Interexpert Agreement on Diagnosis of Bacteriuria and Urinary Tract Infection in Hospitalized Older Adults

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Context: Although bacteriuria with acute coexisting illness is common in hospitalized older adults, distinguishing it from urinary tract infection (UTI) can be challenging.

Objectives: To examine the rate of agreement between two geriatricians in distinguishing UTI from asymptomatic bacteriuria (ASB). To analyze the incidence of associated acute comorbidities and determine if an association exists between clinical manifestations and bacteriuria status on acute hospital admission.

Methods: Two physicians conducted a retrospective analysis of 296 inpatient records, including 142 records from age- and condition-matched nonbacteriuria control subjects. Using consensus criteria to diagnose UTI vs ASB, these independent experts evaluated inpatient records, including admission and discharge diagnoses as well as urinalysis results. A k statistic was used to determine reviewer agreement. Risk assessment was measured by odds ratio with a 95% confidence interval.

Results: Expert agreement for the diagnosis of UTI and ASB was 98% and 44%, respectively. Agreement was reached at a level greater than chance (z=6.74, P<.001, k=0.49). In the 30 cases where interexpert agreement was not reached, half of the subjects had acute pulmonary disease. Symptom crossover for this comorbid condition is the likely cause for lack of diagnostic agreement. Among other conditions observed, delirium was most common in UTI subjects.

Conclusion: Limited interexpert agreement seemed to result from difficulty in diagnosing patients who had no local symptoms but acute comorbid conditions with potential symptom crossover. Among the conditions observed in our sample population, delirium was most closely associated with UTI.

A part from hospitalizations related to childbirth, older adults account for at least one half of all hospital admissions in the United States. Asymptomatic bacteriuria (ASB) is common among this population—as is acute coexisting illness. Although the Infectious Diseases Society of America established guidelines for the clinical management of ASB, many clinicians still face a dilemma because diagnosis is often challenging—and never more so than when patients present with impaired cognition, difficulty explaining their symptoms, or both.

Delays in diagnosing urinary tract infection (UTI) can result in poor clinical outcomes, especially in the frail elderly population. And yet, unnecessary pharmacologic treatment for ASB may lead to adverse effects and an increase in antibiotic resistance.

Earlier studies revealed variations among physicians in the clinical management of UTI and irregular adherence to recommended treatment guidelines. In addition, no information is available regarding levels of clinician agreement with regard to differentiating symptomatic vs asymptomatic bacteriuria and associated acute comorbidities in the hospital setting.

Therefore, we sought to determine the rate of interexpert agreement in distinguishing UTI from ASB in elderly patients with bacteriuria. In addition, we sought to assess acute comorbid conditions associated with bacteriuria in this patient population.

Methods
This retrospective study, approved by the institutional review board at Ohio University College of Osteopathic Medicine in Athens, was conducted at a community hospital in Southeast Ohio.

Inpatient records of 291 potential subjects aged 65 years or older who received a discharge diagnosis of UTI (ICD-9-CM 2007 code: 599.0, Urinary tract infection, site not specified) from January 2003 through December 2005 were reviewed independently for study eligibility by two physicians who specialize in geriatric medicine (J-T.G., W.R.C.).

Because our study was designed in part to establish an association between clinical manifestations and bacteriuria status on acute admission, records documenting the following patient characteristics were excluded: long-term use of an indwelling urinary catheter, catheter placement prior to emergency department (ED) visit or hospitalization, hospital-
acquired UTI, urine culture revealing contaminates, and active cancer (n=137).

Urine specimens were collected by housestaff either as a catheterized urine specimen or as a voiding sample. Most specimens were obtained in the ED or within 24 hours of hospital admission. Urinalysis and urine cultures were processed according to the hospital’s standardized procedures.

For the purposes of the present study, bacteriuria was defined by urinalysis results demonstrating at least 50,000 colony-forming units per milliliter of a single uropathogen, pyuria (urine leukocyte count of at least 2 neutrophils per high power field of spun urine), or nitrite positive test results. Symptomatic bacteriuria or UTI was defined by a positive urine culture and at least one of the following clinical manifestations:

- local symptoms
- fever
- other symptoms (eg, lower abdominal pain, nausea or emesis, falls)\(^{10}\)
- mental status change or delirium\(^{11-14}\)

It is possible that some symptoms (eg, lower abdominal pain, nausea) may be also interpreted in the clinical setting as resulting from comorbidities rather than from UTI (ie, crossover symptoms). In such instances, diagnosis was determined by the principal investigator (J-T.G.).

Finally, ASB was defined by the presence of bacteriuria when the signs and symptoms listed above were not observed.

For the purposes of comparison, a control group (n=142) consisting of age-matched bacteriuria-free patients who were hospitalized during 2003 was also used.

Data extracted from medical records included age, sex, race and ethnicity, residency prior to admission, documented local symptoms of UTI, medical history, urinalysis and urine culture reports, discharge diagnosis, and length of hospital stay. Data from repeat admissions were not used. Blood test results (ie, complete blood count, serum albumin level, serum urea nitrogen/creatinine ratio) were from the first set of blood samples obtained during ED visit or on hospital admission. Repeated urine cultures were not routinely obtained in this study. All UTI or ASB patients identified in the medical records received oral or intravenous antibiotic treatment during their hospital stay.

Acute discharge diagnosis was extracted from physician discharge summaries and diagnoses as well as from medical record discharge “face sheets.” Delirium, acute confusion, or mental status change documented on admission were grouped as “delirium” on discharge diagnosis.

Examiners were two physicians who specialize in geriatric medicine (J-T.G., W.R.C.). All patients were masked and no identifying information was visible during the review process. Although clinical care may have been provided to some of the study subjects by the examiners, neither was able to determine which patients had or had not been under his care because identifying information was not displayed during record review. Established consensus criteria for UTI and ASB were reviewed by each physician before case details were analyzed independently to determine diagnosis retrospectively.

Diagnostic agreement was then compared. Mean (SD) and percentage with frequency were used to report continuous and discrete variables. A \(\chi^2\) test was used when applicable. Unadjusted logistic regression was used to assess the association between binary outcomes and risk factors.

Risk assessment was measured by odds ratio (OR) with a 95% confidence interval (CI). A \(\kappa\) statistic was used to assess reviewer agreement.\(^{15}\)

Statistical significance was set with an \(\alpha\) level of .05. We used SPSS 15 (SPSS Inc, Chicago, Ill) and SAS/ACCESS 9.1 Interface to PC Files (SAS Institute Inc, Cary, NC) to perform the statistical analyses presented.

Results

All 296 inpatient records were reviewed separately by the examiners (J-T.G., W.R.C.). This review took place 2 to 4 years after care was provided.

Diagnostic Agreement

Proportion agreement between reviewers for both study groups (0.804) was greater than chance (\(z=6.74, P<.001, \kappa=0.49\)). Among the 154 bacteriuria cases, both experts agreed that 102 cases qualified for the diagnosis of UTI and 22 cases were ASB. The agreement for the diagnosis of UTI and ASB were 98% (ie, 102 vs 104) and 44% (ie, 22 vs 50), respectively.

Among the remaining 30 disputed cases, 2 were considered UTI by examiner 1 but ASB by examiner 2; 28 were considered ASB by examiner 2 but UTI by examiner 1. Among these disputed cases, 15 patients (50%) had acute pulmonary disease (eg, acute exacerbation of chronic obstructive pulmonary disease, acute bronchitis).

Patient Characteristics

Two comparisons were made for the purposes of this investigation: (1) patients with bacteriuria vs nonbacteriuria control subjects (Table 1), and (2) UTI vs ASB subjects (Table 2). All 296 study subjects were white.

- Patients with bacteriuria vs control subjects—When compared with individuals from the nonbacteriuria control group (Table 1), patients with bacteriuria (either UTI or ASB) were more often:
  - female (84% vs 75%; OR, 1.84; 95% CI, 1.03-3.26)
  - nursing home residents (OR, 1.74; 95% CI, 1.08-2.80)
  - had a history of hypertension (OR, 1.81; 95% CI, 1.14-2.87)
  - received bladder catheterization in the ED or on admission (OR, 1.72; 95% CI, 1.08-2.74)
Although the prevalence of cognitive impairment ranged from 27% to 31% in both study groups, patients with bacteriuria had a higher rate of delirium on admission than nonbacteriuria controls.

The bacteriuria group had a higher, but not statistically significant, frequency of falls without fracture compared to the control group (OR, 2.22; 95% CI, 0.93-5.27).

Ninety-two (60%) of the 154 bacteriuria subjects received antibiotic treatment in the ED, with the fluoroquinolone lev-
ofloxacin as the medication most frequently dispensed.

There was a similar frequency of pulmonary disease and diabetes mellitus with hyperglycemia as well as similar results for serum urea nitrogen/creatinine ratio and electrolyte panel between the two study groups in the acute discharge diagnosis. However, bacteriuria subjects had a lower frequency of acute pulmonary disease than subjects in the control group (OR, 0.53; 95% CI, 0.32-0.86).

**Patients with UTI and ASB**—By way of comparison, the group of 28 individuals whose UTI diagnosis from examiner 2 was under dispute were reassigned to the ASB group because they had symptoms that could overlap with and possibly be explained by acute coexisting illness.

As shown in Table 2, patients with UTI and ASB had similar clinical profiles with respect to mean (SD) age, sex, nursing home residency, and medical history.

On acute discharge diagnosis, delirium was more common in UTI vs ASB subjects. In addition, UTI subjects had a lower rate of pulmonary disease than those with ASB (OR, 0.14; 95% CI, 0.07-0.31). A similar finding was observed with regard to a diagnosis of pneumonia.

In addition, UTI subjects had shorter hospital stays than those with ASB. However, this finding did not remain statistically significant after adjusting for delirium, falls regardless of fracture status, and pulmonary disease (OR, 0.88; 95% CI, 0.768-1.003).

In distinguishing UTI from ASB, pyuria with a urine leukocyte count of at least 2 neutrophils per high power field of spin urine was found in 95 UTI subjects (91%) compared to 34 ASB subjects (68%) (OR, 5.59; 95% CI, 2.19-14.23) with a sensitivity of 91% and a specificity of 32%. The positive and negative predictive values of pyuria for UTI were 74% (95 of 129) and 64% (16 of 25), respectively.

**Comment**

Our study revealed consistent interexpert diagnostic agreement on UTI. However, the distinction between UTI and ASB was problematic in some cases where acute comorbidity was present (eg, acute pulmonary disease without local urinary tract symptoms), probably as a result of symptom crossover. Pyuria was a sensitive, but not a specific, finding for diagnosing UTI, which suggests that urinalysis is a good tool for screening patients when there is a high level of suspicion for UTI.

In our study, women who were nursing home residents had a higher frequency of bacteriuria—but not UTI—than control group subjects.

Delirium was more commonly found in bacteriuria patients than in nonbacteriuria control group subjects. Although delirium and falls without fracture were more common in UTI patients than in those with ASB, it should be noted that no association was observed between delirium and falls in the bacteriuria vs control comparison regardless of fracture status (OR, 1.12; 95% CI, 0.51-2.49).

Our study demonstrated how a potential comorbidity can blur the distinction between UTI and ASB when physicians attempt to diagnose patients who do not present with local urinary tract symptoms.

The problem of distinguishing UTI from ASB shown in the present study could be the result of several methodologic challenges. For example, the broad definition of UTI we adopted and the potential for crossover symptoms from other acute illnesses in this patient population (eg, nausea and emesis in pulmonary disease) may have influenced the outcomes of the present study.

Because of the relatively small sample size and lack of racial and ethnic diversity in our sample population, this diagnostic challenge requires further investigation—preferably in the form of a randomized double-blind clinical trial of antibiotic treatment for patients with atypical symptoms and bacteriuria.

In the present study, individuals in the nonbacteriuria control group had a higher rate of acute pulmonary disease when compared to subjects in the bacteriuria group. And yet, the coexistence of bacteriuria and acute pulmonary disease could also reflect the high prevalence of ASB in the elderly population, especially among functionally impaired nursing home residents. Study wide, among the 101 inpatients with pulmonary disease in the acute discharge diagnosis, 42 had bacteriuria—a result that is similar to previous reports.

A previous surveillance study revealed a 70% prevalence rate among patients with bacteriuria for no urogenital tract symptoms. This finding was similar to a previous study we conducted in which 70% of hospitalized older adults with bacteriuria had no local urinary tract symptoms or fever (J-T. Gau, MD, PhD, unpublished data, June 2007).

One possible explanation for this phenomenon is that patients with cognitive impairment, a condition that increases in prevalence with age, could be difficult to diagnose because of hampered symptom identification. Clinicians rely on clinical symptoms and signs—such as lower abdominal discomfort or pain, nausea, emesis, fever, and mental status change—when considering diagnostic and treatment options. All too often, however, the symptoms noted by patients in this demographic group are nonspecific and overlap other acute comorbidities.

An algorithmic approach and clinical protocol has been proposed and tested for the management of UTIs in long-term care residents. It is not known whether this algorithm can be applied to hospitalized older adults.

Because of the unique challenges involved in distinguishing UTI from ASB in older adults, a proposal to use “a different combination of existing clinical criteria and geriatric manifestations” to define UTI in older adults has been suggested. The particular challenges of differentiating the clinical manifestations of UTI from potential comorbidities in this
population, especially in the context of hospital and long-term care settings, will need to be addressed in any patient care recommendations.

Researchers have shown that UTI is a risk factor for the diagnosis of delirium among older adults who are either hospitalized or receiving care in a psychogeriatric unit. Our findings suggest that older patients exhibiting delirium or a change in mental status receive urinalysis and urine culture to exclude UTI in differential diagnoses.

Table 2

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Urinary Tract Infection (n=104)</th>
<th>Asymptomatic Bacteriuria (n=50)</th>
<th>Crude Odds Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD) Age, y</td>
<td>83 (8)</td>
<td>83 (8)</td>
<td>...</td>
</tr>
<tr>
<td>Female</td>
<td>86 (83)</td>
<td>44 (88)</td>
<td>0.65 (0.24-1.76)</td>
</tr>
<tr>
<td>Nursing Home Resident</td>
<td>42 (40)</td>
<td>26 (52)</td>
<td>0.62 (0.31-1.25)</td>
</tr>
<tr>
<td>Medical History</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>31 (30)</td>
<td>16 (32)</td>
<td>0.90 (0.44-1.87)</td>
</tr>
<tr>
<td>Cardiovascular health</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Congestive heart failure</td>
<td>30 (29)</td>
<td>19 (38)</td>
<td>0.66 (0.32-1.35)</td>
</tr>
<tr>
<td>- Hypertension</td>
<td>65 (63)</td>
<td>28 (56)</td>
<td>1.31 (0.66-2.60)</td>
</tr>
<tr>
<td>- Stroke</td>
<td>22 (21)</td>
<td>8 (16)</td>
<td>1.41 (0.58-3.43)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>26 (25)</td>
<td>19 (38)</td>
<td>0.54 (0.26-1.27)</td>
</tr>
<tr>
<td>Falls</td>
<td>14 (13)</td>
<td>2 (4)</td>
<td>3.73 (0.81-17.11)</td>
</tr>
<tr>
<td>Hospital Care†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bladder catheter</td>
<td>55 (53)</td>
<td>23 (46)</td>
<td>1.32 (0.67-2.59)</td>
</tr>
<tr>
<td>Antibiotic treatment</td>
<td>67 (64)</td>
<td>25 (50)</td>
<td>1.81 (0.91-3.59)</td>
</tr>
<tr>
<td>Mean (SD) length of hospital stay, d</td>
<td>5.0 (2.4)</td>
<td>6.3 (3.4)</td>
<td>0.85 (0.75-0.96)‡</td>
</tr>
</tbody>
</table>

Acute Discharge Diagnosis

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Urinary Tract Infection (n=104)</th>
<th>Asymptomatic Bacteriuria (n=50)</th>
<th>Crude Odds Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyuria†</td>
<td>95 (91)</td>
<td>34 (68)</td>
<td>5.59 (2.19-14.23)‡</td>
</tr>
<tr>
<td>Delirium</td>
<td>40 (38)</td>
<td>6 (12)</td>
<td>4.58 (1.79-11.73)‡</td>
</tr>
<tr>
<td>Heart Disease</td>
<td>32 (31)</td>
<td>21 (42)</td>
<td>0.61 (0.31-1.23)</td>
</tr>
<tr>
<td>Pulmonary Disease</td>
<td>15 (14)</td>
<td>27 (54)</td>
<td>0.14 (0.07-0.31)‡</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>5 (5)</td>
<td>18 (36)</td>
<td>0.09 (0.03-0.26)‡</td>
</tr>
<tr>
<td>Diabetes Mellitus With Hyperglycemia</td>
<td>19 (18)</td>
<td>13 (26)</td>
<td>0.64 (0.28-1.42)</td>
</tr>
<tr>
<td>Anemia</td>
<td>29 (28)</td>
<td>9 (18)</td>
<td>1.76 (0.76-4.08)</td>
</tr>
<tr>
<td>Falls</td>
<td>24 (23)</td>
<td>2 (4)</td>
<td>7.20 (1.63-31.83)‡</td>
</tr>
<tr>
<td>Fracture</td>
<td>7 (7)</td>
<td>1 (2)</td>
<td>3.54 (0.42-29.56)</td>
</tr>
<tr>
<td>No fracture</td>
<td>17 (16)</td>
<td>1 (2)</td>
<td>9.57 (1.24-74.15)‡</td>
</tr>
<tr>
<td>Blood Test Results</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum urea nitrogen/creatinine ratio, ≥20.1</td>
<td>50 (48)</td>
<td>29 (58)</td>
<td>0.67 (0.34-1.32)</td>
</tr>
<tr>
<td>Electrolyte panel (imbalance)</td>
<td>32 (31)</td>
<td>19 (38)</td>
<td>0.73 (0.36-1.47)</td>
</tr>
<tr>
<td>Serum albumin, &lt;3.0 g/dL</td>
<td>36 (35)</td>
<td>18 (36)</td>
<td>0.94 (0.47-1.90)</td>
</tr>
<tr>
<td>Urinalysis Results§</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukocyte esterase (positive)</td>
<td>76 (74)</td>
<td>33 (66)</td>
<td>1.45 (0.70-3.01)</td>
</tr>
<tr>
<td>Nitrite (positive)</td>
<td>55 (53)</td>
<td>17 (50)</td>
<td>1.15 (0.53-2.49)</td>
</tr>
</tbody>
</table>

* Data are presented as No. (%) unless indicated otherwise.
† Bladder catheterization was provided in the emergency department or on hospital admission; antibiotic treatment was dispensed in the emergency department.
‡ Statistically significant difference (P<.05).
§ Diagnosis of pyuria was based on microscopy (ie, urine leukocyte count ≥2 neutrophils per high power field of spun urine).
// Complete laboratory studies were not available for all study subjects. In the urinary tract infection group, leukocyte esterase dipstick test results were available for 103 of the 104 subjects. Although these results were available for all 50 asymptomatic bacteriuria subjects, nitrite results were available for only 34 of these individuals.

As noted elsewhere, data from our study reveal delirium and greater incidence of falls among patients with UTI. The increased frequency of delirium was seen in the bacteriuria
group when compared to the nonbacteriuria control group, suggesting that delirium was associated with bacteriuria rather than a selection bias.

Although a higher frequency of falls without fracture was seen in the discharge diagnosis for the bacteriuria group, the 95% CI ranged between 0.93 and 5.27, which could be a function of the small sample size and lack of power in our study.

Previous studies have suggested a possible indirect link between UTI and falls. To our awareness, no previous studies have demonstrated a direct association. Further studies using National Hospital Discharge Survey Data or a prospective follow-up study may help establish an association.

Evidence is mounting that the increased use of fluoroquinolone antibiotics is associated with the development of *Clostridium difficile* colitis. Therefore, it is important that physicians take care to distinguish UTI from ASB. Current clinical guidelines recommend against the use of antibiotic treatment for ASB.

In addition to the sample size and demographic limitations previously noted, when evaluating the general applicability of our results, readers may wish to consider certain methodologic limitations of our study. First, the “other symptoms” used for the definition of UTI—beyond local symptoms—are not yet well established in the medical literature. Second, it remains to be verified whether patients with bacteriuria and falls at admission diagnosis should be automatically diagnosed with UTI. This conclusion is not supported by our study’s findings. In designing our study, we included falls as a manifestation of UTI mainly because this criterion was used by previous researchers.

Also, data from urinalysis and urine cultures reviewed in this study were not obtained during the course of routine surveillance procedures. As a result, it is possible that our sample population is subject to selection bias. On a related note, our study design did not afford us with the opportunity to repeat urinalysis and urine culture to confirm ASB diagnosis as recommended by current clinical practice guidelines.

Finally, we cannot rule out a type I error in the association between bacteriuria status and acute pulmonary disease among our subjects.

**Conclusion**

Using established consensus criteria, this retrospective, age-matched, case-controlled study demonstrated a high level of interexpert agreement on diagnosis for UTI vs ASB among hospitalized older adults. The distinction between these two conditions can be problematic in this patient population when certain acute comorbidities are present.

Among the acute comorbid conditions observed in the present study, delirium is common in bacteriuria and UTI patients. Our study reveals no association between falls and delirium. Additional research is needed to better define the diagnosis of UTI in hospitalized older patients with multiple acute comorbidities.

**Acknowledgment**

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**References**


