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A suggested approach to the diagnosis of urinary tract infection and empiric use of antibiotics among hospitalized older adults with acute confusion and or underlying cognitive and communication deficits

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REVIEW

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ABSTRACT

Background
The true incidence of urinary tract infection (UTI) among hospitalized older adults remains unknown.

Aims
We aim to present an approach to improve correct identification of UTI diagnosis and empiric use of antibiotics among those who are unable to provide history.

Methods
A comprehensive review of the literature was undertaken.

Results
Our suggested approach appears safe and likely to enhance diagnostic accuracy and judicious use of antibiotics among hospitalized older adults.

Conclusion
Our suggested approach is based on best available literature evidence but requires validation in clinical studies.

Key Words
UTI, confusion, antibiotics

What this review adds:

1. What is known about this subject?
UTI is likely over-diagnosed among hospitalized older adults with acute confusion and or underlying cognitive impairment.

2. What new information is offered in this review?
In an attempt to improving correct identification of UTI, the authors would like to present an approach to the UTI diagnosis and empiric use of antibiotics among such hospitalized older patients, based on best available evidence in the literature.

3. What are the implications for research, policy, or practice?
There is a need to identify markers which can accurately aid in diagnosing UTI among those who cannot provide a clear history. Moreover, our suggested approach needs validation in future clinical studies.

Introduction

Urinary tract infections (UTI) are one of the most common indications for antimicrobial use among hospitalized older adults.[1] Many such patients present with undifferentiated febrile or non-febrile illness and have multiple underlying comorbidities with baseline functional and cognitive deficits.

Evidence suggests that a diagnosis of UTI is made incorrectly in approximately 40 per cent of cases. A consequence is that a large number of patients receive antibiotics inappropriately. Henry et al.[2] in his retrospective study on UTI diagnosis among hospitalized patients noted that it appears to have become accepted wisdom among clinicians that a UTI is a common reason for non-specific deterioration in older adults, yet there has never been reliable evidence to support this. They described misdiagnosis of UTI among 43 patients (37.4 per cent) in their study. David et al.[3] described the frequent reasons to opt for antimicrobial therapy among nursing home residents. These were mainly concerns over missing an infection, delaying treatment, or not meeting a resident's or family's expectations. Clinicians may not consider "watchful waiting," as opposed to taking action. Once antibiotics are empirically initiated, a complete course of antibiotics is often pursued despite negative cultures.[4]

This narrative review aims to explore literature to determine:

1. The literature guidance on UTI diagnosis among confused or cognitively impaired patients?
2. The association of confusion and undifferentiated symptoms with UTI?
3. Whether empiric antibiotics carry survival benefit among stable patients with mild to moderate undifferentiated febrile illness?

Moreover, the authors would like to propose an approach based on the best available literature review in an effort to improving diagnostic accuracy of UTI, judicious antimicrobial prescribing, mitigation of related adverse outcomes and cost effectiveness without compromising patient safety.

UTI diagnosis among cognitively impaired patients

The basis of UTI diagnosis is the presence of compatible new onset localizing genitourinary signs and symptoms (not of existing or chronic urinary symptoms).[5,6] However, it may be challenging not only to assess signs and symptoms but also to devise diagnostic criteria among cognitively impaired or non-communicative older adults. Among hospitalized patients with sepsis, positive blood cultures of uro-pathogenic organisms and or positive imaging may greatly help in confirming upper UTI (pyelonephritis) diagnosis but uncertainty remains in diagnosing lower UTI (cystitis) patients, who usually are not febrile and have non-septic illness. A positive urine culture in this setting may not be a reliable indicator of a symptomatic infection. In this scenario, the clinical practice guidance only comes from expert opinion. Lona Mody et al.,[1] suggested the need for urinary studies among cognitively impaired patients to be done, only in the presence of persistent change in mental status (from the baseline) or change in character of the urine not responsive to other interventions, e.g., hydration) as asymptomatic bacteriuria is highly prevalent in this population.[2,4]

Balogun et al.[7] recommended that in evaluating older patients with delirium, all clinically plausible aetiologies to be considered, and it might make sense to use antibiotics with a positive urine culture only after ruling out all possible other reasons for delirium in a hope to clear delirium.

It has been well described that fever, or raised inflammatory markers are not specific to bacterial infection and may be elevated in many viral or non-infectious aetiologies. Furthermore, inflammatory markers are usually raised only in upper tract UTI, and are less commonly abnormal in cystitis. Absence of fever or normal inflammatory markers do not rule out the diagnosis of cystitis.

Is there any association between confusion and non-localizing symptoms and lower UTI?

Balogun et al.[7] have tried to determine an association between delirium and UTI in their systematic review. Since no randomized controlled trials have evaluated this association, it is difficult to determine with certainty the degree to which urinary tract infection causes delirium and how successful treatment of UTI could lead to improvement in delirium. Though the five studies in their review reported an association between delirium in older patients and UTI, all had significant methodological flaws with potential for biases.

A recent systematic review conducted by Mayne S et al.,[5] noted insufficient evidence to conclude if lower UTI and confusion are linked.

Moreover, a few studies did not find any convincing evidence that non-localizable symptoms such as fever

alone, functional decline, behavioural changes, and mental status changes have a good correlation with UTI.[3]

Empiric use of antibiotics in undifferentiated, non-severe or stable acute febrile illness

The guidance on empiric use of antibiotics among undifferentiated febrile illness comes from expert opinions. It has been suggested that deferring antibiotics might be safe even in stable ICU patients. There is evidence that prescribing antibiotics based on 'just in-case' basis is the norm in the intensive care unit.[8] Leone M et al.[9] suggested that a 'watchful waiting' approach should be the rule in stable ICU patients with a suspected infection, until the diagnosis reaches a high enough level of certainty. Denyy et al.[10] in their narrative review suggested to 'wait and watch' in undifferentiated febrile illness without hypotension in ICU patients until microbiological or source of sepsis confirmation. They have reported that not all patients with suspected infection have an actual infection confirmed later. The watchful waiting strategy might be safe when one is not 100 per cent sure a bacterial infection is present.[10] This strategy was deemed safe among suspected nosocomial infections in ICU and suspected catheter related blood stream infection when patients were not in sepsis.[11,12] A prospective cohort study in Israel did not find benefit of early 'appropriate' empirical treatment among hospitalized elderly with CAUTI on patient's survival and proposed that patients with CAUTI with no other source of infection to be observed without antibiotic treatment. Sepsis trend and culture results will dictate directed antibiotic treatment.[13] Reisfeld et al. did not find mortality benefit with use of empiric antibiotics in the presence of cognitive decline and bacteremic sepsis in the subgroup of patients with decubitus ulcers.[14]

We can extrapolate from the above evidence that empiric antibiotics might be safely held off among stable non-ICU elderly patients with mild to moderate undifferentiated febrile and non-febrile illness. However, close hemodynamic monitoring might be required in febrile patients to detect early deterioration in the absence of empiric antibiotics.

A suggested approach to the UTI diagnosis and empiric use of antibiotics among hospitalized (non-ICU) patients with cognitive impairment

To our knowledge, we are the first ones who have provided a categorical guidance on when to start empiric antibiotics and culture directed antibiotics among undifferentiated presentations among older adults who are often suspected cases of UTI. Though we are confident that this approach is safe, it needs validation ideally through a randomized control trial.

It must be appreciated, that there are no robust diagnostic criterias to identify infection or sepsis. The suspicion of infection is based on clinical features and as well as supporting radiological and microbiological data. The distinction of a bacterial from viral infection is typically reliant on clinical features of the disease and raised inflammatory markers, and sometimes can be difficult at the time of presentation in the absence of microbiological data. There is no evidence to suggest that commonly used inflammatory markers such as C- reactive protein (CRP) or plasma procalcitonin differentiate between symptomatic from asymptomatic bacteriuria. Though, procalcitonin has been evaluated in urosepsis, its use in identification of bacterial infection from non-infectious SIRS in un-differentiated febrile illness (non-septic) remains questionable. The authors prefer the use of CRP in non-septic (non-ICU) patients which is readily available and cost effective.

We have proposed an approach to management, based on risk stratification using clinical judgement aided by assessment of hemodynamic parameters, SIRS (systemic inflammatory response syndrome) and laboratory investigations (inflammatory markers, microbiological studies and radiological evidence). The detailed outline on empiric use of antibiotics and diagnosis of UTI in this unique population has been described in Figure 1.

Conclusion

The diagnosis of UTI among cognitively impaired patients with undifferentiated illness should be a diagnosis of exclusion in the absence of a positive blood culture and or radiological evidence of urinary tract infection.

Empiric use of antibiotics among such cases often leads to over-diagnosis and inappropriate continuation of antibiotics just for the sake of antibiotics course completion.

The 'watchful waiting' approach might be appropriate in many of these cases while trying to treat and investigate all possible alternative causes of an undifferentiated presentation.

We suggest culture directed antibiotics in stable patients once the diagnosis of UTI is substantiated. This approach appears safe and likely to enhance diagnostic accuracy and judicious use of antibiotics.

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PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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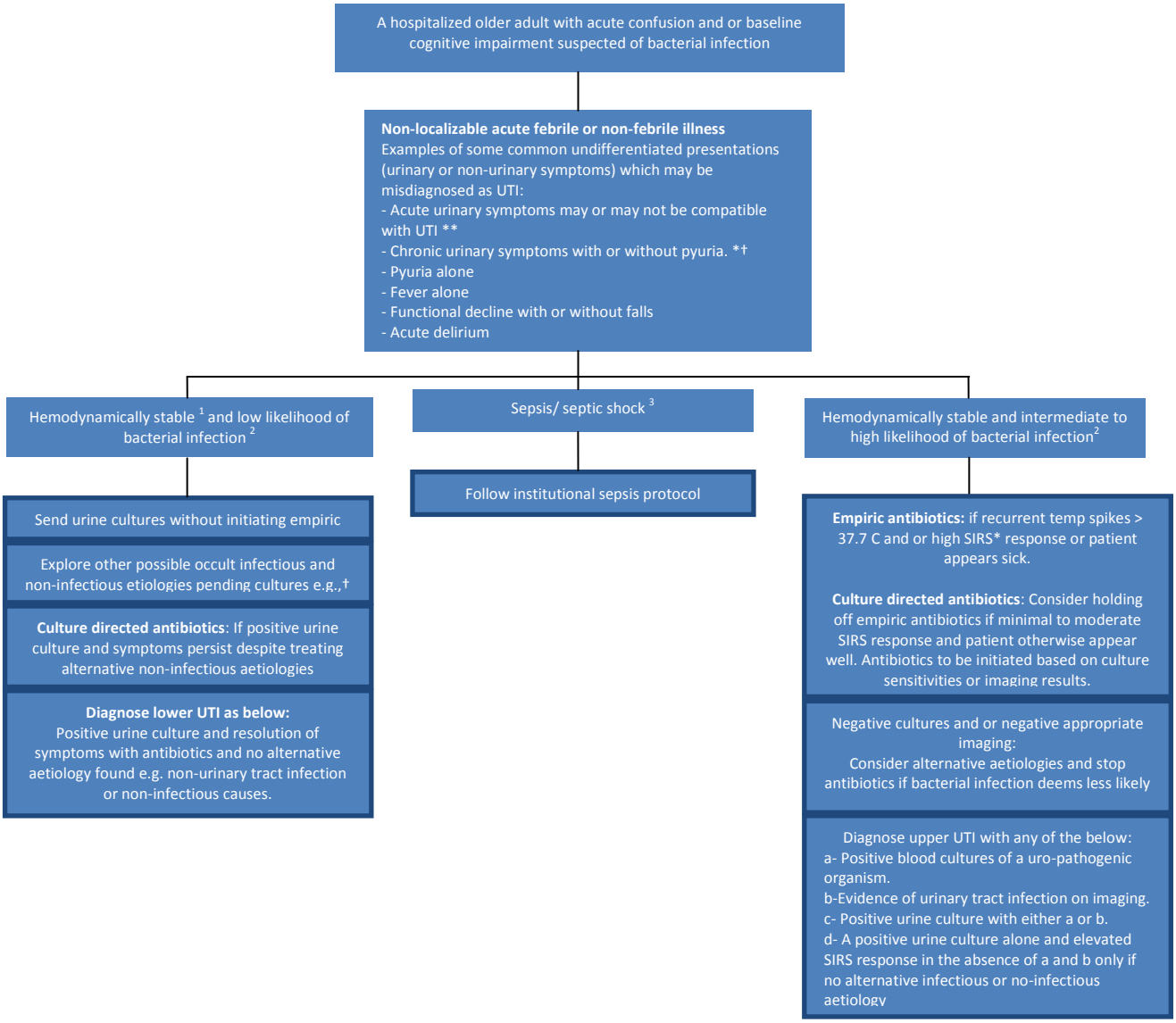
None

Figure 1: A Suggested approach to the diagnosis of upper and lower Urinary tract infections (Catheter and non-catheter related) and empiric use of antibiotics among hospitalized older adults with acute confusion and or underlying cognitive or communication deficits



[1] Adequacy of vital signs (hypotension, tachycardia, tachypnea with low oxygen saturation and extremes of body temperatures) and or surrogates of organ specific perfusion such as reduced urine out-put, severe delirium and elevated lactate.

[2] Based on combination of clinical judgement aided by SIRS (Systemic inflammatory response syndrome) and inflammatory markers.

[3] Life threatening organ dysfunction caused by dysregulated host response to infection. Organ dysfunction is defined as an increase of two or more points in qSOFA (quick sequential (sepsis related)- organ failure assessment score) in the presence of suspected infection.[15]

[*] Systemic inflammatory response syndrome: Pulse rate >90/min, Respiratory rate >20/min, or PaCO2 <32mmHg, Leukocyte count >12000/ul or <4000/ul, Temp> 38C or <36C).

[*†] Chronic urinary symptoms (incontinence, frequency), are not features of UTI.

[**] Haematuria alone, acute urinary retention, urinary sediments, foul smelly or cloudy urine don't necessarily equate to UTI.

[†] Dehydration, drug-drug interactions or related adverse effects, metabolic aetiologies, structural brain disease etc.