



Urinary Tract Infection in Community-Dwelling Elderly Women: A New Old Serious Disease

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Authors' contributions

This work was carried out in collaboration between all authors. Authors LPJM and LMSFV designed the study, and wrote the first draft of the manuscript. Author EPQM managed the literature searches and analyses of the study. Author RMPM managed the proofreading of the manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2015/15316

Editor(s):

- (1) Roberto Manfredi, Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy.
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- (1) Anonymous, Brazil.
(2) Anonymous, Nigeria.
(3) Anonymous, Colombia.

Complete Peer review History: <http://www.sciencedomain.org/review-history.php?iid=911&id=12&aid=7924>

Review Article

Received 19th November 2014
Accepted 21st January 2015
Published 28th January 2015

ABSTRACT

Urinary tract infection (UTI) is a very common infection among women of all ages. However, the incidence increases with older age and account for the substantial raise in morbidity, mortality and health economic costs in elderly people. Almost half of all women have suffered from at least one episode during their reproductive age, a percentage that increases to at least 60% in the postmenopausal period. UTI in elderly women can be a complex problem in terms of approach to diagnosis, treatment and prevention, because these patients often present nonspecific symptoms, resulting in the increase of morbidity and mortality in this group. It is very important to increase the epidemiological and clinical knowledge about UTI in order to help the general practitioner or specialist to make early diagnosis to prevent serious clinical complications secondary to UTI in elderly women.

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Keywords: *Urinary tract infection; asymptomatic bacteriuria; elderly women; diagnosis; therapy.*

1. INTRODUCTION

The elderly population is increasing worldwide. We are witnessing the population aging both in developed and in developing countries. According to the World Health Organization (WHO), the population aged ≥ 60 years has doubled since 1980 and it is estimated to reach two billion by 2050 [1]. The proportion of older people is growing, and infectious diseases may be considered as one of the major health problem in this group as well as being responsible for one third of deaths [2,3]. The treatment of infectious diseases, such as urinary tract infection (UTI), is growing in medical significance and in the healthcare costs to the geriatric population. UTI is the second most common infection of any organ system and the most common urological disease in the United States, where it has been accounted for nearly seven million office visits and one million emergency department visits, resulting in 100,000 hospitalizations per year. Most of these hospitalizations were by the elderly, with a total annual cost of more than \$3.5 billion [4,5].

Among community-dwelling elderly populations, genitourinary infections are the second most common form of infection, accounting for nearly 25% of all identified infections [2]. Asymptomatic bacteriuria is believed to affect up to 50% of geriatric women and 30% of geriatric men. Approximately 11% to 25% of elderly noncatheterized patients develop asymptomatic bacteriuria that generally spontaneously resolves [6,7]. UTI is considered to be the most common bacterial infection in community-dwelling elderly women and it has been associated with the increased morbidity and mortality; there is mounting evidence that UTI is directly associated with Gram-negative bacteria septic events in elderly institutionalized women [8].

Several comorbidities may contribute to the increasing incidence of UTI in elderly women, such as neurological diseases: - dementia, cerebrovascular accidents, difficulty in walking and the decline of cognitive function that hinder personal hygiene - and other functional and organic changes of the genitourinary tract, such as urinary and fecal incontinence, as well as age related immunodeficiency, hormonal changes, malnutrition, and diabetes [8]. The emergence of UTI in older people frequently is presented with a range of atypical symptoms, which delays

diagnosis. When it is effectively diagnosed, its treatment is more difficult and may lead to raised hospitalization and mortality. Therefore, the clinical suspicion of UTI in older people, by the general practitioner or specialist is crucial, so that diagnosis can be made.

Although uncomplicated UTI in women is considered as a relatively benign and self-limiting condition, it has an effect on the quality of life and causes unnecessary suffering, at least in the form of weakness and a feeling of being ill. Any illness, even if short lived and not life-threatening, can have an important impact on the patient's daily activities, social functioning and wellbeing, as well as adverse effects of antibiotics can also affect women's quality of life [9].

2. CLINICAL AND LABORATORIAL DIAGNOSIS

UTI consists of a continuum of conditions in which microorganisms multiply in the urine and invade the tissues of the track and adjacent structures. Urine is a sterile ultrafiltrate of blood. In the absence of infection of the urinary tract, it emerges from the kidney and bladder free of microorganisms. During passage through the urethra and surrounding tissues in the female, small numbers of bacteria may enter the urinary stream as contaminants.

2.1 Collection of Urine Specimens

The objective is to collect a specimen, which reflects, as well as possible the character of urine present in the urinary bladder, and the clean-voided method should be used whenever possible in elderly women; it is necessary to collect a midstream urine after cleaning the perineum and vulva. When the patients presented decline of cognitive function or functional neurologic diseases that may hamper a proper urine collection, the urine must be collected by urethral catheter or, if necessary, by suprapubic puncture [10].

Even the best laboratory techniques, however, are of little value if the urine specimen is not collected properly and delivered to the laboratory without delay. Specimen that cannot be examined and cultured within one hour after voiding must be refrigerated. Multiplication of contaminating organisms in urine left standing at room temperature will invalidate the results of

both microscopic examination and urine culture. The urine examination requires that the urine sample should be collected and processed with as little contamination as possible.

2.2 Urinalysis, Microscopy, Gram Stain and Urine Culture

In the urinalysis assessed by urinary dipstick test in fresh urine, the presence of positive leukocyte esterase and/or nitrite may contribute to the diagnosis of UTI, as well as the presence of a pyuria (≥ 10 leukocyte/hpf) and hematuria (≥ 10 erythrocytes/hpf) from a centrifuged midstream urine sample by microscopy (x 400 magnification), when associated with urinary tract symptoms [11,12].

In the past, the gram stain of urine samples was used as a routine diagnostic test to UTI, since there was a substantial delay of 48-72 hours in obtaining urine culture results. However, nowadays it has been abandoned from routine diagnostic for UTI by most microbiology laboratories and it is only used as a guide to empiric antibiotic therapy [13].

Urine culture is the laboratory test to confirm clinical suspicion of UTI. However, it is necessary to have the presence of Significant Bacteriuria (SB) in order to consider urine culture positive. SB is considered present when ≥ 100.000 colony-forming units (CFU)/mL are isolated in urine culture.

The most common bacterial agent in all the situations that lead to UTI in the elderly is *Escherichia coli*, responsible for 60-90% of infections. Other bacteria represented more frequently in the elderly than in the young: *Proteus*, *Klebsiella*, *Enterobacter cloaca*, *Citrobacter fecundi*, *Providenciae stuartii* and *Pseudomonas aeruginosa* [14]. Among the Gram-positive organisms, *Staphylococcus*, *Enterococcus* and *Streptococcus group B* are the most frequently isolated. *Staphylococcus saprophyticus*, the second most common pathogen in young women is rarely seen in older women, whereas *Enterococcus*, rare in young people, is more frequently associated with infections in the elderly (1515).

2.3 Clinical Diagnosis

By definition, UTI requires the presence of symptoms along with the presence of significant bacteriuria in urine culture; in elderly women it is always considered as complicated UTI by the

presence of several medical comorbidities. The types of UTI in general population are well defined and include urethritis (dysuria and hematuria), cystitis (urethritis with urgency, frequency, and suprapubic pain), pyelonephritis (flank pain, fevers, and nausea/emesis that may or may not be preceded by urethritis/cystitis). Recurrent UTI is defined when two or more UTI episodes are detected in a period of six months or more than three episodes in one year.

It is imperative to distinguish UTI from asymptomatic bacteriuria (ASB) in older women. The ASB diagnosis is defined only when SB is detected in two consecutive urine cultures with seven days of interval without any kind of UTI signs and symptoms. ASB treatment is indicated in pregnancy or when an invasive urologic procedure will be made. Out of these medical indications its increases the rate of adverse drug effects from the use of antimicrobial medicines and the rate of recurrent infections with MDR bacteria; it does not change survival, chronic genitourinary symptoms, or the rate of symptomatic UTI. The UTI diagnosis in elderly women generally poses problems. There are several neurological obstacles that include communication barriers (cognitive deficit, dementia and stroke), high prevalence of chronic genitourinary symptoms at baseline (incontinence, urgency, frequency, nocturia); they frequently present with a range of atypical symptoms and lack of a gold-standard laboratory test to confirm clinical suspicion of UTI, due to the high prevalence of ASB [15].

UTI symptoms (Table 1) are the most important factors to the diagnosis; urinary dipstick test does not increase the likelihood of UTI diagnosis and may delay treatment in patients with UTI. It presented moderately sensitive (75%) but less specific (66%). These results showed that urinary dipstick test may modestly improve diagnostic precision and rule out infection [12]. Physicians must be aware of the atypical symptoms because, when a UTI symptom is not recognized, treatment is delayed and the impact that an apparently trivial illness such as UTI has on the elderly patient increases, accounting significantly for increased mortality and health care costs, and decreased quality of life.

In our study with 598 community-dwelling elderly women we observed a high prevalence (21.06%) of Significant Bacteriuria: (UTI in 99 [16.55%] and AB in 27 [4.51%]) [16]. We studied the presence, sensitivity (se) and specificity (sp) of

the spontaneous urinary symptoms and, in the group with UTI, we observed: foul smelling urine in 60 (sen=60.60; spe=87,7), dysuria in 33 (se=33.33; sp=92,9), frequent urination in 30 (se=30.30; sp=90,1), and urgency to urinate in 29 (se=29.29; sp= 89,4). Cystitis was present in 97 patients, and pyelonephritis in two patients that had presented foul smelling urine two to three weeks before, which was not considered as UTI symptom by the general practitioner [16]. Thus, spontaneous symptoms, such as foul smelling urine, mostly in elderly women without vaginitis and who do not use absorbent pads, must be considered as a UTI symptom.

Table 1. UTI principals signs and symptoms in elderly woman

1.	Dysuria
2.	Frequency
3.	Urgency
4.	Foul smelling urine
5.	Flank pain
6.	Suprapubic pain
7.	Fever
8.	Shaking chills
9.	Gross hematuria
10.	New urinary incontinence
11.	Delirium
12.	Worsening of mental status
13.	Worsening of function status

However, the sensitivity and specificity of any spontaneous urinary symptom in elderly people varies from the place where it is investigated as the emergency ward, long term care facility residents or the community. It is very important to know that in this group the presence of unspecific symptom may be frequent, isolated or associated with other urinary symptom, and its presence can help the physician to suspect about UTI emergence and the clinical suspicion is crucial in order to make an early diagnosis.

UTI diagnosis always requires the presence of urinary symptoms associated with significant bacteriuria (SB) in urine culture. SB definition varies by the method used for collecting the urine sample and the sex. In a midstream urine specimen, the growth of $\geq 100,000$ CFU/mL of a single bacterial species is diagnostic of SB [17].

3. PREDISPOSING FACTORS FOR UTI EMERGENCE

Several non-modifiable factors such as neurological diseases and history of previous

UTIs, and modifiable factors, such as wearing absorbent products, sexual activity, urinary incontinence, have been associated with increased risk of UTIs in elderly women [18].

3.1 Urinary Incontinence

Urinary incontinence is a prevalent debilitating and distressing condition in women, which is often under-reported, undertreated and may increase the risk of UTI emergence OR=1, 74 (1, 44<OR<2, 10) [18]. The presence of a severe urinary incontinence may result in social isolation, psychological impairment, restriction of physical activities and it is associated with sexual dysfunction [18]. Many women wear absorbent products to contain urine leakage and protect their clothes, and it can be difficult to define urinary incontinence intensity because urine volumes, flow, and frequency rates may vary substantially. Light incontinence may encompass occasional monthly leaks (mean rate of urine loss of 2.33 ± 1.12 times per month) of very small amounts (e.g. 1 g to 2 g) and in the severe incontinence monthly mean rate of urine loss was > 4.60 times per month of larger amounts (e.g. 20 g to 50 g) [19].

Light urinary incontinence was observed in 6.02% of elderly women and did not prove to be a UTI risk factor in these women [19]. However, it has been demonstrated that a severe incontinence remains a significant risk factor for UTI and that the frequency, and not the amount of urine lost, is an independent factor associated with UTI risk [19]. These women should be guided to urologic medical evaluation in order to define the cause and treatment to improve urinary incontinence.

There are good evidences that conservative treatment and drug treatments are effective in older people urinary incontinence; older people, however, are often undertreated [20]. First line treatment for stress incontinence is pelvic floor muscle exercises. Bladder retraining, in combination with antimuscarinic drugs, is the first line treatment for urge urinary incontinence. If conservative treatment is unsuccessful, selected surgical interventions may be appropriate in older people [20].

3.2 Sexual Activity

Sexual activity is an accepted predisposing factor for UTI in young women and continues to be remains a significant, albeit less important,

predisposing factor in elderly women, whose frequency of sexual activity is lower with age, but it may increase the risk of UTI emergence OR=1,43 (1,11<OR<1,84) [18]. The prevalence of sexual activity declined with age, from nearly 73% among 57 to 64 years of age, 53% from 65 to 74 years, and 26% from 75 to 85 years [21]. We demonstrated that patients who had little regular sexual activity (from one to three times per month) did not increase UTI risk [16]. It has been demonstrated that only women who did have sexual activity once or more per week were at increased risk [7].

However, sexual activity is increasing in older people, and approximately half of the women have reported at least one bothersome sexual problem directly related to the hormonal changes secondary to menopause that can facilitate the development of hypoestrogenic vaginitis. The presence of hypoestrogenic or infectious vaginitis may increase UTI risk [22] and it is very important that elderly women should be educated about the need for routine gynecologic examinations in order to prevent UTI like as young women.

3.3 Diabetes Mellitus

Diabetic older women are at increased risk for UTI and ASB. In our study the presence of diabetes increased the risk of UTI emergence OR= 1,768 (1,080 <OR < 2,895) [16], and they have similar isolated microorganisms, clinical follow-up, and therapy response to non-diabetic women [16], several alterations due to the "*milieu diabetique*" that can promote immunological and metabolic changes associated to neurological and functional urinary tract abnormalities [23]. The metabolic alterations as the increased formation of advanced glycosylation end products and glucosuria may contribute to the development of UTI, since they induce immunological changes that can lead to disturbances in monocyte migration and cytokine production [24-26] It has been demonstrated that inadequate glycemic control and the presence of obesity increase the risk of the onset of infection [27,28]. Therefore, the appropriate metabolic control is essential to prevent infection in elderly diabetic women.

3.4 Therapy

Almost all epidemiological studies about UTI have shown that *E. coli* is the most frequent infective pathogen in both younger and older

women [18]. Recently, there has been reported of an increase in *E. coli* antimicrobial resistance mainly to trimethoprim-sulfamethoxazole and to fluoroquinolones, the first line therapy for cystitis in several places, this may be due to the unnecessary antibiotic therapy for ASB mostly in older women [29].

Frequently it is necessary to begin antimicrobial therapy in community-acquired UTI before the microbiological test result be known, since it is necessary 48-72 hours to obtain urine culture results after collection. Furthermore, in women with acute uncomplicated cystitis, empiric antibiotic therapy without a pre-therapy urine culture is often used. However, in recurrent UTI it is necessary to collect urine for urine culture in order to guide the antimicrobial therapy [30].

The choice of the antimicrobial for elderly women is complicated by the many of physiological and environmental conditions. The rationale for this approach must be based on the highly predictable spectrum of etiologic agents causing UTI, the use of antibiotics in the preceding month, the antimicrobial resistance in the local community, the antibiotic adverse effects, the antibiotic monetary cost and, when possible, a pre-therapy urine culture [31,32]. When empirical therapy is used, it should be reassessed 48 to 72 hours after initiation, once pre-therapy culture is available. Assessment of therapeutic response to antibiotic therapy is important, since UTI in older patients is usually complicated [32].

The uncomplicated cystitis in older women may be treated with a short course (3 to 6 days) of antibiotic therapy [33]. However, it is very difficult to determine what is uncomplicated UTI in elderly women, in whom the presence of several clinical comorbidities is common, thus it is very frequent to treat cystitis in elderly women for seven days and 14 days for pyelonephritis. An empirical therapy may begin after urine culture collection and, when necessary, it must be changed to an appropriate antibiotic based on the susceptibility testing of the urine culture. Control of the underlying diseases is quite important in the management of UTI in older women. In all cases, antibiotics must be carefully adapted to the patient's clinical situation and titrated to kidney function.

The principal measures for recurrent UTI prophylaxis are intravaginal estrogen replacement [34] and prophylactic antibiotic therapy [35]. The post menopause period reflects

a decrease in circulating estrogen and also a related decrease in lactobacilli colonization associated with lower vaginal pH. Consequently, the vaginal colonization by gastrointestinal uropathogenic bacteria is increased, which may partially account for the generally higher incidence of bacteriuria in elderly women.

Intravaginal estrogen replacement may be the treatment of choice for the prevention of recurrent UTI in postmenopausal women [34]. The use of Cranberry or vaginal and oral vaccine produced from inactivated bacteria or structural components of these microorganisms remains controversial. As the evidence that the benefit for preventing UTI is small, cranberry juice cannot currently be recommended for the prevention of UTI [36].

The changing of life habits, with beneficial general measures, as high fluid intake (more than one liter of water/day) and frequent voiding (voiding at a three to four hour intervals) to maintain bacterial clearance throughout the day, associated with the habit of voiding after coitus and at bedtime, are measures that should always be implemented in order to reduce the number of UTI episodes.

The treatment for ASB in all the patients is not justified and it is one of the principal causes for uropathogenic bacteria acquired antimicrobial resistance. Screening for ASB in elderly patients is limited to those undergoing urological or surgical procedures with material implant. In other situations, examination of the urine is only recommended if signs or symptoms in the urinary tract are present, and when UTI is suspected. Treatment of ASB is only recommended in pregnancy and before invasive urological procedures [37].

5. CONCLUSION

In geriatric population UTI has a high incidence, mostly in women, in whom classical urinary symptoms were infrequent. Thus, it is very important the clinical suspicion based in general symptoms such as abdominal pain, new urinary incontinence, foul smelling urine and delirium. The early diagnosis may prevent the severe clinical complications secondary to UTI and necessity of hospitalization.

In developing effective preventive approaches in elderly women it is necessary to implement measures in order to treat and control the

modifiable factors such as urinary incontinence, vaginitis diagnosed by routine gynecological examinations, avoid absorbent pads use and, increase fluid intake and voiding frequency.

The treatment of UTI in elderly is similar as in other people, and the diagnosis is made mostly by the presence of symptoms associated with significant bacteriuria in urine culture. Urine culture is not a routine laboratory examination to be performed in all people. It must be reserved only to those with UTI clinical suspicion in order to avoid the unnecessary use of antibiotics to treat asymptomatic bacteriuria with its undesirable consequences.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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