
Predicting UTI in symptomatic postmenopausal women

A review of the literature

Evidence-based medicine techniques can help clinicians to accurately predict the presence of UTI in postmenopausal women with atypical symptoms and risk factors.

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More research is needed into the problem of diagnosing urinary tract infections (UTIs) in various subpopulations, such as postmenopausal women. This review looks at the research that is available and offers clinicians a chance to improve their diagnostic skills for this population of women using evidence-based medicine (EBM) methods. A blend of peer-reviewed literature, patient perspective, and clinician experience, EBM represents an effort to more accurately predict disease patterns. In this instance, it enables clinicians to review the probability of bias inherent in predicting a UTI diagnosis based on presenting symptoms, risk factors, and office-based dipstick urinalysis.

Urinary tract infection: An overview

Acute UTI accounts for approximately 3.6 million office visits annually by US women 18 to 75 years old. Bladder problems reportedly cost an estimated \$16 billion a year in health-related expenses.¹ Although nonbacterial forms of UTI exist, bacterial infections are far more common. UTIs often manifest in an uncomplicated form, which can be successfully treated empirically. They are more common in women than in men, a result of differences in anatomy, hormones, and behavior.

Clinicians should bear a number of facts in mind in order to provide effective and appropriate care.² The accuracy of a diagnosis based on clinical assessment is often uncertain. Overtreatment and consequent antibiotic resistance are becoming increasingly common, and undertreatment also poses the threat of complications, particularly in postmenopausal women. A methodical approach to improved diagnostic and therapeutic efficacy may include the application of evidence-based principles.

Uncomplicated acute UTI Also termed acute cystitis, this type of infection involves only the bladder. It is not associated with signs or symptoms of upper UTI (fever, chills, or flank pain) or with characteristics suggesting a high risk of upper urinary tract or complicated infection (eg, diabetes, pregnancy, immunosuppression, previous pyelonephritis, symptoms lasting longer than 14 days, or structural abnormalities of the urinary tract).³

Recurrent UTI Consisting of multiple episodes, this kind of infection is subclassified as persistent, reinfection, or unresolved. Reinfection is the most common type of recurrent UTI. It differs from persistent infection by the source of the bacterial pathogens—which is outside the urinary tract—and is primarily due to bacterial resistance.

Bacterial UTI A bacterial UTI includes the inflammatory response and the associated signs and symptoms that result from the presence of the bacteria. Bacteriuria, the presence of bacteria in the urine, may be asymptomatic, particularly in elderly adults. Bacterial

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Key Points

- This literature review offers an opportunity for clinicians to improve their diagnostic decision-making skills through evidence-based medicine methods.
- Postmenopausal women with UTI may not present with typical symptoms and may have risk factors specific to their subgroup.
- Dipstick testing in combination with clinical assessment is superior to clinical assessment alone for diagnosing UTI.

Competencies

Medical knowledge	◆◆◆◆
Interpersonal & communication skills	◆
Patient care	◆◆
Professionalism	◆◆
Practice-based learning and improvement	◆◆◆◆
Systems-based practice	◆◆◆◆

For an explanation of competencies ratings, see the table of contents.

uropathogens likely originate in the GI tract and ascend via the fecal-urethral route.³ *Escherichia coli* is the most prevalent organism associated with community-acquired UTIs; additional common uropathogens include *Enterococcus faecalis* and *Proteus*, *Klebsiella*, *Staphylococcus*, and *Pseudomonas* species.² In an observational study, *E coli* was the etiologic agent in 209 of 252 cases of bacteriuria (82%).⁴

Genetic factors, such as the presence of Lewis nonsecretor status and specific human leukocyte antigens, are responsible for biochemical changes at the cell surface that can contribute to susceptibility. For example, women who do not secrete Lewis blood group antigens (nonsecretors) experience significantly more recurrent UTIs.⁵

Estrogen also plays a role in maintaining the pH balance of the vagina. A normal vaginal flora depends on a normal pH, which in turn regulates colonization by uropathogens. Postmenopausal women have decreased amounts of estrogen, reducing vascularity and leading to atrophy of urethral epithelium and vaginal mucosa. This results in increased uropathogen colonization.⁶

The difficulty of diagnosis based on presenting symptoms

A good deal of research demonstrates the difficulty of diagnosing UTI in postmenopausal women based on presenting symptoms (see Table 1, page 53). One reason is that these women may not have the typical symptoms

of urgency, frequency, and dysuria. Atypical symptoms and signs such as back pain, confusion, and fever may be the only clues.⁷ An observational study of women aged 18 to 87 years within a primary health care setting revealed that a generalized sense of “feeling out of sorts” was frequent in adult women with acute uncomplicated lower UTI, irrespective of the presence of bacteriuria.⁴

Symptoms that are present may also be misinterpreted. A case-based descriptive study of adult women in a primary care setting revealed that clinicians often fail to assess contributing factors and treat unfamiliar and elderly patients with UTI symptoms more frequently than their pretest probability of infection would warrant.⁸

Infection probability correlates with symptoms. A systematic MEDLINE (1966-2001) review revealed that four symptoms (dysuria, frequency, hematuria, and back pain) and one sign (costovertebral angle tenderness) significantly increase the probability of UTI. The authors concluded that in women who present with one or more symptoms of UTI, the probability of infection is approximately 50%; specific combinations of symptoms may increase the probability of UTI to more than 90%.⁹

A prospective, multicenter, randomized, double-blind, placebo-controlled study in women aged 18 years or older calculated the spontaneous cure rate of symptoms and bacteriuria at 24%.¹⁰ The authors concluded that laboratory tests were required to establish the diagnosis of lower UTI.¹⁰

Evidence of risk factors

Although extensively studied in younger women and older debilitated women, the risk factors for UTI among healthy, community-dwelling postmenopausal women have not been well described (see Table 2, page 53). Information gleaned from the literature includes the following:

- A population-based case-control study of women aged 55 to 75 years revealed through likelihood ratio calculations that postmenopausal women with recurrent UTI were more likely to have been sexually active, to have a history of UTI, to have diabetes mellitus, and to be incontinent; the study also found that oral estrogen replacement did not reduce UTI risk.¹¹
- A case-control study from the Group Health Cooperative of Puget Sound also included women aged 55 to 75. It found that women who used oral hypoglycemic agents and insulin had a higher risk of UTI than both nondiabetic postmenopausal women and women with untreated diabetes or diabetes treated by lifestyle changes.¹²
- The Heart and Estrogen/progestin Replacement study of postmenopausal women revealed that hormone therapy did not reduce the frequency of UTIs. Potentially modifiable risk factors in postmenopausal

women were different from those in younger women and included diabetes, vaginal symptoms, and urge incontinence.¹³

- A case-control study that included postmenopausal women with a history of UTI found that urinary incontinence, a history of UTI before menopause, and nonsecretor status were most strongly associated with recurrent UTI in postmenopausal women.¹⁴
- Finally, a population-based, prospective cohort study consisting of 55- to 75-year-old postmenopausal women enrolled in an HMO found that having insulin-treated diabetes and a lifetime history of UTI were independent predictors.¹⁵

Urine dipstick testing

A systematic review of studies of urine dipstick testing classified them as follows:

- Grade A: at least 1 randomized controlled trial (RCT) is available as part of consistent, high-quality evidence
- Grade B: evidence comes from appropriate clinical trials with non-RCT designs
- Grade C: evidence comes from a published consensus of experts.

The literature revealed that a urine culture was not necessary to diagnose uncomplicated UTI (grade B) (see Table 3, page 54). Under general practice conditions, a positive nitrite result on a urine dipstick test had a high positive predictive value (90%-100%) and low sensitivity (46%); a positive leukocyte esterase result was very sensitive (93%). If both test results were negative, the probability of UTI was low (grade A).¹⁶

Dipstick equal to urinalysis In a prospective observational study of symptomatic women, urine dipstick testing was as accurate as urinalysis in diagnosing UTI.¹⁷ Another prospective study, of adults in an emergency department (ED) setting, confirmed that dipstick testing in combination with clinical assessment was superior to clinical assessment alone for diagnosing UTI.¹⁸ A positive result on a dipstick test indicated that the likelihood of UTI was 25% higher than the pretest probability, and a negative result indicated that the likelihood of infection was 25% lower than the pretest probability.¹⁹

Dipstick testing versus analysis of a clean-catch specimen The clean-catch technique for collecting a urine sample is time-consuming to explain, frequently not performed correctly by patients, costly for supplies, often embarrassing for patients and staff, not effective at reducing contamination, and of unproven benefit in outpatient women whose symptoms suggest a UTI.²⁰ Interobserver error has also contributed to potential inaccurate testing and overall bias.²¹

A prospective, observational study of adult women presenting to an ED with symptoms of UTI calculated sensitivity, specificity, and predictive values at positive

test cutoff points for combinations of leukocyte esterase, nitrite, and blood on dipstick testing. Based on defined dipstick cutoff points, overtreatment and undertreatment rates limited the accuracy of diagnosis.²²

A systematic MEDLINE and EMBASE review demonstrated that the urine dipstick test alone seemed to be useful for excluding infection when the results were negative for both nitrites and leukocyte esterase. However, even with high pretest probabilities and high sen-

TABLE 1

Findings from studies that evaluated presenting symptoms

When clinicians knew the patient, they were four times more likely to correctly predict the test result and 12 times less likely to prescribe antibiotics. Clinicians were six times more likely to prescribe antibiotics for older women.⁸

Generalized symptoms of "feeling out of sorts" were frequent in adult women with acute, uncomplicated lower urinary tract infection (UTI). These symptoms were equally frequent in all age groups, whether bacteriuria was present or not.⁴

Four symptoms and one sign significantly increased the probability of UTI: dysuria, frequency, hematuria, back pain, and costovertebral angle tenderness. The two most powerful historical factors were a history of vaginal discharge and a history of vaginal irritation, each of which significantly decreased the likelihood of UTI when present.⁹

The spontaneous cure rate for symptoms and bacteriuria was calculated at 24%, and laboratory tests were required to establish the diagnosis of UTI.¹⁰

TABLE 2

Findings from studies that evaluated risk factors

Postmenopausal women with current urinary tract infection (UTI) were more likely to be sexually active, to have a history of UTI, to have diabetes mellitus, and to be incontinent. Oral estrogen replacement did not reduce UTI risk.¹¹

Potentially modifiable risk factors in postmenopausal women were different from those in younger women and included diabetes, vaginal symptoms, and urge incontinence.¹³

Urinary incontinence, a history of UTI before menopause, and nonsecretor status were most strongly associated with recurrent UTI in postmenopausal women.¹⁴

Independent predictors of UTI included using oral hypoglycemic agents or insulin and having a lifetime history of UTI.¹⁵

sitivity, the usefulness of the urine dipstick test alone to rule in infection remains doubtful.²³

Discussion

The author reviewed the literature in an effort to summarize the evidence available on factors that predict, and variables that influence, the clinician's ability to diagnose community-acquired, uncomplicated, and recurrent lower UTIs in symptomatic postmenopausal women within the primary care setting. The focus was on literature related to presenting symptoms, risk factors, and office-based dipstick urinalysis. MEDLINE (1975-2005) and EMBASE (1990-1999) databases were researched. The search was limited to RCTs reported in English and conducted in humans. Although this review was not completely successful in identifying research consistent with its inclusion criterion and area of interest, it offers the reader a practical, EBM approach to calculating the probability of a UTI based on presenting symptoms, risk factors, and urine dipstick test findings.

While some good evidence existed for our study topic, it was limited by methodologic problems and a failure to address many of the factors that impact various subgroups (such as postmenopausal women). The studies in this review did not define terms consistently, nor did they provide a comprehensive definition of their target diagnosis, suggesting the threat of differential

bias. In addition, applying conclusions to subgroups not adequately represented in the original study may result in inaccurate diagnoses based on selection and spectrum biases, lack of test procedure definition, imprecise execution of test procedure, and inadequate description of the patient survey process.

Conclusion

The literature states that postmenopausal women may not present to the clinician with "typical" UTI symptoms, may have risk factors based on physiologic changes related to aging, and may harbor organisms in the bladder that are not detected by the office dipstick test. Misdiagnosis of uncomplicated lower UTI in an older population may contribute to the development of complicated infections that require advanced and costly therapeutic intervention. Therefore, clinicians should consider including a gold standard diagnostic intervention to reduce misdiagnosis and to ensure a high quality of care for populations with atypical presentations. □

TABLE 3

Findings from studies that evaluated urine dipstick testing

Urine dipstick testing was as accurate as urinalysis in diagnosing urinary tract infection (UTI) in symptomatic women, and confirming a dipstick test with a urinalysis appeared to be unnecessary.¹⁷

Dipstick testing combined with clinical assessment was superior to clinical assessment alone for diagnosing UTI.¹⁸

A positive result on a dipstick test indicates that infection is 25% more likely than the pretest probability would indicate, and a negative result indicates that infection is 25% less likely than the pretest probability would indicate.¹⁹

Based on defined dipstick cutoff points, overtreatment and undertreatment rates may create limitations in the accuracy of a diagnostic decision.²²

The urine dipstick test alone was useful for excluding infection if the results for nitrites and leukocyte esterase were both negative. Although positive results for both nitrites and leukocyte esterase are very sensitive in family practice, the usefulness of the dipstick test alone to rule in infection remains doubtful, even with high pretest probabilities.²³

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