

- I. Carry out questioning and physical examination, to evaluate the neurological history of the patient with urological dysfunction of the urinary tract, carry out a voiding diary and current status of their bladder and sexual function, as well as a general and system physical examination, emphasizing:
 - a. Background:
 - i. High or low urinary infections.
 - ii. Previous use of antibiotics or urinary antiseptics.
 - iii. Urological surgeries and associated complications.
 - iv. Current method of bladder evacuation (voluntary urination or not, if it is with the help of evacuation maneuvers: Valsalva or Credé), if it is by permanent or intermittent catheterization, if it is due to overflow, if there is a sensation or not of a full bladder, episodes of urgency/incontinence, if your bladder capacity or volume is quantified, as well as the presence of post-voiding residue, as well as related dysautonomic disorders).
 - v. Previous urine cultures
 - b. Studies to be carried out in the evaluation:
 - i. Culture and Uroculture.
 - ii. Renal, bladder and prostate ultrasound. Measure postvoid residue.
 - iii. Direct vaginal discharge and culture (for women).
 - iv. Serum prostate antigen (PSA) if you are a man.
 - v. It is necessary to record the clinical data of the presence of neurogenic intestine, and method of intestinal evacuation.
- II. Once all these results have been received and with the updated voiding diary:
 1. The neurogenic bladder type will be clinically classified [9,10].
 2. The results of the cyturia and urine culture will be evaluated, making clinical correlation and classification of the infection if they are positive, to decide treatment according to recommendation guidelines.
 3. The diagnosis of the clinical form of urinary infection will be made according to clinical, microbiological criteria [11].
- III. Additional urological studies will be requested if the initial evaluation finds: kidney or bladder lithiasis, dilation or stenosis of the excretory system, malformations or tumors, or in any situation that the attending physician trained in the management of neurogenic bladder considers, for the subsequent specialized assessment.

Table 1: Neuro-urological evaluation protocol.

episode. Fever as the only presenting symptom or associated with headache, chills, general malaise, lumbar pain, abdominal pain, hematuria or atypical symptoms. Lower urinary tract infection occurred in 84 episodes (75%), in different clinical forms: recurrent symptomatic bacteriuria (29.4%) and cystitis (16.9%), especially after removal of a catheter; with increased of frequency, dysuria; atypical symptoms with increased spasticity or muscle spasms, incontinence episodes, difficulty passing the catheter, dysautonomic disorders (dysreflexia) with hypertension, bradycardia, sweating, anxiety and changes in the physical characteristics of the urine; Asymptomatic bacteriuria present in 13.3% of the episodes, with

positive culture in the absence of symptoms, others such as vaginitis, urethritis or epididymitis, with a lower prevalence.

With respect to sex, infection prevailed in males (31 male and 12 female patients with a 1.3/1 ratio), unlike the UTI shown by the general population, which is related to the constitution of the sample, where 74.41% were patients with spinal cord injuries, a disease predominantly male.

The most frequently occurring risk factors (Table 3), VN with permanent catheter in 23.2% or intermittent in 62.7%, history of a previous diagnostic procedure or surgery in 18.5% of patients,

	Men	Woman	%
Acute pyelonephritis	16	12	25
Lower UTI	48	36	75
Cystitis	11	8	16.9
Urethritis	2	2	3.5
Vaginitis	-	9	8.03
Recurrent symptomatic bacteriuria	21	12	29.4
Asymptomatic bacteriuria	10	5	13.3
Epididymo-orchitis	4	3.5	
Total	64	48	-

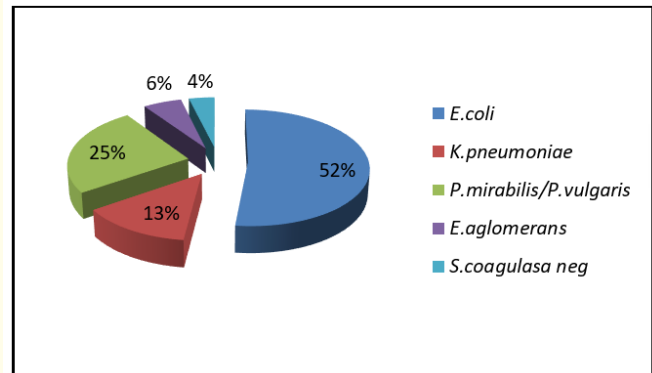
Table 2: Clinic presentation of urinary infection.

other abnormalities such as diverticula, lithiasis, stenosis urethral were found in 4.6%, 11.6% and 4.6% respectively. The susceptibility pattern of *E. coli* and *Proteus* spp is shown, whose sensitivity to amikacin and carbapenems is found in 100% of the isolated strains (See graph 2 and 3), in relation to cefepime, the sensitivity remains above 80%, while for sulfaprim the resistance of *E. coli* is greater than 70%, nalidixic acid 80% and fluoroquinolones type ciprofloxacin between 60 - 75%, which prevents the empirical or prophylactic use of these antimicrobials in urinary infections. In relation to penicillins with beta-lactamase inhibitors (IBL), the germs showed a resistance between 40% for amoxicillin/IBL in *E. coli* and 60% for piperacillin/IBL for *Proteus* sp.

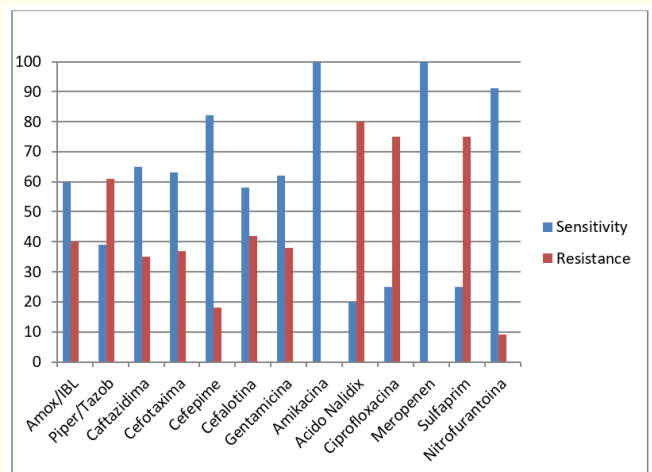
Risk Factors	No. Patients	Percent
Indwelling catheter	10	23.2
Diverticula and Pseudodiverticula	3	4.6
Renal or bladder lithiasis	5	11.6
Previous cystography	6	13.9
Intermittent catheterization	27	62.7
Surgical procedure	2	4.6
Immunosuppression	3	7.5
Only neurogenic bladder	8	18.6
Urethral stenosis	2	4.6
Others (double excretory system)	2	4.6
Pressure ulcer*	8	18

Table 3: Risk factors in patients with urinary tract infections associated with neurogenic bladder.

*: Comorbidity present in patients with spinal cord injury.



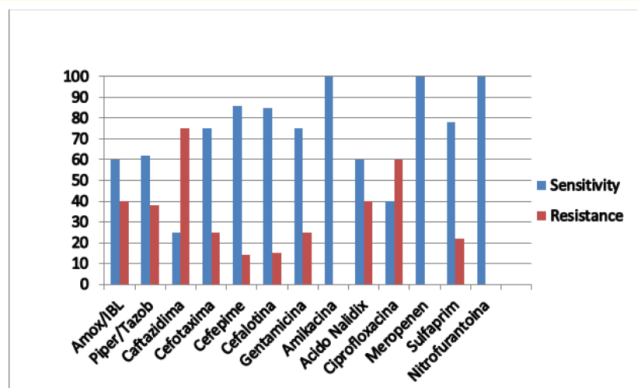
Graph 1: Microorganisms isolated in urocultures.



Graph 2: Sensitivity-resistance pattern of *E. coli*.

Discussion

Recurrent symptomatic bacteriuria and acute pyelonephritis are the most frequent clinical forms of cUTI in patients with neurogenic bladder, with a predominance of lower urinary tract involvement, which involves pathogenic mechanisms typical of enterobacteria, the presence of virulence factors that intervene in the adherence of microorganisms to the uroepithelium, the presence of biofilms that favor colonization as well as the reduction of the defenses of a functionally and nutritionally affected bladder [14-



Graph 3: Sensitivity resistance pattern for *Proteus* spp.

16] but regardless of the contribution that each pathogenic pathway has in the historical model of infection, it has been proposed that in these patients, they only explain approximately 50% of the episodes of recurrence of symptoms, where the bacterial strains are genetically identical [17]. It has been observed that both relapses and re-infections are related to the existence of an intracellular reservoir of bacteria in the bladder mucosa, which would explain the frequency of therapeutic failure and antimicrobial resistance [5,18].

This pathogenic mechanism would cause a cascade of events that promote infection and recurrence: bacterial replication in the bladder lumen, adherence and invasion of the uroepithelium, internalization with endosome formation, intracellular bacterial replication, bacterial morphological and functional modifications, with resistance to the mechanisms of host defense, escapes from antimicrobial action and defense mechanisms, to restart the process [8,19].

In asymptomatic bacteriuria (AB) from the pathogenic point of view in the patient with NB, it has been proposed in the first place that uropathogens lose the expression of many virulence factors and have little capacity to stimulate an adequate immune response in the mucosa uroepithelial, causing that some of these patients can be asymptomatic carriers for long periods of time, and secondly, the lack of response of the mucosa, being also a protective mechanism to avoid kidney damage; this has been demonstrated in studies conducted in BA children [20]. Therefore, therapeutic or prophylactic antimicrobial treatment is not recommended in asymptomatic bacteriuria, except in special populations (patients who will undergo invasive procedures of the urinary tract where bleeding, immunosuppression, vesico-ureteral reflux are expect-

ed).

Therefore, therapeutic or prophylactic antimicrobial treatment is not recommended in asymptomatic bacteriuria, except in special populations (patients who will undergo invasive procedures of the urinary tract where bleeding, immunosuppression, high-grade vesico-ureteral reflux, pregnancy) are expected, since it does not reduce the incidence of the symptomatic episode and the subsequent recurrence by more resistant germs is avoided [21].

Microbiological isolates from patients with neurogenic bladder-associated UTI tend to be similar to uncomplicated infections, however these microorganisms have greater resistance to antibiotics and higher rates of treatment failure when the underlying abnormality cannot be corrected; In the reported series, *E. coli* is maintained as the predominant germ, however in a much lower proportion in relation to other reports, with an increased trend of isolations of other enterobacteria such as *Proteus sp*, *K. pneumoniae* and *E. agglomerans*, (Graph 1), behavior that could be explained by recurrent episodes of asymptomatic bacteriuria and infection with repeated therapeutic courses of antibiotics that occur in patients with cUTI, and that favor changes in the intestinal flora as well as the appearance of emerging uropathogens [22].

We must bear in mind that in UTI of patients with permanent and prolonged catheterization, the frequent use of antibiotics, treatment with corticosteroids, comorbidities such as diabetes mellitus, fungal infections and especially candiduria are a possibility to take into account, not only as colonizing agent (asymptomatic candiduria) of any segment of the urinary tract, but can be the cause of abscesses, infection of the lithiasis and can become a symptomatic and invasive pathogen, (23-24) which was evaluated and ruled out in 10 patients of this report, by mycological cultures of the urine [25].

The presence of immunosuppression documented with studies of cellular and humoral immunity, due to the use of steroids and immunosuppressants for a long time, was present in 7.5% of the episodes, in a patient with demyelinating disease, as well as in two patients with SCI associated with alterations of the nutritional status due to co-morbidities such as pressure ulcer (present in 18% of the episodes), the latter affecting the emotional state with chronic depression, both situations favor the immune alterations of the host and constitute risk factors added to the VN, that compromise the host's defenses against infection [26].

Isolated enterobacteria have a sensitivity of 83 - 100% for cefepime, amikacin and meropenem, constituting an excellent therapeutic resource when decision-making is necessary for patients

with severe obstructive forms of pyelonephritis, as well as a sensitivity of 90 - 100% for nitrofurantoin; resistance to nalidixic acid, ciprofloxacin, sulfaprim, penicillins and cephalosporins between 60 - 80%; behavior according to the institutional microbial map and according to a study carried out previously of the different resistance patterns of *E. coli* from urine cultures in hospital isolates, where there is a growing increase in resistance that is expressed from one to seven combinations of antimicrobials [27,28].

The resistance mechanisms of the most frequent *Enterobacteriaceae* are related to resistance genes against antibiotics used in the urinary tract; plasmid-encoded or chromosomally encoded beta-lactamases, with broad activity against penicillins and cephalosporins [29,30] and function by fractionation of the β -lactam ring, thus inactivating antibiotics, these plasmids carry other resistance genes that provide activity against other families of antimicrobials such as aminoglycosides, sulfonamides and quinolones, by transferring resistance to other antibiotics, which could be the mechanism of multi-resistance in these pathogens [31,32].

Conclusion

Recurrent symptomatic bacteriuria and acute pyelonephritis are the most frequent clinical forms of cUTI in patients with neurogenic bladder, with *E. coli* being the most common germ, with an increase in the proportion of isolates of other enterobacteria. Associated risk factors are related to the use of intermittent or permanent catheterizations. Isolated *Enterobacteriaceae* are 80 - 100% sensitive to amikacin, meropenem, cefepime, and nitrofurantoin, and 60 - 80% resistant to various families of commonly used antimicrobials: nalidixic acid, ciprofloxacin, sulfaprim, penicillins and cephalosporins.

The clinical evaluation and antimicrobial treatment for NV UTI should be based on therapeutic protocols reasoned according to the form of presentation, microbial circulation and behavior of the sensitivity/resistance pattern, avoiding prophylactic use in asymptomatic forms and thus promoting optimization of antibiotics, essential tools of the program to reduce resistance in urinary infections at the hospital and global level.

Interest Policy

There are no conflicts of interest between the authors of the work.

Ethical Conflicts

All patients included in this series have in their medical history the informed consent document, for their incorporation into the neurological restoration program, which is signed by the patient and the family member.

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