Scientific Research Publishing

Open Journal of Obstetrics and Gynecology, 2023, 13, 1547-1568
https://www.scirp.org/journal/ojog
ISSN Online: 2160-8806
ISSN Print: 2160-8792

Mechanisms and Associated Factors of Nocturia in Women Attending Two Urogynecology Clinics: A Cross-Sectional Study

Ingrid Antunes da Silva*, José Rodrigo de Moraes, Renato Augusto Moreira de Sá, Carlos Augusto Faria

School of Medicine, Federal Fluminense University, Niterói, Brazil
Email: *ingrid_antunes@id.uff.br

How to cite this paper: da Silva, I.A., de Moraes, J.R., de Sá, R.A.M. and Faria, C.A. (2023) Mechanisms and Associated Factors of Nocturia in Women Attending Two Urogynecology Clinics: A Cross-Sectional Study. *Open Journal of Obstetrics and Gynecology*, **13**, 1547-1568.
https://doi.org/10.4236/ojog.2023.139130

Received: August 17, 2023
Accepted: September 17, 2023
Published: September 20, 2023

Abstract

Introduction: Nocturia has a multifactorial etiology, and its diagnostic approach involves, in addition to medical history and physical examination, the use of a bladder diary to define the pathophysiological mechanisms present in each case. Methods: This study investigated the prevalence of nocturia, its mechanisms, and associated factors in women with lower urinary tract symptoms attending two urogynecology clinics in the state of Rio de Janeiro, Brazil. Anamnesis, physical examination, and a 24-hour bladder diary were conducted. Two definitions of nocturia were considered: one or more nighttime voids and two or more nighttime voids. Mann-Whitney and Chi-square tests were used, with p-value ≤ 0.05 considered significant. Results: A total of 133 participants were included. The majority were aged 60 years or older (61.4%) and had three or more comorbidities (66.7%), with systemic arterial hypertension being the most prevalent (59.1%). Of the total participants, 54 (41.4%) completed the bladder diary. Among those with one or more nighttime voids (70.7%), the prevalence of nocturnal polyuria was 69.1%, reduced nocturnal bladder capacity was 17.3%, and global polyuria was 12.9%. Among participants with two or more nighttime voids (56.4%), the prevalences were respectively 68.2%, 19.1%, and 13.6%. Among the mechanisms, associations were found only with global polyuria, namely: use of insulin, body mass index and tobacco consumption. An association was also found between recurrent urinary tract infection and global polyuria in participants with two or more nighttime voids. Conclusions: The prevalence of nocturia was higher than that reported in general population studies and specialized services for lower urinary tract symptoms. Nocturnal polyuria was the most prevalent mechanism. Associations were observed between the use of insulin, body mass index, tobacco consumption, and recurrent urinary tract infection with global po-

lyuria. No associations were found between any clinical or demographic variables and nocturnal polyuria or reduced nocturnal bladder capacity.

Keywords

Nocturia, Polyuria, Lower Urinary Tract Symptoms, Women's Health

1. Introduction

Nocturia is a urinary symptom characterized by urination that occurs during the primary sleep period [1]. Although a single episode of urination is considered nocturia, studies assessing quality of life generally indicate significant discomfort from two or more episodes [2].

In population-based studies, the prevalence of one or more episodes of nocturia was 57.3% in the general population of Malaysia [3], 69.6% in women in the United States [4], and 76% in a multicenter study conducted in the United States, United Kingdom, and Switzerland [5]. The prevalence of two or more episodes was 23.2%, 28.8%, and 34%, respectively. In a study conducted in the general Brazilian population, 32.4% of women had two or more episodes [6].

The causes of nocturia can be urological, such as overactive bladder syndrome [7] and underactive bladder [8], as well as non-urological. The latter largely involve alterations in water or sodium homeostasis, such as endocrine [9], cardiovascular [10], sleep [11], and renal pathologies, as well as the medications used in their treatment [12]. There are also associated factors, such as older age, lower income, and lower education level [4]. Other factors that should be included in the investigation of nocturia are caffeine consumption, as the substance increases glomerular filtration rate [13], and tobacco consumption, which can interfere with the circadian rhythm of blood pressure [14].

These factors are related to nocturia through one or more of the following physiological mechanisms: global polyuria, nocturnal polyuria, and reduced nocturnal bladder capacity. Evaluation of these mechanisms is important in defining the diagnostic strategy for possible etiologies.

To assist in this definition, a bladder diary is an extremely important tool. It records the individual's activities, any urinary symptoms they may experience (urgency, stress urinary incontinence, urge incontinence), volume of urine voided, and the timing of voids.

Global polyuria can be defined as a urine volume exceeding 40 ml/kg in 24 hours [15]. This condition is present in more than 20% of patients with lower urinary tract symptoms and is generally caused by excessive water consumption for a variety of reasons, mostly behavioral. Additionally, it can be caused by various clinical conditions such as uncontrolled diabetes mellitus, advanced stages of chronic kidney disease, and diabetes insipidus [16].

Nocturnal polyuria is assessed through the percentage relationship between nocturnal urine volume and 24-hour urine volume and varies according to age:

greater than 20% in patients younger than 65 years old [15] or greater than 33% in those aged 65 years or older. The majority of cases are associated with one or more comorbidities. According to a large population-based study, in women, the association of nocturnal polyuria with overactive bladder syndrome is more prevalent than that with diabetes mellitus, systemic arterial hypertension, heart failure, and obstructive sleep apnea [17] [18].

Reduced nocturnal bladder capacity is evaluated through the nocturnal bladder capacity index, calculated from the number of nocturia episodes, nocturnal urine volume, and the highest 24-hour urine volume. Values of this index above 1.3 indicate a higher probability that nocturia is influenced by nocturnal bladder capacity [15]. This, in turn, can occur due to alterations in the circadian cycle of mechanisms involved in detrusor contractility, sodium and water transport across the bladder wall, and perception of urinary volume and composition [19].

Given the diversity of associated factors and physio-pathological mechanisms involved in nocturia, the inclusion of a bladder diary in the diagnostic arsenal for the condition is essential. It provides a wealth of information, and its standardization allows for comparison among different populations.

Therefore, the present study aims to evaluate the prevalence of nocturia in women attending urogynecology clinics, the prevalence of the three main mechanisms causing nocturia, and the factors associated with them.

2. Methods

This is a cross-sectional study involving women with lower urinary tract symptoms attending two urogynecology clinics in the state of Rio de Janeiro, Brazil, between July 2021 and January 2023. The exclusion criteria were age below 18 years, ongoing pregnancy, history of pelvic radiotherapy, surgery for pelvic cancer, neurological disease, and impaired cognitive capacity.

The project was approved by the Research Ethics Committee of the School of Medicine at the Federal Fluminense University with CAAE 43177721.5.0000.5243, and all participants completed the Informed Consent Form.

Participants underwent a medical history and physical examination as part of a comprehensive gynecological evaluation. Sociodemographic data, such as data collection location, age, and education level, were recorded. In addition to nocturia, the presence of other lower urinary tract symptoms, pelvic organ prolapse [20], evacuation symptoms [21], comorbidities, and medications used were investigated. Two definitions of nocturia were used: one or more episodes of urination and two or more episodes of urination. Polypharmacy was defined as the concomitant use of five or more medications [22]. The consumption of caffeine in mg/day and tobacco in packs/year were estimated.

During the physical examination, weight and height were evaluated, and body mass index (BMI) was calculated and stratified as normal, overweight, and obese [23]. Pelvic organ prolapse, when present in the examination, was staged using the Pelvic Organ Prolapse Quantification (POP-Q) system [24].

In addition, participants with the symptom of nocturia were instructed to fill out a 24-hour bladder diary, including the times they went to bed and woke up, the frequency of daytime and nighttime urination, and the urine volumes.

All urinations after lying down to sleep, provided that they were followed by a period of sleep or intention to sleep, were considered part of the nocturnal urinary frequency. The daytime volume was calculated from the second urination of the day until the last urination before going to bed. The nocturnal volume considered was the sum of the volumes of nocturnal urinations plus the volume of the first daytime urination of the following day, according to the ICIQ [25] standardization. The 24-hour bladder diary data allowed for the evaluation of the presence of global polyuria, nocturnal polyuria, and reduced nocturnal bladder capacity.

Regarding statistical analysis, caffeine consumption and tobacco consumption were treated as continuous variables, while all other variables were dichotomized. Frequency distribution tables were constructed for the clinical and sociodemographic variables of the participants. For the analysis of women with nocturia, for quantitative characteristics, the mean and standard deviation (mean ± SD) were calculated in general and among women with/without global polyuria, with/without nocturnal polyuria, and with greater/lesser nocturnal bladder capacity. Additionally, the Mann-Whitney test was applied to compare the values of caffeine consumption and tobacco consumption between patients with nocturia in the mentioned groups.

Finally, the Pearson chi-square test (with Yates' continuity correction) was adopted to evaluate the association between sociodemographic and clinical characteristics of patients with the outcomes of global polyuria, nocturnal polyuria, and reduced nocturnal bladder capacity. For all these analyses, a significance level of 5% was considered.

3. Results

A total of 133 women agreed to participate in the study, of which 94 (70.7%) reported at least one nocturnal urination and 75 (56.4%) reported at least two nocturnal urinations. Out of the total participants, 70 (52.6%) were 60 years or older, and 73 (53.9%) had lower education levels. The remaining clinical and sociodemographic variables are presented in **Table 1**.

Out of the total participants, 54 (41.4%) filled out the bladder diary. Among the bladder diaries of participants with nocturia defined by one or more voids, 54 had information on 24-hour urine volume, and 52 had information on nighttime bladder capacity. Among participants with nocturia defined by two or more voids, 42 out of 44 bladder diaries had information on nighttime bladder capacity.

Among women with one or more episodes of nocturia, the most prevalent mechanism was nocturnal polyuria, present in 38 (69.1%) participants, followed by reduced nighttime bladder capacity in 9 (17.3%) participants and global

Table 1. Descriptive analysis of sociodemographic and clinical characteristics in women attending two urogynecology clinics (N = 132). Niterói (RJ) and Petrópolis (RJ), Brazil, 2021-2023.

Characteristics		Number of participants and percentage or mean and standard deviation
Location	Niterói	45 (33.83%)
	Petrópolis	88 (66.17%)
Age	Less than 60 years old	63 (47.37%)
	60 years old or older	70 (52.63%)
Education level	Up to incomplete primary school	60 (45.11%)
	At least completed primary school	73 (54.89%)
Nocturia 1	No urination	39 (29.32%)
	One or more urinations	94 (70.68%)
Nocturia 2	Up to one urination	58 (43.61%)
	Two or more urinations	75 (56.39%)
Stress urinary incontinence	No	110 (82.71%)
	Yes	23 (17.29%)
Urgency urinary incontinence	No	115 (86.47%)
	Yes	18 (13.53%)
Mixed urinary incontinence	No	59 (44.36%)
	Yes	74 (55.64%)
Overactive bladder syndrome	No	35 (26.32%)
	Yes	98 (73.68%)
Hesitation	No	118 (88.72%)
	Yes	15 (11.28%)
Slow stream	No	110 (82.71%)
	Yes	23 (17.29%)
Feeling of incomplete bladder emptying	No	59 (44.36%)
	Yes	74 (55.64%)
Post-voiding incontinence	No	91 (68.42%)
	Yes	42 (31.58%)
Pelvic organ prolapse (symptom)	No	91 (68.42%)
	Yes	42 (31.58%)
Anterior vaginal wall prolapse	Up to stage II	119 (89.47%)
	Stage III or IV	14 (10.53%)
Posterior vaginal wall prolapse	Up to stage II	130 (97.74%)
	Stage III or IV	3 (2.26%)
Apical prolapse	Up to stage II	130 (97.74%)
	Stage III or IV	3 (2.26%)

Continued

Fecal incontinence	No	124 (93.23%)
	Yes	9 (6.77%)
Constipation (Bristol stool scale)	No	107 (80.45%)
	Yes	26 (19.55%)
Constipation (bowel movement frequency)	No	105 (78.95%)
	Yes	28 (21.05%)
Recurrent urinary tract infection	No	116 (87.22%)
	Yes	17 (12.78%)
Systemic arterial hypertension	No	54 (40.60%)
	Yes	79 (59.40%)
Diabetes mellitus	No	93 (69.92%)
	Yes	40 (30.08%)
Congestive heart failure	No	131 (98.50%)
	Yes	2 (1.50%)
Chronic kidney disease	No	130 (97.74%)
	Yes	3 (2.26%)
Chronic venous insufficiency	No	90 (67.67%)
	Yes	43 (32.33%)
Depression/Anxiety	No	115 (86.47%)
	Yes	18 (13.53%)
Number of comorbidities	Up to two	25 (33.30%)
	Three or more	107 (66.70%)
Antidepressant	No	107 (80.45%)
	Yes	26 (19.55%)
Diuretic	No	93 (69.92%)
	Yes	40 (30.08%)
Calcium channel blocker	No	110 (82.71%)
	Yes	23 (17.29%)
Benzodiazepine	No	119 (89.47%)
	Yes	14 (10.53%)
Angiotensin II receptor blocker	No	73 (54.89%)
	Yes	60 (45.11%)
Beta-blocker	No	111 (83.46%)
	Yes	22 (16.54%)
Hypoglycemic agent	No	94 (70.68%)
	Yes	39 (29.32%)
Insulin	No	126 (94.74%)

Continued

	Yes	7 (5.26%)
Angiotensin-converting enzyme inhibitor	No	126 (94.74%)
	Yes	7 (5.26%)
Polypharmacy	No	91 (68.42%)
	Yes	42 (31.58%)
Caffeine (mg/day)		163.1 ± 77.8
Tobacco (packs/year)		4.4 ± 13.5
Body mass index (BMI)[a]	Normal	20 (15.15%)
	Obesity	52 (39.39%)
	Overweight	60 (45.46%)
Risk of obstructive sleep apnea	Low	54 (40.60%)
	Intermediate/High	79 (59.40%)

[a]133 patients in the database − 1 (no BMI information) = 132 patients.

polyuria in 7 (12.9%).

Regarding two or more episodes of nocturia, the mechanisms followed the same order of prevalence, present in 30 (68.2%), 8 (19.1%), and 6 (13.6%) participants, respectively.

Among participants with nocturia defined by one or more voids, an association was observed between global polyuria and recurrent urinary tract infection, insulin use, body mass index, and tobacco consumption (Table 2).

In those with nocturia defined as two or more urinations, an association was found between the use of insulin, BMI, and tobacco consumption with global polyuria (Table 3).

There was no statistically significant association observed between the studied variables and nocturnal polyuria or reduced nocturnal bladder capacity.

4. Discussion

The study analyzed the prevalence of nocturia in women seeking care at two urogynecology outpatient clinics for lower urinary tract symptoms. Among these women, the study evaluated the prevalence of the three main mechanisms through which nocturia occurs and factors associated with them.

The prevalence of nocturia defined by one or more episodes (70.7%) was similar to a cross-sectional study conducted by Daugherty *et al.* (2021) in the United States (69.6%), which included 7620 adult women [4], and another cross-sectional study conducted by Cruz *et al.* (2020) in the state of Rio de Janeiro, Brazil (68.4%), which included 411 women over 45 years old [26]. However, the prevalence of two or more episodes was higher than that of the Brazilian study (56.4% versus 49%) and nearly double that of the American study (28%).

Table 2. Association between sociodemographic and clinical characteristics and presence of global polyuria in women with nocturia (one or more voids) attended at two urogynecology clinics (N = 54). Niterói (RJ) and Petrópolis (RJ), Brazil, 2021-2023.

Characteristics	% of patients (n = 54*) or Mean ± SD	Global polyuria		p-value** (c2)
		Absent (n = 47)	Present (n = 7)	
Location				
Niterói	38.9	90.5	9.5	0.854
Petrópolis	61.1	84.8	15.2	
Age				
Under 60 years	40.7	90.9	9.1	0.772
60 years or older	59.3	84.4	15.6	
Education				
Up to incomplete primary school	51.9	85.7	14.3	1.000
At least completed primary school	48.1	88.5	11.5	
Hesitation				
Absent	88.9	85.4	14.6	0.720
Present	11.1	100	0	
Slow stream				
Absent	72.2	84.6	15.4	0.688
Present	27.8	93.3	6.7	
Feeling of incomplete bladder emptying				
Absent	35.2	94.7	5.3	0.414
Present	64.8	82.9	17.1	
Post-voiding incontinence				
Absent	61.1	84.8	15.2	0.854
Present	38.9	90.5	9.5	
Pelvic organ prolapse (symptom)				
Absent	68.5	86.5	13.5	1.000
Present	31.5	88.2	11.8	
Anterior vaginal wall prolapse				
Up to stage II	90.7	85.7	14.3	0.836
Stage III or IV	9.3	100.0	0.0	
Posterior vaginal wall prolapse				
Up to stage II	96.3	86.5	13.5	1.000
Stage III or IV	3.7	100	0	
Apical prolapse				
Up to stage II	96.3	86.5	13.5	1.000
Stage III or IV	3.7	100.0	0.0	
Fecal incontinence				

Continued

Absent	90.7	85.7	14.3	0.836
Present	9.3	100.0	0.0	
Constipation (Bristol stool scale)				
Absent	75.9	90.2	9.8	0.440
Present	24.1	76.9	23.1	
Constipation (bowel movement frequency)				
Absent	77.8	92.9	7.1	0.058
Present	22.2	66.7	33.3	
Recurrent urinary tract infection				
Absent	81.5	93.2	6.8	**0.022**
Present	18.5	60.0	40.0	
Systemic arterial hypertension				
Absent	37.0	90.0	10.0	0.938
Present	63.0	85.3	14.7	
Diabetes mellitus				
Absent	64.8	88.6	11.4	0.975
Present	35.2	84.2	15.8	
Heart failure				
Absent	96.3	86.5	13.5	1.000
Present	3.7	100.0	0.0	
Chronic kidney disease				
Absent	94.4	88.2	11.8	0.844
Present	5.6	66.7	33.3	
Chronic venous insufficiency				
Absent	64.8	88.6	11.4	0.975
Present	35.2	84.2	15.8	
Depression/Anxiety				
Absent	85.2	89.1	10.9	0.598
Present	14.8	75.0	25.0	
Number of comorbidities				
Up to 2 comorbidities	20.4	100.0	0.0	0.352
3 or more	79.6	83.7	16.3	
Antidepressant				
Absent	81.5	88.6	11.4	0.832
Present	18.5	80.0	20.0	
Diuretic				
Absent	70.4	86.8	13.2	1.000

Continued

Present	29.6	87.5	12.5	
Calcium channel blocker				
Absent	75.9	82.9	17.1	0.261
Present	24.1	100.0	0.0	
Benzodiazepine				
Absent	88.9	85.4	14.6	0.720
Present	11.1	100	0	
Angiotensin II receptor blocker				
Absent	53.7	86.2	13.8	1.000
Present	46.3	88.0	12.0	
Beta blocker				
Absent	81.5	86.4	13.6	1.000
Present	18.5	90.0	10.0	
Hypoglycemic agent				
Absent	64.8	88.6	11.4	0.975
Present	35.2	84.2	15.8	
Insulin				
Absent	94.4	90.2	9.8	**0.049**
Present	5.6	33.3	66.7	
Angiotensin-converting enzyme inhibitor				
Absent	92.6	86.0	14.0	0.977
Present	7.4	100	0	
Polypharmacy				
Up to 4 medications	63.0	94.1	5.9	0.110
5 or more medications	37.0	75.0	25.0	
Body mass index				
Normal	16.7	66.7	33.3	
Overweight	27.8	80.0	20.0	**0.040**
Obesity	55.6	96.7	3.3	
Risk of obstructive sleep apnea				
Low	31.5	82.4	17.6	0.796
Moderate or high	68.5	89.2	10.8	
Stress urinary incontinence				
Absent	87.0	87.2	12.8	1.000
Present	13.0	85.7	14.3	
Urgency urinary incontinence				
Absent	88.9	85.4	14.6	0.720

Continued

Present	11.1	100	0	
Mixed urinary incontinence				
Absent	29.6	93.8	6.2	0.611
Present	70.4	84.2	15.8	
Overactive bladder syndrome				
Absent	14.8	87.5	12.5	1.000
Present	85.2	87.0	13.0	
Quantitative characteristics:				
Caffeine (mg/day)***	153.2 ± 71.3	154.0 ± 70.3	150.0 ± 84.2	0.728
Tobacco (packs/year)***	4.2 ± 10.9	3.3 ± 8.3	10.4 ± 22.1	**0.046**

*54 female patients with nocturia (one or more urinations) and information on global polyuria; **p-value of Pearson's chi-square test (with Yates continuity correction); ***For the variables caffeine consumption and tobacco, the nonparametric Mann-Whitney test was applied.

Considering that the prevalence of nocturia increases with age [4] [5], it is noteworthy that the present study had a higher percentage (52.6%) of participants aged 60 years or older compared to the Brazilian study (43.3%). In the American study, age stratification was not provided. However, the mean age of participants with information on nocturia was 48.3 years, which is lower than the mean age of the present study, which was 58.4 years.

Patients in older age groups usually have a higher number of comorbidities and, consequently, are more likely to use polypharmacy. The association of these factors may explain the higher prevalence of nocturia in the study population. Furthermore, Daugherty *et al.* (2021) provided the descriptive analysis of sociodemographic and clinical factors, from which we could make additional comparisons. In the present study, the prevalences of systemic arterial hypertension (59.1% versus 43.3%) and obesity (45.5% versus 37.5%) were higher, two factors known to be associated with nocturia [4] [26].

When compared to a study conducted by Clemens *et al.* (2020) in a specialized urogynecology service in the United States, the prevalences were higher in the present study, with 70.7% versus 41.5% for one or more episodes of nocturia, and 56.4% versus 14.3% for two or more episodes in women [27]. Lower income and education levels of the population included in the present study, variables associated with a higher prevalence of nocturia in the literature, may contribute to explaining these differences [4]. Another factor to consider is the method used to measure episodes of nocturia, which was self-reported by patients in the present study, while in the US study, it was estimated by the average episodes recorded in a three-day bladder diary.

Another relevant information is that in Clemens *et al.*'s (2020) study, the mean age was 60.4 years, but it did not distinguish between men and women. This hinders the comparison between studies, as the causes of nocturia differ

Table 3. Association between sociodemographic and clinical characteristics and the presence of global polyuria in women with nocturia (two or more urinations) attended at two urogynecology outpatient clinics (N = 54). Niterói (RJ) and Petrópolis (RJ), Brazil, 2021-2023.

Characteristics	% patients (n = 44*) or Mean ± SD	Global polyuria		p-value** (c2)
		Absent (n = 38)	Present (n = 6)	
Location				
Niterói	36.4	87.5	12.5	1.000
Petrópolis	63.6	85.7	14.3	
Age				
Less than 60 years old	38.6	88.2	11.8	1.000
60 years or older	61.4	85.2	14.8	
Education				
Up to incomplete primary school	50.0	86.4	13.6	1.000
At least completed primary school	50.0	86.4	13.6	
Hesitation				
Absent	88.6	84.6	15.4	0.801
Present	11.4	100.0	0.0	
Slow stream				
Absent	75.0	84.8	15.2	1.000
Present	25.0	90.9	9.1	
Feeling of incomplete bladder emptying				
Absent	29.5	100.0	0.0	0.220
Present	70.5	80.6	19.4	
Post-voiding incontinence				
Absent	61.4	85.2	14.8	1.000
Present	38.6	88.2	11.8	
Pelvic organ prolapse (symptom)				
Absent	70.5	87.1	12.9	1.000
Present	29.5	84.6	15.4	
Anterior vaginal wall prolapse				

Continued

Up to stage II	93.2	85.4	14.6	1.000
Stage III ou IV	6.8	100.0	0.0	
Posterior vaginal wall prolapse				
Up to stage II	97.7	86.0	14.0	1.000
Stage III ou IV	2.3	100.0	0.0	
Apical prolapse				
Up to stage II	97.7	86.0	14.0	1.000
Stage III ou IV	2.3	100.0	0.0	
Fecal incontinence				
Absent	90.9	85.0	15.0	0.945
Present	9.1	100.0	0.0	
Constipation (Bristol stool scale)				
Absent	77.3	88.2	11.8	0.886
Present	22.7	80.0	20.0	
Constipation (frequency of bowel movements)				
Absent	75.0	90.9	9.1	0.310
Present	25.0	72.7	27.3	
Recurrent urinary tract infection				
Absent	81.8	91.7	8.3	0.109
Present	18.2	62.5	37.5	
Systemic arterial hypertension				
Absent	40.9	88.9	11.1	1.000
Present	59.1	84.6	15.4	
Diabetes mellitus				
Absent	63.6	85.7	14.3	1.000
Present	36.4	87.5	12.5	
Heart failure				
Absent	97.7	86.0	14.0	1.000

Continued

Present	2.3	100.0	0.0	
Chronic kidney disease				
Absent	93.2	87.8	12.2	0.874
Present	6.8	66.7	33.3	
Chronic venous insufficiency				
Absent	68.2	90.0	10.0	0.577
Present	31.8	78.6	21.4	
Depression/Anxiety				
Absent	81.8	88.9	11.1	0.641
Present	18.2	75.0	25.0	
Number of comorbidities				
Up to 2 comorbidities	22.7	100.0	0.0	0.365
3 or more	77.3	82.4	17.6	
Antidepressant				
Absent	77.3	88.2	11.8	0.886
Present	22.7	80.0	20.0	
Diuretic				
Absent	72.7	84.4	15.6	0.893
Present	27.3	91.7	8.3	
Calcium channel blocker				
Absent	75.0	81.8	18.2	0.310
Present	25.0	100.0	0.0	
Benzodiazepine				
Absent	86.4	84.2	15.8	0.684
Present	13.6	100.0	0.0	
Angiotensin II receptor blocker				
Absent	61.4	85.2	14.8	1.000
Present	38.6	88.2	11.8	

Continued

Beta-blocker				
Absent	84.1	86.5	13.5	1.000
Present	15.9	85.7	14.3	
Hypoglycemic agent				
Absent	63.6	85.7	14.3	1.000
Present	36.4	87.5	12.5	
Insulin				
Absent	95.5	90.5	9.5	0.010
Present	4.5	0.0	100.0	
Angiotensin-converting enzyme inhibitor				
Absent	90.9	85.0	15.0	0.945
Present	9.1	100.0	0.0	
Polypharmacy				
Up to 4 medications	59.1	92.3	7.7	0.350
5 or more medications	40.9	77.8	22.2	
Body mass index				
Normal	18.2	62.5	37.5	
Overweight	31.8	78.6	21.4	0.018
Obesity	50.0	100.0	0.0	
Risk of obstructive sleep apnea				
Low	34.1	80.0	20.0	0.674
Moderate or high	65.9	89.7	10.3	
Stress urinary incontinence				
Absent	86.4	86.8	13.2	1.000
Present	13.6	83.3	16.7	
Urgency urinary incontinence				
Absent	90.9	85.0	15.0	0.945
Present	9.1	100.0	0.0	

Continued

Mixed urinary incontinence				
Absent	27.3	91.7	8.3	0.893
Present	72.7	84.4	15.6	
Overactive bladder syndrome				
Absent	13.6	83.3	16.7	1.000
Present	86.4	86.8	13.2	
Quantitative characteristics:				
Caffeine (mg/day)***	151.9 ± 65.7	153.0 ± 62.5	142.0 ± 89.6	0.538
Tobacco (packs/year)***	4.8 ± 11.8	3.7 ± 8.8	12.1 ± 23.6	0.037

*44 female patients with nocturia (two or more urinations) and information on global polyuria; **p-value of Pearson's chi-square test (with Yates continuity correction); ***For the variables caffeine consumption and tobacco, the nonparametric Mann-Whitney test was applied.

between men and women and vary with age [18] [27].

Regarding the mechanisms through which nocturia can occur, the prevalence of nocturnal polyuria was 69.1%, reduced nighttime bladder capacity was 17.3%, and global polyuria was 12.9% (nocturia defined as one or more voids) and 68.2%, 19.1%, and 13.6%, respectively, for nocturia defined as two or more voids. The order of prevalences remained consistent in studies conducted by Drangsholt *et al*. (2019), who conducted a retrospective chart analysis of records of women with nocturia treated at a functional urology clinic and evaluated 72 bladder diaries, and also consistent with the findings of Clemens *et al*. (2020), which included 217 diaries from women. Drangsholt *et al*. (2019) found prevalences of 75% for nocturnal polyuria, 40.2% for reduced nighttime bladder capacity, and 18.1% for global polyuria in women with one or more nocturnal voids. Excessive fluid intake was identified as the primary cause of most cases of global polyuria [28]. Clemens *et al*. (2020) found prevalences of 77%, 36%, and 22%, respectively, in participants with two or more voids [27].

It is worth noting that the prevalences of the mechanisms of nocturia were all lower in the present study compared to the other two, particularly the reduced nighttime bladder capacity compared to the study by Drangsholt *et al*. (2019). This study included women with a mean age of 73.3 years compared to the mean age of 58.4 years in the present study, indicating that they were in the long postmenopausal period when a higher prevalence of the three mechanisms causing nocturia is expected. Furthermore, although it excluded patients with predominantly daytime symptoms, the inclusion criteria were women with urgency urinary incontinence with nocturia. Lastly, the criterion used to define reduced bladder capacity (greater urinary volume in 24 hours < 300 mL) was the

most sensitive among the studies. This justifies a disproportionately higher prevalence of this mechanism [28].

In the study by Clemens *et al*. (2020), where the mean age was similar to the present study and less sensitive criteria were used for nocturnal polyuria (>33% of 24-hour urine volume) and reduced nighttime bladder capacity (nocturnal bladder capacity index >2), lower prevalences of these mechanisms would be expected. However, the rates were not stratified by sex. It is known that in men, prostate disease is associated with reduced bladder capacity, while in women, there are specific conditions such as hypoestrogenism and genital prolapse.

In the three studies that evaluated bladder diaries, nocturnal polyuria was the most prevalent mechanism. It is believed that nocturnal polyuria results from changes in the circadian rhythm of antidiuretic hormone. This is a heterogeneous condition that can result from excessive fluid intake, be induced by medications such as diuretics taken in the late afternoon, or be part of a global polyuria picture. Systemic diseases that have the potential to alter electrolyte and water homeostasis, such as heart failure, venous stasis in the lower limbs, and obstructive sleep apnea, may be factors involved in nocturnal polyuria [29].

In a study involving women with nocturnal polyuria in the US (2023), 72.7% had the condition associated with overactive bladder syndrome, and 10.8% had it associated with other comorbidities (diabetes mellitus, systemic hypertension, heart disease, or obstructive sleep apnea). Among patients with at least two voids, 75.3% had the condition associated with overactive bladder syndrome, and 11% had it associated with other comorbidities [17]. In the present study, no association of any variables with nocturnal polyuria was observed.

Among the studied population, 66.7% had three or more comorbidities. The most prevalent comorbidities were systemic hypertension (59.1%), obesity (45.5%), and chronic venous insufficiency (32.6%). Additionally, the majority (59.1%) of participants had a moderate or high risk for obstructive sleep apnea. According to the literature, these mentioned conditions are known to be associated with nocturia. The most commonly used medications were angiotensin II receptor blockers (44.7%), diuretics, and hypoglycemic agents (both 29.5%) [9] [10] [11] [12].

In terms of urinary symptoms, there was a substantial prevalence of overactive bladder syndrome (73.5%), which can be associated with reduced bladder capacity [7]. The sensation of incomplete bladder emptying was also highly prevalent (55.3%), a symptom that may be associated with hypoactive bladder and consequently reduced bladder capacity [8]. Pelvic organ prolapse was reported by 31.8% of participants, with the highest prevalence of stage 3 or 4 prolapse being in the anterior vaginal wall (10.6% of participants) upon physical examination.

Our analyses found an association between normal body mass index, insulin use, and higher tobacco consumption with global polyuria both in participants with defined nocturia as one or more voids and in those with two or more voids. On the other hand, the association between a history of recurrent urinary tract

infection and global polyuria occurred only when nocturia was considered as one or more voids.

Several studies have observed an association between obesity and nocturia in women [5] [26] [30]. Moon *et al*. (2019) even found a positive association between increasing body mass index and the likelihood of having two or more voids in adjusted analyses for age, sex, and various comorbidities [31]. The association found between normal body mass index and polyuria may be related to factors that were not part of the scope of the present study, such as the measurement of fluid intake in the bladder diary, as well as the hormonal status of the participants related to menopause [9].

The observed association between insulin use and the presence of global polyuria contradicts current evidence, which suggests that the medication reduces polyuria associated with osmotic dieresis [32]. On the other hand, Chang *et al*. (2017) found that among diabetic women, those with more than 10 years since the diagnosis of diabetes mellitus had a 1.9 times higher chance of reporting nocturia compared to those diagnosed within 10 years [33]. It is possible that among insulin users, there was a high proportion of participants with long-standing diabetes mellitus and diabetic nephropathy, which may explain our findings.

Regarding the association between smoking and global polyuria, a population-based study conducted in China (2014) also found an association in individuals with nocturia using both definitions [34]. The relationship between smoking and changes in the physiological nighttime drop in blood pressure, a possible cause of nocturia, is still controversial and would be partly attributed to sympathetic nervous system activation [35] [36]. It is possible that such changes contribute to the occurrence of polyuria, but the exact mechanisms still need to be further studied.

According to the literature, a history of recurrent urinary tract infection is associated with nocturia. Madhu *et al*. (2015), in a multicenter study, found increasing frequencies of this condition as the number of nighttime urinations increased [5]. The mechanism through which these variables are related seems to be a reduction in nighttime bladder capacity. Another hypothesis suggests that urothelial dysfunction and underlying chronic inflammation justify both recurrent urinary tract infection and lower urinary tract symptoms in the context of hypersensitivity to bladder distension [29] [37].

The association between recurrent urinary tract infection and global polyuria in the present study can be understood in light of hypoestrogenism, which can be associated with both conditions. Vaginal epithelium has reduced epithelial glycogen production, leading to a decrease in *Lactobacillus* population and making the environment more vulnerable to uropathogens [38]. On the other hand, global polyuria can occur due to impaired secretion of antidiuretic hormone, resulting in predominantly free water diuresis, and due to decreased activation of the renin-angiotensin-aldosterone axis, leading to increased solute excretion. Both mechanisms are modulated by estrogen. Furthermore, oral mucosa and sa-

livary glands contain estrogen receptors, and decreased activation of these receptors leads to dry mouth after menopause, which can result in increased fluid intake throughout the 24-hour period [9].

However, there are certain limitations in this study that need to be mentioned. It was not possible to determine the postmenopausal duration for a significant percentage of the participants due to a high prevalence of women who had previously undergone hysterectomy. Comorbidities were self-reported by the participants, thereby potentially leading to an underestimation or overestimation of their prevalence. The research team observed a relative difficulty in correctly filling out the bladder diary, which resulted in a reduced number of available diaries.

On the other hand, this study contributes to a better understanding of the prevalence of nocturia in a population attending specialized services in Brazil, as well as it's associated factors. It also investigated the prevalence of the three main causative mechanisms of nocturia and a wide range of potential associations. Such information can support investigative protocols for nocturia and raise awareness among different medical specialties regarding the relevance of this topic.

5. Conclusions

The prevalence of nocturia was higher than that observed in previous studies conducted in both the general population and referral services for the treatment of lower urinary tract symptoms, especially when the condition was defined as the presence of two or more urinations. Nocturnal polyuria was the most prevalent cause of nocturia. Associations were found between global polyuria and normal body mass index, insulin use, higher tobacco consumption, and recurrent urinary tract infection.

Therefore, in patients with documented global polyuria, based on these findings, it becomes important to advise smoking cessation, assess the possible presence of recurrent urinary tract infection, provide appropriate clinical management, and evaluate the adequacy of therapeutic targets in diabetic patients. On the other hand, for patients with such conditions, it can be interesting to assess the possibility of polyuria associated. Lastly, no associations were found with nocturnal polyuria or reduced nocturnal bladder capacity.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Hashim, H., Blanker, M.H., Drake, M.J., Djurhuus, J.C., Meijlink, J., Morris, V., *et al.* (2019) International Continence Society (ICS) Report on the Terminology for Nocturia and Nocturnal Lower Urinary Tract Function. *Neurourology and Urodynamics*, **38**, 499-508. https://doi.org/10.1002/nau.23917

[2] Tikkinen, K., Johnson, T.M., Tammela, T.L.J., Sintonen, H., Haukka, J., Huhtala, H., *et al*. (2010) Nocturia Frequency, Bother, and Quality of Life: How Often Is Too Often? A Population-Based Study in Finland. *European Urology*, **57**, 488-498. https://doi.org/10.1016/j.eururo.2009.03.080

[3] Yow, H.Y., Tiong, J.J.L., Mai, C.W., van der Werf, E., Zainuddin, Z.M., Toh, C.C., *et al*. (2021) Prevalence of Nocturia among Community-Dwelling Adults: A Population-Based Study in Malaysia. *BMC Urology*, **21**, Article No. 95. https://doi.org/10.1186/s12894-021-00860-1

[4] Daugherty, M., Ginzburg, N. and Byler, T. (2021) Prevalence of Nocturia in United States Women: Results from National Health and Nutrition Examination Survey. *Female Pelvic Medicine and Reconstructive Surgery*, **27**, e52-e58. https://doi.org/10.1097/SPV.0000000000000792

[5] Madhu, C., Coyne, K., Hashim, H., Chapple, C., Milsom, I. and Kopp, Z. (2015) Nocturia: Risk Factors and Associated Comorbidities; Findings from the EpiLUTS Study. *International Journal of Clinical Practice*, **69**, 1508-1516. https://doi.org/10.1111/ijcp.12727

[6] Soler, R., Gomes, C.M., Averbeck, M.A. and Koyama, M. (2017) The Prevalence of Lower Urinary Tract Symptoms (LUTS) in Brazil: Results from the Epidemiology of LUTS (Brazil LUTS) Study. *Neurourology and Urodynamics*, **37**, 1356-1364. https://doi.org/10.1002/nau.23446

[7] Irwin, D.E., Abrams, P., Milsom, I., Kopp, Z. and Reilly, K. (2008) Understanding the Elements of Overactive Bladder: Questions Raised by the EPIC Study. *BJU International*, **101**, 1381-1387. https://doi.org/10.1111/j.1464-410X.2008.07573.x

[8] Offiah, I., Drake, M.J. and Gammie, A. (2022) Implications of Underactive Bladder Syndrome for Nocturia. Do We Need Urodynamic Assessment? *European Urology Focus*, **8**, 86-88. https://doi.org/10.1016/j.euf.2021.12.013

[9] Pauwaert, K., Goessaert, A.S., Ghijselings, L., Monaghan, T.F., Depypere, H. and Everaert, K. (2021) Nocturia through the Menopausal Transition and Beyond: A Narrative Review. *International Urogynecology Journal*, **32**, 1097-1106. https://doi.org/10.1007/s00192-020-04640-7

[10] Reyes, P.B.G., Butcher, K., Cotterill, N., Drake, M.J., Gimson, A., Gogola, L., *et al*. (2022) Implications of Cardiovascular Disease for Assessment and Treatment of Nocturia in Primary Care: Systematic Review and Nominal Group Technique Consensus. *European Urology Focus*, **8**, 26-32. https://doi.org/10.1016/j.euf.2021.12.014

[11] Papworth, E., Dawson, S., Henderson, E.J., Eriksson, S.H., Selsick, H., Rees, J., *et al*. (2022) Association of Sleep Disorders with Nocturia: A Systematic Review and Nominal Group Technique Consensus on Primary Care Assessment and Treatment. *European Urology Focus*, **8**, 42-51. https://doi.org/10.1016/j.euf.2021.12.011

[12] Dawson, S., Duncan, L., Ahmed, A., Gimson, A., Henderson, E.J., Rees, J., *et al*. (2022) Assessment and Treatment of Nocturia in Endocrine Disease in a Primary Care Setting: Systematic Review and Nominal Group Technique Consensus. *European Urology Focus*, **8**, 52-59. https://doi.org/10.1016/j.euf.2021.12.008

[13] Hashimoto, Y., Tanaka, M., Yamazaki, M., Nakano, K., Ushigome, E., Okada, H., *et al*. (2016) Caffeine Intake Enhances the Benefits of Sodium Glucose Transporter 2 Inhibitor. *Diabetes/Metabolism Research and Reviews*, **32**, 694-699. https://doi.org/10.1002/dmrr.2789

[14] Kanbay, M., Turgut, F., Erkmen Uyar, M., Akcay, A. and Covic, A. (2008) Causes and Mechanisms of Nondipping Hypertension. *Clinical and Experimental Hypertension*, **30**, 585-597. https://doi.org/10.1080/10641960802251974

[15] Nguyen, L.N., Randhawa, H., Nadeau, G., Cox, A., Hickling, D., Campeau, L., *et al*. (2022) Canadian Urological Association Best Practice Report: Diagnosis and Management of Nocturia. *Canadian Urological Association Journal*, **16**, E336-E349. https://doi.org/10.5489/cuaj.7970

[16] Fisch, G.Z., Fang, A.H., Miller, C.D., Choi, C., Monaghan, T.F., Smith, E.F., *et al*. (2022) Polyuria in Patients with Lower Urinary Tract Symptoms: Prevalence and Etiology. *Neurourology and Urodynamics*, **42**, 256-262. https://doi.org/10.1002/nau.25078

[17] Mueller, E.R., Weiss, J.P., Bosch, J., Chughtai, B., Rosenberg, M.T., Bacci, E.D., *et al*. (2023) Nocturnal Polyuria in Women: Results from the EpiNP Study. *International Urogynecology Journal*, **34**, 1743-1751. https://doi.org/10.1007/s00192-022-05432-x

[18] Weiss, J.P., Bosch, J., Chapple, C.R., Bacci, E.D., Simeone, J.C., Rosenberg, M.T., *et al*. (2022) The Prevalence of Nocturnal Polyuria in the United States: Results from the Epidemiology of Nocturnal Polyuria Study. *European Urology Focus*, **8**, 1415-1423. https://doi.org/10.1016/j.euf.2021.12.016

[19] Vahabi, B., Jabr, R., Fry, C., McCloskey, K., Everaert, K., Agudelo, C.W., *et al*. (2020) ICI-RS 2019 Nocturia Think Tank: How Can Experimental Science Guide Us in Understanding the Pathophysiology of Nocturia? *Neurourology and Urodynamics*, **39**, S88-S95. https://doi.org/10.1002/nau.24274

[20] ICS Glossary. ICS|International Continence Society. https://www.ics.org/glossary

[21] Aziz, I., Whitehead, W.E., Palsson, O.S., Törnblom, H. and Simrén, M. (2020) An Approach to the Diagnosis and Management of Rome IV Functional Disorders of Chronic Constipation. *Expert Review of Gastroenterology & Hepatology*, **14**, 39-46. https://doi.org/10.1080/17474124.2020.1708718

[22] Delara, M., Murray, L., Jafari, B., Bahji, A., Goodarzi, Z., Kirkham, J., *et al*. (2022) Prevalence and Factors Associated with Polypharmacy: A Systematic Review and Meta-Analysis. *BMC Geriatrics*, **22**, Article No. 601. https://doi.org/10.1186/s12877-022-03279-x

[23] Abarca-Gómez, L., Abdeen, Z.A., Hamid, Z.A., Abu-Rmeileh, N.M., Acosta-Cazares, B., Acuin, C., *et al*. (2017) Worldwide Trends in Body-Mass Index, Underweight, Overweight, and Obesity from 1975 to 2016: A Pooled Analysis of 2416 Population-Based Measurement Studies in 128.9 Million Children, Adolescents, and Adults. *The Lancet*, **390**, 2627-2642. https://doi.org/10.1016/S0140-6736(17)32129-3

[24] Madhu, C., Swift, S., Moloney-Geany, S. and Drake, M.J. (2018) How to Use the Pelvic Organ Prolapse Quantification (POP-Q) System? *Neurourology and Urodynamics*, **37**, S39-S43. https://doi.org/10.1002/nau.23740

[25] ICS Standards 2022. ICS|International Continence Society. https://www.ics.org/members/shop/icsstandards2022

[26] Cruz, R., Garcia-Rosa, M. and Faria, C. (2020) Prevalence and Associated Factors in Community-Dwelling Subjects—A Population-Based Study. *Revista da Associação Médica Brasileira*, **66**, 830-837. https://doi.org/10.1590/1806-9282.66.6.830

[27] Clemens, J.Q., Wiseman, J.B., Smith, A.R., Amundsen, C.L., Yang, C.C., Bradley, M.S., *et al*. (2020) Prevalence, Subtypes, and Correlates of Nocturia in the Symptoms of Lower Urinary Tract Dysfunction Research Network Cohort. *Neurourology and Urodynamics*, **39**, 1098-1107. https://doi.org/10.1002/nau.24338

[28] Drangsholt, S., Peyronnet, B., Arcila-Ruiz, M., Sussman, R.D., Palmerola, R., Pape, D.R., *et al*. (2019) Nocturia in Female Patients: Current Clinical Features, Treatment Patterns and Outcomes at a Tertiary Referral Centre. *Arab Journal of Urology*, **17**, 82-86. https://doi.org/10.1080/2090598X.2019.1589792

[29] Oelke, M., De Wachter, S., Drake, M.J., Giannantoni, A., Kirby, M., Orme, S., *et al*. (2017) A Practical Approach to the Management of Nocturia. *International Journal of Clinical Practice*, **71**, e13027. https://doi.org/10.1111/ijcp.13027

[30] Azuero, J., Santander, J., Trujillo, C.G., Caicedo, J.I., Zuluaga, L., Becerra, A.M., *et al*. (2021) Potential Associations of Adult Nocturia. Results from a National Prevalence Study. *Neurourology and Urodynamics*, **40**, 819-828. https://doi.org/10.1002/nau.24624

[31] Moon, S., Chung, H.S., Yu, J.M., Ko, K.J., Choi, D.K., Kwon, O., *et al*. (2019) The Association between Obesity and the Nocturia in the U.S. Population. *International Neurourology Journal*, **23**, 169-176. https://doi.org/10.5213/inj.1938062.031

[32] Erdogan, B.R., Liu, G., Arioglu-Inan, E. and Michel, M.C. (2022) Established and Emerging Treatments for Diabetes-Associated Lower Urinary Tract Dysfunction. *Naunyn-Schmiedeberg's Archives of Pharmacology*, **395**, 887-906. https://doi.org/10.1007/s00210-022-02249-9

[33] Chang, C.J., Pei, D., Wu, C.C., Palmer, M.H., Su, C.C., Kuo, S.F., *et al*. (2017) Correlates of Nocturia and Relationships of Nocturia with Sleep Quality and Glycemic Control in Women with Type 2 Diabetes. *Journal of Nursing Scholarship*, **49**, 400-410. https://doi.org/10.1111/jnu.12302

[34] Wang, Y., Hu, H., Xu, K., Zhang, X., Wang, X., Na, Y., *et al*. (2014) Prevalence, Risk Factors, and Symptom Bother of Nocturia: A Population-Based Survey in China. *World Journal of Urology*, **33**, 677-683. https://doi.org/10.1007/s00345-014-1411-5

[35] Musameh, M.D., Nelson, C.P., Gracey, J., Tobin, M., Tomaszewski, M. and Samani, N.J. (2016) Determinants of Day-Night Difference in Blood Pressure, a Comparison with Determinants of Daytime and Night-Time Blood Pressure. *Journal of Human Hypertension*, **31**, 43-48. https://doi.org/10.1038/jhh.2016.14

[36] Omvik, P. (1996) How Smoking Affects Blood Pressure. *Blood Pressure*, **5**, 71-77. https://doi.org/10.3109/08037059609062111

[37] Kuo, H.C., Ke, Q.S. and Lee, C.L. (2021) Recurrent Urinary Tract Infection in Women and Overactive Bladder—Is There a Relationship? *Tzu Chi Medical Journal*, **33**, 13-21. https://doi.org/10.4103/tcmj.tcmj_38_20

[38] Jung, C. and Brubaker, L. (2019) The Etiology and Management of Recurrent Urinary Tract Infections in Postmenopausal Women. *Climacteric*, **22**, 242-249. https://doi.org/10.1080/13697137.2018.1551871