Characteristics of Symptomatic and Asymptomatic Bacteriuria in Patients with Neurogenic Bladder under Neurorehabilitation

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Research article

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Abstract

Background: The definitions of urinary tract infections (UTI) and asymptomatic bacteriuria (ABU) are problematic to apply in patients with neurogenic bladder (NB). Here, we carried out a comparative analysis of the main clinical and laboratory data of NB patients with UTI and ABU.

Methods: One hundred ninety five patients with neurogenic bladder were evaluated in the Urology Sector at a neurorehabilitation hospital. Patients were divided into either ABU or UTI group based on clinical and laboratory data. The sociodemographic data, clinical history, and laboratory test results were collected and used in the comparative analysis.

Results: Of the patients evaluated, 161 (82.6%) had ABU. Patients of different age groups were affected, predominantly young adults (20-39 years). The median time of bladder involvement was 8.9 years (0-35). Neurogenic bowel was observed in 97.5% of cases and renal lithiasis in 11.3%. The main underlying pathologies leading to urologic involvement were spinal cord injury, myelomeningocele, stroke, and neoplasms. Only 16.4% of patients were not on intermittent catheterization, in which the risk of recurrent infection was higher than in patients who were under for intermittent bladder catheterization ($p = 0.016$, OR 2.65). Infection rates were significantly different between patients with histories of recurrent urinary tract infections (asymptomatic bacteriuria 29.8% vs 52.9% infection, $p = 0.016$). Leukocyturia was frequent in both groups, however, our data suggested that only values ≤ 30 cells/high power field excluded infection.

Conclusions: In summary, intermittent catheterization was observed to be essential in the prevention of recurrent UTI, as well as the need to adjust the reference values for leukocyturia in the definition of the infectious condition.

Background

Neurogenic bladder (NB) is a neurologic disorder that affects the bladder emptying. Thus, it contributes as a predisposing factor for bacterial colonization of the urinary tract. The majority of NB patients requires intermittent catheterization to empty the bladder, thus restoring the physiology of the urinary tract. Such management may also contribute to inducing bacterial colonization of the urinary tract by increasing the risk of recurrent urinary tract infection (UTI) [1, 2]

Escherichia coli is the most frequent pathogen to cause symptomatic urinary tract infection (UTI), but can also lead to asymptomatic bacteriuria (ABU) [3]. Clinically, while UTI is characterized by the presence of host inflammatory responses against microorganisms triggering relevant signs and symptoms [3], asymptomatic bacteriuria (ABU) is a clinical condition in which bacteria are isolated from a properly collected urine sample and the patient has no signs or symptoms related to the urinary tract [4, 5]. Such clinical definitions are problematic to apply, particularly in patients in whom ABU originates from predisposing situations, as the use of a bladder catheter. Another important aspect is that some

hospitalized and/or institutionalized patients may be unable to verbalize their symptoms and, consequently, can be mistakenly diagnosed as having ABU or UTI [6].

The clinical heterogeneity among the NB patients and the scarcity of studies make it difficult to establish specific and reliable guidelines. There is a significant variation in the diagnosis, management, and treatment of UTI in these patients between urological rehabilitation centers. Management of this population seems to be largely based on the particularities of each clinical center rather than on existing evidence and guidelines [7, 8]. Thus, we compared the main clinical and laboratory data of the NB patients from a neurorehabilitation hospital with symptomatic and asymptomatic bacteriuria by *E. coli*.

Methods

Study, sampling and hospital setting

This is a descriptive, analytical, and cross-sectional study with patients with neurogenic bladder who underwent urine culture. The study consisted of two groups of patients clinically defined as UTI or ABU carriers. The participants were selected after receiving conventional care by the hospital team, with the purpose of admission, monitoring, and vesical education. Bacterial strains were isolated from urine cultures requested according to the context of clinical follow-up. Other laboratory tests were also requested, according to the clinical condition of each patient.

In 2013, the Sarah Network of Rehabilitation Hospitals located in the city of São Luís – Maranhão, Northeast Brazil, carried out a total of 1,730 urine culture exams. During this period, 354 (20.5%) patients with neurogenic bladder had bacteriuria with the growth of only *E. coli*. Based on these data, the minimum number required for to perform this study, with a confidence level of 95% and a sample error of 5%, was 169 patients. The group for analysis included 195 patients selected among those who had growth of only *E. coli* and with colony counts greater than or equal to 100,000 colony forming units per milliliter ($\geq 10^5$ CFU/mL). Clinical samples were collected from July 2014 to February 2015. Patients who did not consent to participate in the study urine and cultures with polymicrobial growth were excluded from the study.

Epidemiological and clinical data

The sociodemographic data, clinical history, and laboratory test results were collected. The following clinical and demographic characteristics were investigated: gender, age, type of lesion, time of evolution of the lesion that led to bladder involvement, type and need for catheterization, number of UTIs per year, presence of neurogenic bowel, use of diapers, and occurrence of renal lithiasis. Despite the difficulty in clinically classifying the type of urinary infection [7], we used the previously established criteria as described below [8, 9]:

- ABU: patients with counts greater than or equal to 10^5 CFU/mL without relevant clinical manifestations in the urinary tract.

- UTI: patients with the same characteristics as for ABU accompanied by the following manifestations: fever (temperature greater than or equal to 38 °C), dysuria, bacteremia, significant leukocyturia (≥ 10 leukocytes/high power field - HPF), tissue invasion, abdominal pain, sweating, hypotension, and dysreflexia or spasticity.

The laboratory tests used were: white blood cell (WBC) counting, C-reactive protein, procalcitonin, cystatin C, and urinalysis (automated counting using the iQ 200 Iris device and evaluation by using bright field microscopy (x 400) for confirming the presence of leukocyturia and hematuria).

Statistical analysis

Descriptive statistical analysis was performed for all variables using the NCSS 11 Statistical Software - 2016 (NCSS, LLC. Kaysville, Utah, USA). The Lilliefors test was applied to evaluate the data distribution, and as the distribution was not normal ($p < 0.05$), the time of bladder involvement was evaluated using the Mann-Whitney test. The screening test was used to determine sensitivity, specificity, positive predictive value, negative predictive value and accuracy, and the ROC curve was used to determine a cut-off point. The Chi-square test (c^2) was used for independent samples and to evaluate the similarity of the groups regarding demographic variables.

Results

Out of the 195 patients evaluated, 161 (82.6%) were clinically classified as having ABU and 34 (17.4%) as UTI. The median time of bladder impairment in both clinical populations was 8.9 years (0-35). The occurrence of bacteriuria by *E. coli* was similar between genders, with 103 male patients (52.8%) and 92 female patients (47.2%). Other data regarding age, duration of vesical involvement, type of urination, neurogenic bowel, recurrent UTI, use of diapers, and presence of renal lithiasis are described in Table 1.

Of 163 patients under intermittent catheterization, 136 were classified as having ABU and 27 as UTI. Of the 195 patients, 66 (33.8%) had a history of recurrent UTI, of which 29.8% were among the patients with ABU (48/161) and 52.9% were among those with UTI (18/34). This finding was considered statistically significant when comparing both groups (OR = 2.65, p = 0.016). Neurogenic bowel was observed in 97.5% (190/195) of patients (Table 1).

The main underlying pathology that led to bladder involvement in the patients evaluated was spinal cord injury (SCI) in 93 (47.7%) patients, of which 78 had ABU (48.4%) and 15 had UTI (44.1%), followed by other pathologies, such as myelomeningocele, stroke, and neoplasms. Among the patients with SCI 15.4% (12/78) with ABU were tetraplegics and 40% (6/15) with UTI presented the same condition (p= 0.038 and OR = 3.67) (Table 1).

Table 1 Characteristics of 195 patients with symptomatic and asymptomatic bacteriuria due to *Escherichia coli*.

Variable	Patients		p	OR
	Asymptomatic n = 161	Symptomatic n = 34		
Gender				
Male	83 (51.5%)	20 (59.0%)	0.560	1.34
Female	78 (48.5%)	14 (41.0%)		
Mean age ± SD (years)	34.7 ± 20.5	29.2 ± 18.4	0.151	
Duration of vesical involvement (years)	7.0 (3 – 12.5)	7.0 (1 – 13)	0.518	
Intermittent catheterization	136 (84.5%)	27 (79.4%)	0.639	0.71
Recurrent UTI	48 (29.8%)	18 (52.9%)	0.016	2.65
Neurogenic bowel	156 (96.9%)	33 (97.1%)	0.620	1.06
Diaper use	117 (72.7%)	28 (82.4%)	0.338	1.76
Lithiasis	18 (11.2%)	4 (11.8%)	0.841	1.06
Basic pathology				
Spinal cord injury (SCI)*	78 (48.4%)	15 (44.1%)		
Myelomeningocele	47 (29.2%)	9 (26.5%)	0.313	
Other**	34 (21.1%)	12 (35.3%)		

* Among SCI patients those with tetraplegia had a significant risk for infection (p = 0.038, OR = 3.7.) - 12 patients with ABU (15.4%) versus 6 patients with UTI (40.0%)

** Stroke, neoplasms, arthrogryposis multiplex congenita, tropical spastic paraparesis caused by human T cell-lymphotropic virus.

Considering only the 163 patients who were on intermittent catheterization (136 with ABU and 27 with UTI), the most suggested cut-off point (ROC curve) for the evaluation of leukocyturia as a parameter to distinguish between UTI and ABU was 30 leukocytes/HPF with the highest area under the curve (AUC =

0.875 ± 0.035, p = 0.0001 CI 95% = 0.806 – 0.943) (Fig. 1). This value corresponded to a sensitivity of 81.5%, specificity of 77.2%, positive predictive value of 41.5%, negative predictive value of 95.5%, and accuracy of 77.9% (Table 2).

Table 2 Diagnostic performance of leukocyturia values of 163 patients who underwent intermittent catheterization

Leukocyturia cut-off values *	Measurements (%) **				
	Sensitivity	Specificity	PPV	NPV	Accuracy
≥ 10 WBC/HPF	96.3	51.4	28.3	98.6	58.9
≥ 30 WBC/HPF	81.5	77.2	41.5	95.5	77.9
≥ 100 WBC/HPF	46.4	96.4	66.7	99.4	89.1

* WBC: white blood cells; HPF: High-Power Field

** PPV: Positive Predictive Value; NPV: Negative Predictive Value

The main clinical and laboratory findings identified in the 34 patients with UTI are described in Table 3. Renal function impairment with changes in proteinuria and cystatin C tests was observed in 20.6% (7/34) of cases. In 11.8% (4/34) there was evidence of more severe and systemic clinical impairment, and possible bacteremia, which was evidenced by alterations in the procalcitonin tests (Table 3).

Table 3 Clinical and laboratory characteristics of 34 patients with UTI due to E. coli.

Characteristics	Symptomatic (n = 34)
Symptoms	
Irritating	31 (91.2)
Abdominal and/or lumbar pain	16 (47.1)
Fever (≥ 38 °C)	13 (38.2)
Without ≥ 2 symptoms	13 (38.2%)
Urinalysis	
Leukocyturia (WBC/HPF)*	33
≥ 10	34 (97.1%)
≥ 30	22 (64.7%)
≥ 100	12 (35.3%)
Nitrite	28 (82.4%)
Hematuria (≥ 3 cells/HPF)	23 (67.6%)
Kidney function	
Cystatin C (≥ 1.11 mg/L)	7 (20,6%)
Proteinuria	7 (20.6%)
Inflammatory activity	
C-Reactive Protein (≥ 0.5 mg/dL)	19 (55.9%)
Procalcitonin (> 0.5 ng/mL)	4 (11.8%)
Leukocytosis (patient's age)	8 (23.5%)

* WBC: white blood cells; HPF: High-Power Field

Discussion

We have shown that leukocyturia with less than 30 cells/HPF suggested exclusion of UTI in NB patients. The majority of patients evaluated were clinically diagnosed with ABU. An important factor that influenced this finding is that these patients were already being assisted in the urologic rehabilitation program, with 83.6% already under intermittent catheterization, thus achieving more adequate control of urinary functions with consequent lower UTI rates.

The normal innate immune response that is stimulated by bacterial components results in pro-inflammatory signaling and in leukocyte recruitment in patients with neurogenic bladder [10]. It is important to emphasize that, in populations routinely using a catheter, bacteriuria and leukocyturia (or pyuria) should not serve as isolated parameters for the clinical diagnosis of ABU or UTI [11]. Despite this recommendation, this indicator is commonly used in clinical practice to diagnose UTI in patients without changes in the urinary tract, using a threshold value of ≥ 10 leukocytes/HPF in the urinary sediment [12].

Clear criteria for the diagnosis of ABU and UTI in patients with NB and standardized data on clinical presentation are still scarce in the literature. Although the prevalence of ABU in this population is high [5], it may vary due to factors such as age, gender, metabolic diseases, spinal cord injury, frequent use of a catheter, pathogenic potential of the microorganism, and the condition of the institutionalized patient [13].

During this study, we observed that there is no consensus in the literature on the definition of diagnostic criteria for UTI in patients with NB and under catheterization. Giusto et al, in a systematic review of 1,425 studies correlating spinal cord injury and UTI, observed that only 43.9% of the studies established diagnostic criteria for this condition [14]. Even so, there were 11 different criteria used, which suggests that the definition of UTI in this population is variable, inconsistent, and limits the diagnostic reliability.

Criteria for defining UTI, as described by Bickenbach and cols [9], rely on the results of urine culture and urinalysis, as well as on the presence of clinical symptoms. However, such clinical/laboratory findings were not always present in the patients of this study to allow an ideal definition of this clinical condition. Madden-Fuentes et al. found similar results in patients with myelomeningocele [7].

The main pathology found in both groups that triggered bladder dysfunction was spinal cord injury associated with paraplegia, followed by myelomeningocele (more prevalent in patients aged under 16 years), a result consistent with previous studies [15]. Among spinal cord injury patients, quadriplegia implicated a higher relative risk for the onset of infection.

Little attention is paid to the influence of neurogenic bladder associated with neurogenic bowel [16]. Keren et al found that children with neurogenic bowel were at a higher risk of developing recurrent UTI [17]. In this study, neurogenic bowel was found in almost all cases (97.5%).

The use of diapers [15] and the presence of renal lithiasis [10] are described as predisposing factors for UTI in NB patients, which was not observed among the patients of this study.

Patients who were not on intermittent catheterization faced a relatively higher risk of having re-current UTI, despite the fact that this procedure is recommended in the neurological practice of patients with neurogenic bladder and is indicated as the main factor in reducing the occurrence of UTI [9]. Patients who were not on intermittent catheterization showed resistance to the completion of the procedure or had not yet started urological rehabilitation at the time of data collection in this study.

Conclusions

Knowledge of the sociodemographic conditions of patients with neurogenic bladder increases the understanding of risk factors for the development of the infection. The findings of this study suggest that follow-up should be permanent, as low adherence to intermittent catheterization is a significant risk factor for recurrent UTI. It is also important to note that, in cases of bladder dysfunction, the assessment of intestinal function should always be considered and, if the neurogenic intestine is identified, monitoring and control measures must be implemented.

Although the confirmation of infection should not be based solely on pyuria, the presence of less than 30 leukocytes/HPF in urine sediment significantly excludes infection. The detailed evaluation of signs and symptoms with the presence of laboratory changes is essential to define the infectious process in NB patients.

Abbreviations

ABU: Asymptomatic bacteriuria; CFU/mL: Colony forming units per milliliter; HPF: High power field; NB: Neurogenic bladder; OR: Odds ratio; ROC: Receiver operating characteristic; SCI: Spinal cord injury; UTI: Urinary tract infection; WBC: White blood cell

Declarations

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors contributions

All authors were involved in the design of the study. FOBL, MTS, VMLSP, and RJDA reviewed all the patient data. FOBL, MRQB, SGM, and VM-N performed the analysis, and wrote the first draft. All authors reviewed the final version of the manuscript and approved it for publication.

Ethics approval and consent to participate

This study was approved by the Research Ethics Committee of the Sarah Network Rehabilitation Hospitals, under decision no. 708.539/2014. An informed consent form was applied, and all patients and/or family members involved in this study gave their consent.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

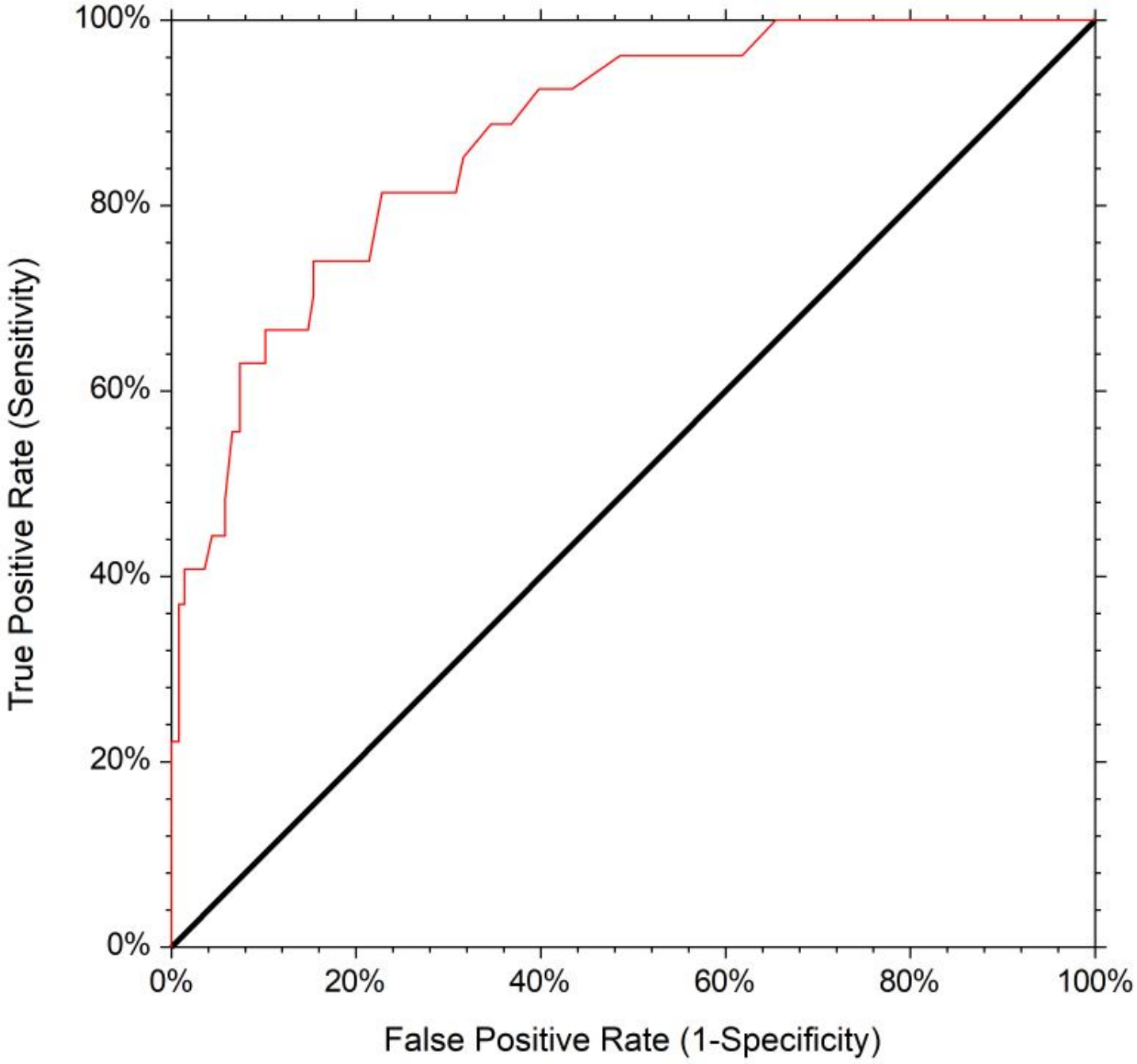

Figure 1

Receiver Operating Characteristic (ROC) curve for performance of leukocyturia to predict ABU and UTI (AUC = 0.875 ± 0.035 p = 0.0001 CI 95% = 0.806 – 0.943).