Clinical and Microbiological Outcomes of Asymptomatic Bacteriuria in Elderly Stroke Patients

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ABSTRACT: **Background:** The optimal approach to the evaluation of asymptomatic bacteruria in stroke patients is uncertain.

Objectives: To compare elderly patients after an acute stroke with and without asymptomatic bacteriuria for the development of symptomatic urinary tract infections (UTI).

Methods: We prospectively monitored patients over 65 years of age admitted to our rehabilitation hospital after an acute stroke, with and without asymptomatic bacteriuria, for the development of symptomatic UTIs. The prevalence of bacteriuria was determined by urine cultures obtained 2 and 4 weeks after admission. Patients with and without persistent bacteriuria were compared to identify variables associated with bacteriuria.

Results: Fifty-five patients were included in the study. The prevalence of asymptomatic bacteriuria at baseline was 20%. Of all 55 stroke patients, 13 (23.6%) developed a symptomatic UTI during the 30 day follow-up. Patients with stroke and asymptomatic bacteriuria at baseline had an increased risk of developing a symptomatic UTI (54.5% with asymptomatic bacteriuria vs. 15.9% without, $P = 0.011$). To exclude the effects of several confounders, we performed multivariate Cox regression analysis, which showed that bacteruria remained a significant covariate for symptomatic UTI (hazard ratio 2.86, 95% confidence interval 0.71–10.46, $P = 0.051$). When subjects who experienced symptomatic urinary infection were included, the prevalence of bacteriuria in the study cohort declined to 45.5% by 30 days.

Conclusion: Elderly patients with stroke and asymptomatic bacteriuria have an increased risk of developing a symptomatic UTI compared to those without asymptomatic bacteriuria during a 30 day post-stroke follow-up.

IMAJ 2017; 19: 147–151

KEY WORDS: asymptomatic bacteriuria, elderly, stroke, urinary tract infection (UTI)

Urinary tract infections (UTI) are consistently found to be one of the most frequent complications in stroke patients, with rates of 1–24% within the first week to 1 month [1-4]. UTI is a common cause of morbidity in stroke patients and may have more significant consequences resulting from infection.

Variables associated with an increased likelihood of UTI after stroke are female gender, older age, functional dependence before stroke, stroke severity, poor cognitive function, and catheterization [3,4]. Patients with stroke are at particularly high risk for developing UTI in the hospital, whether catheterized or not, with more than double the odds when compared with the general medical and surgical populations. Several explanations are suggested for this increased risk: immunosuppression, increased bladder dysfunction, and increased likelihood of having a bladder catheter [5-8].

Asymptomatic bacteriuria is defined as isolation of a specified quantitative count of bacteria in an appropriately collected urine specimen from an individual without symptoms or signs of urinary tract infection. The quantitative thresholds are different for voided clean-catch specimens and catheterized specimens. Asymptomatic bacteriuria in women is defined by the 2005 Infectious Diseases Society of America (IDSA) guidelines as two consecutive clean-catch voided urine specimens with isolation of the same organism in quantitative counts ≥ 10^5 cfu/ml [9]. In men, a single clean-catch voided urine specimen with isolation of a single organism in quantitative counts ≥ 10^5 cfu/ml is sufficient. In asymptomatic catheterized men or women, bacteriuria is defined as a single catheterized specimen with isolation of a single organism in quantitative counts ≥ 10^2 cfu/ml [9]. The presence of pyuria (≥ 10 leukocytes/mm^3 of uncentrifuged urine) is not sufficient for the diagnosis of bacteriuria since 60% of urine samples from asymptomatic elderly women with pyuria have no bacteriuria [10].

Most experts agree that screening for and treatment of asymptomatic bacteriuria is appropriate only for pregnant women and for patients undergoing urologic procedures where mucosal bleeding is anticipated [9,11]. Screening for or treatment of asymptomatic bacteriuria is not indicated for the following populations: non-pregnant women, diabetic patients, the elderly, or patients with spinal cord injury or indwelling urethral catheters [12].

The optimal approach to the evaluation of asymptomatic bacteriuria in stroke patients is uncertain, and there are no data from large trials to clarify this issue. Although higher frequencies of bacteriuria were observed in older patients suffering a stroke [13], it is not known whether asymptomatic

bacteriuria leads to symptomatic UTI and/or other consequences in these patients. The natural history and outcome of the microbiology of asymptomatic bacteriuria in these patients is also an interesting issue that has not been well described. The aims of the present study were to compare stroke patients with and without asymptomatic bacteriuria for the development of symptomatic UTIs and after a 30 day follow-up period, and to assess and describe the microbiological outcomes in stroke patients with asymptomatic bacteriuria not treated with antimicrobials.

PATIENTS AND METHODS

Data had been prospectively collected over a 6 month period at the Fliman Rehabilitation Geriatric Hospital (a 175-bed public geriatric facility affiliated with the Technion's Rappaport Faculty of Medicine and located in Haifa, Israel). All patients over 65 years old admitted consecutively to the five geriatric rehabilitation wards with a diagnosis of acute stroke were eligible for inclusion. Exclusion criteria were known urinary tract abnormalities, symptoms of a UTI, use of antimicrobials for non-urinary infection, or the use of antimicrobial drugs in the previous 14 days.

Patients' baseline medical histories were obtained from the hospital records using a standardized questionnaire and included age, type and time since stroke occurrence, secondary complications of the stroke, medication(s), and use of a urine-collecting system. During hospitalization, antimicrobial therapy was prescribed by a primary care practitioner after diagnosing a UTI in symptomatic patients by means of urinary diagnostic tests (urine culture or microscopic analysis). Urine specimens were collected and a clinical review was performed on admission day and 2 and 4 weeks later. Patients with asymptomatic bacteriuria were not treated during the study period.

LABORATORY METHODS

A mid-stream voided or urinary catheter urine specimen was collected and transported promptly to the laboratory. Standard microbiological methods were used, including semi-quantitative urine culture, organism identification, and susceptibility testing.

DEFINITIONS

- Asymptomatic bacteriuria in women was defined by a researcher (a physician) as two consecutive clean-catch voided urine specimens with isolation of the same organism in quantitative counts ≥ 10^5 cfu/ml [9]. In men it was defined by the same researcher (a physician) as a single clean-catch voided urine specimen with isolation of a single organism in quantitative counts ≥ 10^5 cfu/ml. In asymptomatic catheterized men or women, bacteriuria was defined as a single catheterized specimen with isolation of a single organism in quantitative counts ≥ 10^2 cfu/ml [9].
- Date of event was defined as the date when the first clinical evidence (signs/symptoms) of the UTI appeared, or the date the specimen was collected and used to make or confirm the diagnosis, whichever comes first.
- Urinary tract infections were defined using a combination of clinical signs and symptoms and laboratory criteria defined by the July 2013 CDC/NHSN Protocol Clarifications on Surveillance Definitions for Specific Types of Infections [14].
- Symptomatic UTI (SUTI) was defined when the patient manifested signs and symptoms such as acute dysuria, new and/or marked increase in urinary frequency, suprapubic tenderness, etc., which localize the infection to the urinary tract. These events could occur in patients without urinary devices or managed with urinary devices other than indwelling urinary catheters (suprapubic catheters, straight in-and-out catheters, and condom catheters) [14].

STATISTICAL ANALYSIS

Comparing patients with and without asymptomatic bacteruria for the development of UTIs

Absolute and relative values between baseline and follow-up were compared between stroke patients with and without asymptomatic bacteriuria, using the Mann-Whitney test for categorical variables and the χ^2 test for dichotomous variables. Asymptomatic bacteriuria as a risk factor for the development of a UTI was investigated using a Cox proportional hazards analysis, in which patients were excluded when antimicrobial therapy was started for any reason, which resulted in a hazard ratio as the approximation of the relative risks. The cumulative incidence of UTI during 30 days was described using a Kaplan-Meyer life table analysis. A comparison of the number of UTIs between groups was performed using a multivariate Poisson regression model. In multivariate analyses, age category (65–74 vs. ≥ 75), gender, previous stroke, stroke location, bladder-emptying method, and functional status on admission were regarded as possible covariates for the multivariate analysis. $P < 0.05$ was considered statistically significant.

Assessing the microbiological outcomes of asymptomatic bacteruria

The initial analysis included a description of infecting organisms and the proportion of subjects remaining bacteriuric at each sampling time. Outcomes at 2 and 4 weeks after admission were described as follows: persistence of the original bacterial strain, spontaneous resolution of the initial strain in the absence of antimicrobial therapy, and resolution of bacteriuria with treatment of symptomatic urinary infection. Standard statistical methods were used for significance testing and calculation of odds ratios (OR) and 95% confidence intervals (95%CI).

Table 1. Characteristics of stroke patients followed for 30 days

Variable	Control (n=44)	Bacteruria (n=11)	*P* value
Age, yrs (mean ± SD)	78.4 ± 8.7	74.4 ± 9.5	0.223
Female (%)	56.8	45.45	0.735
Previous stroke	12	3	1
Risk factors and other diseases (%)			
Heart disease	49	4	0.148
Hypertension	40	9	0.075
Hyperlipidemia	36	10	0.785
Smoking	10	3	0.751
Renal failure	20	6	0.84
Diabetes mellitus	49	4	0.148
Etiology (%)			
Atheromatosis	2	2	0.364
Embolus	4	2	0.746
Lacunar infarct	6	0	0.449
Hemorrhage	2	2	0.364
Undetermined	30	5	0.293
Location (%)			
Total anterior circulation	18	5	0.785
Partial anterior circulation	26	5	0.634
Lacunar syndrome	0	1	0.449
Side of lesion			
Right	24	5	0.839
Left	20	6	0.894
Bladder-emptying method			
Spontaneous	24	3	0.200
Indwelling catheter	20	8	0.200
Functional status on admission (mean ± SD)			
ADL	0.66 ± 0.86	0.55 ± 0.82	0.939
FIM	50.55 ± 21.83	42.36 ± 19.66	0.244

ADL = activities of daily living, FIM = functional independence measure

RESULTS

Follow-up results were available for 55 patients admitted for rehabilitation following a stroke. The descriptive characteristics of all patients are listed separately for those with and without asymptomatic bacteriuria in Table 1. Baseline characteristics of participants in each group were similar.

CLINICAL OUTCOMES

Patients with asymptomatic bacteriuria developed UTIs significantly more often ($P = 0.011$) during the 1 month follow-up period than patients without asymptomatic bacteriuria at the time of inclusion. The presence of asymptomatic bacteriuria at baseline increased the risk of UTI incidence in patients with stroke (relative risk 3.42, 95%CI 0.96–12.27, $P = 0.058$) [Table 2, Figure 1]. The figure indicates that the increased risk of UTI remained high during the follow-up period and started immediately after inclusion of the patients. The hazard ratio of the bacteruria to the control group did not change significantly: 2.86 (95%CI 0.71–10.46, $P = 0.051$) after adjustment for age, gender, previous stroke, stroke location, bladder-emptying method, and functional status on admission [Table 2].

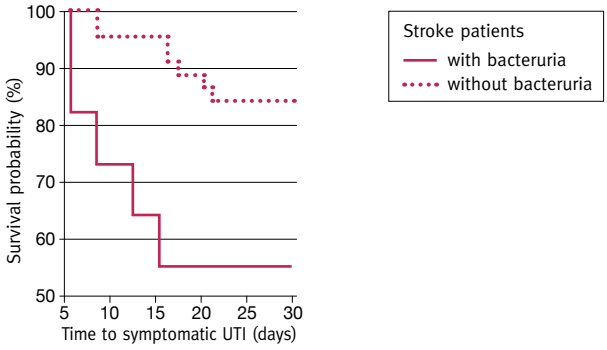
Table 2. Outcome for stroke patients with and without bacteruria followed for 30 days

Outcome	No bacteruria group (n=44)	Bacteruria group (n=11)	*P* value
Symptomatic UTI	7	6	
Hazard ratio for UTI (95%CI)			
Unadjusted	1	3.42 (0.96–12.27)	0.058
Adjusted*	1	2.86 (0.71–10.46)	0.051

* Adjusted for age, gender, previous stroke, stroke location, bladder-emptying method and function status on admission

95%CI = confidence interval

Figure 1. Cumulative incidence of symptomatic UTI during 30 days follow-up (x-axis) of stroke patients with bacteruria (lower curve) and without bacteruria (upper curve) at baseline ($P = 0.011$, log-rank test)



In the entire study population (n=55) (those with and without asymptomatic bacteriuria), 13 patients (23.6%) developed at least one symptomatic UTI. All symptomatic UTIs were cystitis – 6 of the 11 patients with asymptomatic bacteriuria (54.5%) and 7 of the 44 patients without (15.9%).

PREVALENCE OF BACTERIURIA AND INFECTING ORGANISMS

The infecting organisms isolated initially from patients with bacteriuria and the microbiologic outcome at 30 days are summarized in Table 3. Gram-negative bacteria were isolated from 91% of initial specimens. No specific bacteria were more common in symptomatic recurrences. By 30 days the prevalence had declined to about 45.5%. When subjects who experienced symptomatic urinary infection were excluded, the initial strain persisted in three of five patients at 30 days [Table 3].

This analysis is compromised by the small study numbers. We were unable to compare patients experiencing spontaneous resolution of the initial bacteriuria with patients who had persistent bacteriuria in order to identify variables potentially associated with early resolution.

DISCUSSION

We compared the development of symptomatic UTIs in stroke patients with asymptomatic bacteriuria with that in stroke

Table 3. Organisms isolated from patients with stroke and untreated asymptomatic bacteriuria and the microbiologic outcome after 30 days

Organism	Initial bacteruria (n=11)	Subsequent infection			
		Asymptomatic (n=5)		Symptomatic (UTI) (n=6)	
		Bacteruria (n=3)	Resolution (n=2)	Bacteruria (n=2)	Resolution (n=4)
Gram-negative	10	3	2	1	4
Escherichia coli	2	1	0	1	0
Enterobacter	3	1	0	0	2
Providencia	1	0	1	0	0
Klebsiela proteus	2	1	1	0	0
Proteus mirabilis	1	0	0	0	1
Citrobacter	1	0	0	0	1
Gram-positive	1	0	0	1	0
Enterococcus	1	0	0	1	0

patients without, during a 30 day follow-up period. We found that stroke patients with asymptomatic bacteriuria have a greater chance of developing a symptomatic UTI than stroke patients without asymptomatic bacteriuria. To the best of our knowledge, although not large, this is the first follow-up study of stroke patients with and without asymptomatic bacteriuria where higher frequencies of UTIs were observed in older stroke patients with asymptomatic bacteriuria.

Early infections, especially pneumonia and urinary tract infections, occur in 30% of stroke patients and are associated with worse functional outcome, increased mortality, longer hospitalization, and increased costs for medical care [15]. This increased vulnerability to infection may be at least partially explained by stroke-induced immunodepression [16-18].

Evidence that the occurrence of infection after stroke is associated with poor functional outcome and mortality prompted investigators to assess the preventive use of antimicrobials in patients with acute stroke. A Cochrane meta-analysis concluded that although studies differed in populations analyzed, type of antimicrobial used and definition of infection, the overall antimicrobial prophylaxis reduced the infection rate from 36% to 22% (relative risk 0.58) [19]. However, it remains uncertain whether or not preventive antimicrobials reduce the risk of poor functional outcome after stroke. A recent study found that preventive ceftriaxone did not improve functional outcome at 3 months in adults with acute stroke [20].

An early biomarker predicting post-stroke infections could help in selecting patients for prophylactic therapy. Such biomarkers include heart rate variability (HRV) indices suggestive of a sympathovagal imbalance with parasympathetic overweight after ischemic stroke [21], increased sympathetic activity [7,22] and, as found in a recent study, a high circulating natural killer cell count followed by a drop in all lymphocyte subsets in these patients [23]. None of these studies addressed bacteruria as an early simple marker predicting post-stroke urinary tract infection.

Since the optimal approach to the evaluation of asymptomatic bacteriuria in stroke patients is uncertain, and as it was unknown whether asymptomatic bacteriuria leads to symptomatic UTI in these patients, our finding that stroke patients with asymptomatic bacteriuria compared to those without asymptomatic bacteriuria were at increased risk of developing a symptomatic UTI is important. This study suggests that screening for and treatment of asymptomatic bacteriuria might be appropriate following a stroke, and that bacteruria may serve as a biomarker predicting post-stroke urinary infections and helping in the selection of patients for prophylactic therapy after a stroke.

We must recognize and consider the diagnostic challenges of asymptomatic bacteriuria and urinary infection in this population. The diagnosis of UTI in patients after a stroke is often complicated by the lack of typical symptoms and a clear history. Moreover, the presence of cognitive impairment and communication difficulties makes it even more difficult to obtain an accurate history. Some stroke patients may have UTI without localizing urinary symptoms, while other – especially older – patients may have chronic genitourinary symptoms and it is important to recognize that this might not be synonymous with infection.

The strength of our study is that we cultured the urine sample of every stroke patient admitted and of every patient immediately after he or she developed symptoms of a UTI. The most important limitation is that it was not a large study and the analysis was compromised by the small study numbers. Another limitation is that we followed our patients for only 30 days. This period of follow-up was chosen according to observations that most urinary tract infections developed in stroke patients within the first week to 1 month. Clearly, larger and longer follow-up studies are needed to definitively answer these questions.

CONCLUSIONS

Patients with a stroke and asymptomatic bacteruria were at increased risk of developing a symptomatic UTI compared to those without asymptomatic bacteruria.

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