinence, new or increased	15 (4.1)
Vomiting	13 (3.6)
Offensive urine	11 (3.0)
Polyuria	7 (1.9)
Chills or rigors	7 (1.9)
No symptoms	17 (4.6)
Duration of symptoms in days	
(n = 349, excluding 17 with no symptoms)	
Median (IQR) (n = 321, excluding 28 with duration not recorded)	4.0 (3.0-10.0)
duration of symptoms not recorded	28 (8.0)
1-3	146 (41.8)
4-7	93 (26.7)
8-14	30 (8.6)
15-60	35 (10.0)
> 60	17 (4.9)

*one or more of hesitancy, poor stream, flow not normal, output reduced, or dribbling.

Figure 2. Flow chart for selection of consultations and subjects with suspected urinary tract infection, in urban primary care in Malaysia, July-December 2016.
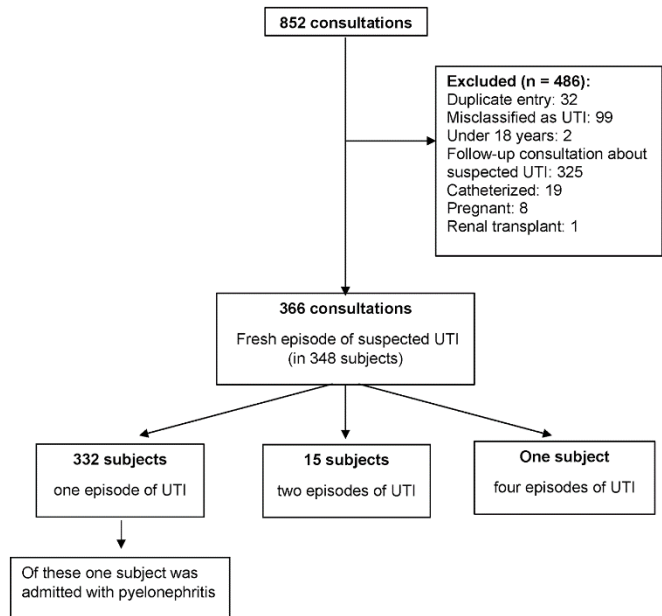

major co-morbidities were hypertension (37.1%), prostatic enlargement in males (35.5%) and impaired renal function (31.3%) (Table 1). Additional co-morbidities and complicating factors of interest included relevant cancer (urogenital, pelvic or disseminated) (2.6%), use of immunosuppressant medication(s) (2.3%), atrophic vaginitis in females (2.9%), overactive bladder (1.4%) and confirmed history of STI (0.9%).

Symptoms recorded during consultation

Symptoms were reported in 349/366 consultations (95.4%) (Table 2). The most common symptoms were dysuria (59.0%), frequency (51.1%) and supra-pubic pain (27.3%). An unexpected finding was the complaint of 'incomplete voiding', in 43 (11.7%) consultations.

Some doctors recorded symptoms suggesting other diagnoses. In 24 (6.6%) consultations, subjects were asked about sandy particles in the urine, and one reported this. In consultations with women, 44/289 (15.2%) were asked about vaginal discharge (eight reported it), and 13 (4.5%) about vulval irritation (nine reported it). Three women reported use of topical products (oestrogen-based vaginal cream or 'feminine wash'). There was no record about spermicide use. In consultations with men, 11/77 (14.3%) were asked about urethral discharge (one reported it). Sexual history was recorded in 24/366 (6.6%) consultations. Two men were recorded as men who have sex with men. One woman reported that she had had more than

one sexual partner. No other high-risk behaviour was recorded.

In 17 (4.6%) consultations, no relevant symptoms were recorded, though urinary symptoms were enquired for. In most of these it appears that UTI was considered because of a UFEME which had been requested in advance of follow-up appointments for hypertension or diabetes. Of these 17 patients, 15 had hypertension and/or diabetes, and 13 had UFEME prior to the consultation. In the whole series 37 (10.1%) UFEMEs were taken in advance; among these, 32 had hypertension and/or diabetes.

Appropriateness of antibiotic prescription

Antibiotics were prescribed in 307 consultations, which was appropriate in 227/307 (73.9%) consultations, where the subject had at least one symptom, and leucocytes were raised in UFEME (Table 3). In 7 (2.3%) consultations appropriateness of antibiotics could not be determined as UFEME was not available.

The remaining 73 (23.8%) who had antibiotics inappropriately, fell into several groups. There were 14 (4.6%) who were asymptomatic; they all had evidence of bacteriuria, either nitrite positive 11 (3.6%), or bacteria seen on microscopy 3 (1%). These 14 all had hypertension and/or diabetes, and UFEME had apparently been ordered routinely. A further 17 (5.5%) had symptoms but urine was clear (nitrite negative, and on microscopy leucocytes and erythrocytes not raised and bacteria not seen). In the remaining 42 (13.7%) the patient had symptoms, and leucocytes were not raised, but the urine showed some abnormality (nitrite positive 14 (4.6%), nitrite negative but erythrocytes raised 18 (5.9%), or no abnormality except bacteria seen on microscopy 10 (3.3%)).

Requests for urine culture

Urine culture was requested in 75/366 (20.5%) consultations, comprising 16/77 (20.8%) consultations with males, and 59/289 (20.4%) consultations with females.

Antibiotic choice

This analysis excludes the subject who was admitted, as the antibiotic was chosen in the ward. From the 306 antibiotic prescriptions given in the clinic, 126 (41.2%) antibiotics were one of the three recommended (nitrofurantoin 68 (22.2%), co-amoxiclav 48 (15.7%), and cefuroxime 10 (3.3%)). The other 180 (58.8%) included cephalexin 159 (52.0%), fosfomycin as a single 3g dose 13 (4.2%), amoxicillin 4 (1.3%), co-trimoxazole 2 (0.7%), erythromycin 1 (0.3%) and ciprofloxacin 1 (0.3%). The prescription of ciprofloxacin was regarded as not following recommendations, as it was not evident that the patient had pyelonephritis. For three prescriptions, data on duration was missing; otherwise duration complied with guidelines except for 13 (4.2%), who were males given courses shorter than seven days. One subject received a 'delayed' prescription, i.e., the patient was advised to wait two days, and then take the antibiotics if the symptoms were not resolving.

Symptomatic treatment

Pharmacological management other than antibiotics was prescribed in 231 (63.1%) consultations. The most common prescriptions were urinary alkalinisers (49.2%) and paracetamol (23.5%). Non-pharmacological management included advice to increase fluid intake (39.1%) and to address local hygiene (6.8%).

Discussion

Using our operational definition, requiring at least one symptom, and pyuria, we found 73.9% of decisions to prescribe antibiotics in suspected UTI were appropriate. Inappropriate prescribing occurred either in subjects with asymptomatic bacteriuria (ABU), or in subjects with symptoms but non-confirmatory urine. When antibiotics were given for ABU, this followed a

Table 3. Appropriateness of decision to prescribe antibiotics for suspected urinary tract infection, in urban primary care in Malaysia, July-December 2016.

		Antibiotics given (307) n (%)	Antibiotics not given (59)
Appropriate to give antibiotics	Symptomatic and raised leucocytes	227 (73.9)	15
Inappropriate to give antibiotics	Asymptomatic	14* (4.6)	2
	Symptomatic, but urine clear	17 (5.5)	28
	Symptomatic, some abnormality in urine but leucocytes not raised	42 (13.7)	12
No urine full examination and microscopic examination (UFEME)		7 (2.3)	2

Decision rule for the appropriateness of antibiotic: at least one symptom present, and leucocytes in UFEME raised (> 3/μL in male, > 10/μL in female); *all were routine UFEME for hypertension and/or diabetes mellitus.

UFEME requested 'routinely' for hypertension or diabetes. Our other main finding was that choice of antibiotics followed local guidelines in 41.2% of prescriptions.

Other studies have reported antibiotics given inappropriately in ABU. A review [19] of 30 studies, mostly of hospital inpatients in developed countries, found a pooled prevalence of inappropriate prescribing for ABU of 45%. A study in Irish general practice [4] reported inappropriate antibiotic prescribing in adults with symptoms of UTI but non-confirmatory urine. In this study all subjects were tested for pyuria and culture. Of 481 who received antibiotics, 158 (32.8%) had culture confirmation, a further 55 (11.4%) showed pyuria, while 268 (55.7%) had no laboratory evidence of UTI. A study [1] in the USA assessed appropriateness of initiating antibiotics for suspected UTI in the emergency department (ED). Requiring at least one symptom, and either leucocytes or nitrites on immediate urine testing, the study found 55/94 (58.5%) patients started antibiotics inappropriately. Many patients had urinalysis before seeing a clinician. The authors suggested some tests were unnecessary and led to unnecessary antibiotics, which resembles our finding that 'routine' UFEME appeared to lead to inappropriate antibiotics. Our report seems to be the first to highlight the pitfall of inappropriate prescribing for ABU found on routine urinalysis in hypertension and diabetes.

In Malaysia, national guidelines for hypertension and diabetes encourage routine UFEME testing. The hypertension guideline [30] recommends testing for albuminuria or microalbuminuria, and checking for microsopic haematuria with respect to possible renal disease. The diabetes guideline [31] recommends testing for albuminuria or microalbuminuria, and advises annual urine microscopy. These policies could be reviewed, and if regular microscopy is still required, doctors should learn not to treat ABU.

In suspected UTI doctors should consider alternative diagnoses. We found few consultations assessed possible STI symptoms, or sexual history. This suggests opportunities were missed to diagnose and treat STI. Similarly, a study [32] in the USA among adult women presenting to ED, found over-diagnosis of UTI and under-diagnosis of STI. Another American study [33], reviewing ED consultations where young women with dysuria had been diagnosed with UTI, found sexual history was only recorded in 17%.

An unexpected finding in our study was the symptom 'incomplete voiding' in 11.7% consultations. It was recorded in English but appears to represent the Malay phrase *'tidak lawas'* (personal communication from clinic doctors, 2017). It is unclear whether it represents strangury, i.e., slow, painful urination caused by muscular spasms of the urethra and bladder [34], which occurs in cystitis, or a voiding problem related to an anatomical or neurological problem. This needs further study.

Regarding whether doctors should use C&S to increase accuracy of diagnosis, we note that C&S was requested in 20.8% of consultations with males, and 20.4% of consultations with females. This is surprising since the MMOH guideline [29] suggests that C&S should be requested in all males, but only selected females. We cannot say whether doctors knew the guidance, or if other factors operated, e.g., doubt whether patients would return to review C&S result. In terms of managing uncertainty, only one consultation used delayed prescription [20,23-25]. The doctors may not have considered this option, as it does not feature in the Malaysian guideline [29], or maybe it seemed impractical since patients collect their prescription from the attached pharmacy on the day. Symptomatic treatment was extensively used, though we note that for alkalinisers there is insufficient evidence to support their use [35].

Our finding on antibiotic choice, that 41.2% of antibiotic prescriptions followed local guidelines, can be compared with other studies: in Malaysia 43.3% antibiotic choices for UTI followed guidelines [5], in Israel 40.5% [2], and in Ireland 37.2% [4]. In our study the first-generation cephalosporin, cephalexin, was prescribed extensively though not recommended, while the second-generation cefuroxime, which is recommended, was used little. It emerged that until June 2016, just before our study period, the more expensive cefuroxime was not available for prescription in this clinic. When the cheaper generic form became available, it was added to the approved formulary, but we found the clinic doctors had not yet adopted it very much. Antibiotic choice might be improved using information technology, e.g., reminders integrated into patient management software, as demonstrated in Ireland [6].

A strength of our study is the inclusion of adult males and females of all ages, which highlighted the complexity of diagnosing UTI in older patients with many co-morbidities. A limitation is the incompleteness of medical records, as illustrated in 28 (8.0%) consultations where duration of symptoms was omitted (Table 2). Another limitation is the difficulty of setting a decision rule for UTI diagnosis. We accepted one symptom only, but some definitions in the elderly [7] require at least two symptoms.

Conclusion

A retrospective review found incomplete adherence to local guidelines for management of suspected UTI. Pitfalls included inappropriate antibiotic prescribing in patients with ABU, and in patients with non-confirmatory urine. The majority of antibiotics chosen were not recommended. To improve antibiotic stewardship doctors should avoid antibiotics in ABU, and where urine is non-confirmatory they should seek other diagnoses. The practice of 'routine' UFEME needs review. These findings are probably relevant to primary care in many countries, but in Malaysia specifically further research needs to clarify what 'incomplete voiding' means.

Acknowledgements

References

1. Kiyatkin D, Bessman E, McKenzie R (2016) Impact of antibiotic choices made in the emergency department on appropriateness of antibiotic treatment of urinary tract infections in hospitalized patients. J Hosp Med 11: 181-184.
2. Kahan E, Kahan NR, Chinitz DP (2003) Urinary tract infection in women--physician's preferences for treatment and adherence to guidelines: a national drug utilization study in a managed care setting. Eur J Clin Pharmacol 59: 663-668.
3. Llor C, Rabanaque G, Lopez A, Cots JM (2011) The adherence of GPs to guidelines for the diagnosis and treatment of lower urinary tract infections in women is poor. Fam Pract 28: 294-299.
4. Vellinga A, Cormican M, Hanahoe B, Bennett K, Murphy AW (2011) Antimicrobial management and appropriateness of treatment of urinary tract infection in general practice in Ireland. BMC Fam Pract 12: 108.
5. Teng CL, Tong SF, Khoo EM, Lee V, Zailinawati AH, Mimi O, Chen WS, Nordin S (2011) Antibiotics for URTI and UTI - prescribing in Malaysian primary care settings. Aust Fam Physician 40: 325-329.
6. Vellinga A, Galvin S, Duane S, Callan A, Bennett K, Cormican M, Domegan C, Murphy AW (2016) Intervention to improve the quality of antimicrobial prescribing for urinary tract infection: a cluster randomized trial. CMAJ 188: 108-115.
7. Mody L, Juthani-Mehta M (2014) Urinary tract infections in older women: a clinical review. JAMA 311: 844-854.
8. Alatab S, Pourmand G, El Howairis Mel F, Buchholz N, Najafi I, Pourmand MR, Mashhadi R, Pourmand N (2016) National profiles of urinary calculi: a comparison between developing and developed worlds. Iran J Kidney Dis 10: 51-61.
9. Chalmers L, Cross J, Chu CS, Phyo AP, Trip M, Ling C, Carrara V, Watthanaworawit W, Keereecharoen L, Hanboonkunupakarn B, Nosten F, McGready R (2015) The

10. Knottnerus BJ, Geerlings SE, Moll van Charante EP, Ter Riet G (2013) Toward a simple diagnostic index for acute uncomplicated urinary tract infections. Ann Fam Med 11: 442-451.
11. Little P, Turner S, Rumsby K, Warner G, Moore M, Lowes JA, Smith H, Hawke C, Mullee M (2006) Developing clinical rules to predict urinary tract infection in primary care settings: sensitivity and specificity of near patient tests (dipsticks) and clinical scores. Br J Gen Pract 56: 606-612.
12. McIsaac WJ, Moineddin R, Ross S (2007) Validation of a decision aid to assist physicians in reducing unnecessary antibiotic drug use for acute cystitis. Arch Intern Med 167: 2201-2206.
13. Deville WL, Yzermans JC, van Duijn NP, Bezemer PD, van der Windt DA, Bouter LM (2004) The urine dipstick test useful to rule out infections. A meta-analysis of the accuracy. BMC Urol 4: 4.
14. Struthers JK, Weinbren MJ, Taggart C, Wiberg KJ (2012) The urine specimen. In Struthers JK, Weinbren MJ, Taggart C, Wiberg KJ editors. Medical Microbiology Testing in Primary Care. London: Manson Publishing Ltd. 46-65.
15. European Association of Urology. (2015) Guidelines on urological infections. Available: https://uroweb.org/wp-content/uploads/19-Urological-infections_LR2.pdf. Accessed: 20 March 2018.
16. Trautner BW, Grigoryan L. (2014) Approach to a positive urine culture in a patient without urinary symptoms. Infect Dis Clin North Am 28: 15-31.
17. Cai T, Mazzoli S, Mondaini N, Meacci F, Nesi G, D'Elia C, Malossini G, Boddi V, Bartoletti R (2012) The role of asymptomatic bacteriuria in young women with recurrent urinary tract infections: to treat or not to treat? Clin Infect Dis 55: 771-777.
18. Harding GK, Zhanel GG, Nicolle LE, Cheang M, Manitoba Diabetes Urinary Tract Infection Study Group (2002) Antimicrobial treatment in diabetic women with asymptomatic bacteriuria. N Engl J Med 347: 1576-1583.
19. Flokas ME, Andreatos N, Alevizakos M, Kalbasi A, Onur P, Mylonakis E (2017) Inappropriate Management of Asymptomatic Patients With Positive Urine Cultures: A Systematic Review and Meta-analysis. Open Forum Infect Dis 4: ofx207.
20. Little P, Moore MV, Turner S, Rumsby K, Warner G, Lowes JA, Smith H, Hawke C, Leydon G, Arscott A, Turner D, Mullee M (2010) Effectiveness of five different approaches in management of urinary tract infection: randomised controlled trial. BMJ 340: c199.
21. Gagyor I, Bleidorn J, Kochen MM, Schmiemann G, Wegscheider K, Hummers-Pradier E (2015) Ibuprofen versus fosfomycin for uncomplicated urinary tract infection in women: randomised controlled trial. BMJ 351: 6544.
22. Kronenberg A, Butikofer L, Odutayo A, Mühlemann K, da Costa BR, Battaglia M, Meli DN, Frey P, Limacher A, Reichenbach S, Jüni P (2017) Symptomatic treatment of uncomplicated lower urinary tract infections in the ambulatory setting: randomised, double blind trial. BMJ 359: 4784.
23. Little P (2017) Antibiotics or NSAIDs for uncomplicated urinary tract infection? BMJ 359: 5037.
24. National Institute for Health and Care Excellence (2016) Antimicrobial Stewardship. Available:

https://www.nice.org.uk/guidance/qs121/resources/antimicrobial-stewardship-pdf-75545353537477. Accessed: 3 October 2018.

25. Public Health England (2017) Diagnosis of urinary tract infections. Available: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/619772/Urinary_tract_infection_UTI_guidance.pdf. Accessed: 20 March 2018.

26. Ministry of Health Malaysia (2014) National antibiotic guideline. Available: https://www.scribd.com/doc/266005740/National-Antibiotic-Guideline-2014-Full-Version. Accessed: 20 March 2018.

27. Ministry of Health Malaysia (2016) National antibiotic resistance surveillance report 2016. Available: http://www.imr.gov.my/images/uploads/NSAR/NSAR_2016/NSAR_report_2016.pdf. Accessed: 27 February 2018.

28. University of Malaya Medical Centre (2017) Antibiotic guideline. Available: http://farmasi.ummc.edu.my/antibioticguideline. Accessed: 22 March 2018.

29. Ministry of Health Malaysia (2014) Protocol on antimicrobial stewardship program in healthcare facilities. Available: https://www.pharmacy.gov.my/v2/en/documents/protocol-antimicrobial-stewardship-program-healthcare-facilities.html. Accessed: 11 January 2018.

30. Ministry of Health Malaysia (2013) Clinical practice guidelines. Management of hypertension. Available: http://www.moh.gov.my/penerbitan/CPG2017/Hypertension1.pdf. Accessed: 3 October 2018.

31. Ministry of Health Malaysia (2016) Clinical practice guideline. Management of type 2 diabetes mellitus. Available: http://www.moh.gov.my/penerbitan/CPG/CPG%20T2DM%202015.pdf. Accessed: 3 October 2018.

32. Tomas ME, Getman D, Donskey CJ, Hecker MT (2015) Overdiagnosis of urinary tract infection and underdiagnosis of sexually transmitted infection in adult women presenting to an emergency department. J Clin Microbiol 53: 2686-2692.

33. Wilbanks MD, Galbraith JW, Geisler WM (2014) Dysuria in the emergency department: missed diagnosis of *Chlamydia trachomatis*. West J Emerg Med 15: 227-230.

34. Car J (2006) Urinary tract infections in women: diagnosis and management in primary care. BMJ 332: 94-97.

35. O'Kane DB, Dave SK, Gore N, Patel F, Hoffmann TC, Trill JL, Del Mar CB (2016) Urinary alkalisation for symptomatic uncomplicated urinary tract infection in women. Cochrane Database Syst Rev 4: CD010745.

Corresponding author
Assoc. Prof. Sajaratulnisah Othman,
Department of Primary Care Medicine, Faculty of Medicine,
University of Malaya,
50603 Kuala Lumpur, Malaysia.
Tel: +603-79492306
Fax: +603-79494368
Email: sajaratul@ummc.edu.my

Conflict of interests: No conflict of interests is declared.