

ORIGINAL RESEARCH

Nocturia in men and associated comorbidities: a southeast Michigan study

Daniel Fortney¹, Prasun Sharma^{1,*}, Alexander Geisenhoff²,
Bernadette M.M. Zwaans^{1,2}, Michael D Lutz³

¹Oakland University William Beaumont
School of Medicine, Rochester, MI
48309, USA

²Corewell Health William Beaumont
University Hospital, Royal Oak, MI
48073, USA

³Michigan Institute of Urology,
Rochester Hills, MI 48307, USA

***Correspondence**

Prasunsharma@oakland.edu
(Prasun Sharma)

Abstract

Nocturia is a highly prevalent condition associated with poor quality of life and increased adverse health outcomes. Our study investigates the prevalent condition of nocturia and its profound impact on individuals' quality of life and adverse health outcomes. We explore the correlation between nocturia and various comorbidities in a southeast Michigan population by analyzing data from 1023 participants who completed self-administered questionnaires during the 2021 Michigan Institute of Urology's Men's Health Event; 892 participants responded to the nocturia questionnaire. Categorizing participants based on the severity of nocturia into three groups—no nocturia, nocturia once per night, and multiple nocturia episodes per night—we employed Pearson's Chi-square test to examine the relationship between nocturia severity and the presence of comorbidities. Our findings demonstrate significant associations between increasing episodes of nocturnal voids and the prevalence of hypertension, non-insulin-dependent diabetes and anxiety. Additionally, arthritis and colorectal polyps exhibit notable links with multiple nocturia episodes, while participants with a family history of hypertension show decreased prevalence as nocturnal voids increase, and a family history of myocardial infarction is notably associated with nocturia, particularly in the nocturia once per night group. Our research highlights the widespread impact of nocturia and its strong associations with diverse comorbidities, underscoring the importance of further investigation to comprehend the underlying mechanisms and enhance patient outcomes.

Keywords

Nocturia; Comorbidities of nocturia; Quality of life; Men's health

1. Introduction

Nocturia, defined as waking up during the night to void, is a prevalent condition affecting a considerable proportion of the population. According to the International Continence Society (ICS), the first episode of nocturia must be preceded by sleep, and subsequent episodes must be followed by the intention of returning to sleep, in order to account [1]. One meta-analysis assessing the prevalence of nocturia showed 2–16.6% of men and 4.4–18% of women between the ages of 20 and 40 voided two or more times at night, and the prevalence rates for men and women between 70 and 90 were higher at 29–59.3% and 28.3–61.5%, respectively [2]. Thus, nocturia is frequently seen in both men and women and increases in prevalence with age, though nocturia is not simply a disease of the elderly population. Given the commonality of nocturia, it is imperative to understand the harmful outcomes associated with this symptom.

Nocturia has four main underlying causes: 1. 24-hour polyuria (production of abnormally high volumes of urine), 2. Nocturnal polyuria, 3. Diminished bladder capacity, and 4.

Sleep disorders [3]. These categories encompass a myriad of conditions, which complicates the diagnosis and treatment of nocturia.

While waking up at night to void may be harmless, many studies have demonstrated that nocturia is associated with poor health outcomes, most commonly due to interrupted sleep [4]. Consistent sleep disturbances are related to various issues, including somatic diseases, mood disorders, cardiovascular disease, mortality and diminished quality of life [5]. Other comorbidities that have consistently been associated with nocturia include hypertension, obesity and diabetes [6, 7]. Consequently, nocturia places a significant economic burden on the U.S Healthcare System and affected patients. Jhaveri *et al.* [8] demonstrated that patients with nocturia had 60% greater hospitalization rates and 19% higher rates of outpatient visits. These individuals were also affected economically *via* reduced work productivity, lower employment odds, and fewer hours worked per week. On a larger scale, the overall economic burden of nocturia was estimated between \$94.0–\$231.1 billion based on varying prevalence rates with an average cost of \$3491 per patient [8].

While some studies have not consistently aligned on the associations between nocturia and specific comorbidities, the overall agreement on the negative health outcomes and economic strain caused by untreated nocturia remains significant [9]. To shed further light on this subject, we aimed to investigate the relationship between nocturia and various conditions, including cardiovascular disease, myocardial infarction (MI), hypertension, stroke, diabetes, arthritis, colorectal polyps, prostate cancer, depression, anxiety and chronic obstructive pulmonary disease (COPD)/asthma, using data from the 2021 Men's Health Event in Detroit, MI.

2. Methods

The data for our study was compiled from Michigan Institute of Urology's 2021 Men's Health Event Questionnaire (See **Supplementary material**). MIU's Men's Health Event is an annual event designed to create awareness through screening, educating and informing the greater Detroit male community on men's health-related issues. It provides a unique opportunity to collect data from a diverse patient population in Southeast Michigan on a large scale.

The study population included males age 18 or older who physically attended the 2021 Men's Health Event. Those excluded from the study were women, and men under the age of 18. Voluntary consent to participate in the study was performed the same day prior to the screening. Participants self-reported their demographic information, which included age, race and ethnicity. Medical history, including cardiovascular disease, myocardial infarction, hypertension, stroke, type 1 diabetes, type 2 diabetes, arthritis, colorectal polyps, prostate cancer, depression, anxiety, COPD and asthma, was also self-reported. Nocturia-related questions addressed the history and frequency of nocturia. A total of 1023 visitors participated in the screening, of which 892 completed the questions related to nocturia.

Data analysis was conducted using SPSS 26.0 software (IBM, New York City, NY, USA), focusing on establishing associations between nocturia and the included comorbidities. Further analysis examined whether the prevalence of participants with a family history of the target variables had significant associations with the frequency of nocturnal voids. Study participants were divided into three groups: no nocturia, nocturia once per night, and multiple nocturia episodes per night. Pearson's Chi-square test was utilized to assess significant differences in the incidence of co-morbidities among the three nocturia groups. Statistical significance was set at $p < 0.05$.

3. Results

A total of 896 participants consented to participate, completed the nocturia questions, and were subsequently included in this study. The overall average age of study participants was 56.7 years of age (Standard Deviation (SD) 12.7), with over 60% of study participants being 51–70 years of age (Table 1). Study participants were further divided into 3 groups based on the prevalence of nocturia. The groups included participants who did not experience nocturia ($N = 203$; 22.8%), those who

experienced 1 episode of nocturia per night ($N = 414$; 46.4%), and those who had 2 or more episodes of nocturia per night ($N = 275$; 30.8%). The average age with standard deviation, distribution of age among the groups, and demographics of the participants are shown in Table 1. Based on these results, the incidence of nocturia was higher in older age groups ($p < 0.0001$). Sixty-one percent of study participants had African American/Black race, followed by 35.7% White and 2.6% Asian. The prevalence of nocturia did not differ significantly between African American/Black and White study participants ($p = 0.2709$). Approximately 8.8% of all study participants actively used medication to manage nocturia symptoms, with the majority (17.8%) in the ≥ 2 voids/night group ($p < 0.0001$).

Two-thirds of study participants reported to have 1 or more co-morbidities (Table 1). The incidence of comorbidities was significantly higher in participants with nocturia compared to men without nocturia ($p < 0.0019$). Of the co-morbidities analyzed, several were significantly associated with increasing episodes of nocturia (Fig. 1). The prevalence of hypertension ($p = 0.0084$), non-insulin-dependent diabetes ($p = 0.0080$), and anxiety ($p = 0.0099$) was positively associated with severity of nocturia. Arthritis also exhibited a significant association with nocturia ($p = 0.0088$), with a prevalence of 11% in the no nocturia and $1 \times$ nocturia groups, and 20% in the ≥ 2 nocturia group (Fig. 1A). Similarly, the prevalence of subjects with colorectal polyps was statistically significant ($p = 0.0001$) with incidence of 16%, 13% and 26% in the respective nocturia categories (Fig. 1B). Non-insulin-dependent diabetes and anxiety showed increasing prevalence with the severity of nocturia, ranging from 9% to 10% and 18% and 1% to 9% and 14%, respectively (Fig. 1C,D). The incidence of reported hypertension increased from 31% in the no nocturia group to 37% in the $1 \times$ per night nocturia group and 46% in the ≥ 2 per night nocturia group (Fig. 1E).

Further analysis was performed to determine if the prevalence of participants with only a family history of the target comorbidities had any significant associations with the frequency of nocturnal voids (Fig. 2). The intent of this analysis was to determine if the presence of nocturia may be an early symptom of later developing one of these underlying conditions. The prevalence of a family history of hypertension ($p = 0.0077$) decreased from 46% to 43% to 32% in the no nocturia, $1 \times$ nocturia and ≥ 2 nocturia groups, respectively. Additionally, the percentage of subjects with a family history of myocardial infarction ($p = 0.0420$) changed from 34% to 48% to 37% among the respective nocturia groups.

4. Discussion

This study retrospectively analyzed the incidence of nocturia and its associations with comorbidities in a predominantly African American male community. Our findings indicate that several chronic illnesses are significantly associated with increasing nocturnal voids, including hypertension, non-insulin-dependent diabetes and anxiety. Additionally, the prevalence of arthritis and colorectal polyps is significantly associated with ≥ 2 voids per night. As the frequency of nocturnal voids increased, there was a notable decrease in the prevalence of participants with a family history of hypertension. Further-

TABLE 1. Patient characteristics based on age and race.

	All	No Nocturia	Nocturia		p-value
			1×/night	≥2/night	
Age	N = 892	N = 203	N = 414	N = 275	
Average Age (SD)	56.7 (12.7)	52.2 (13.9)	55.9 (12.2)	60.1 (11.3)	<0.0001*
Under 40	95	37 (38.9%)	44 (46.3%)	14 (14.7%)	
41–50	145	36 (24.8%)	75 (51.7%)	34 (23.4%)	
51–60	293	73 (24.9%)	138 (47.1%)	82 (28.0%)	<0.0001
61–70	254	42 (16.5%)	114 (44.9%)	98 (38.6%)	
71+	105	15 (14.3%)	43 (41.0%)	47 (44.8%)	
Race/ethnicity	N = 854	N = 195	N = 395	N = 264	
Black/African American	522 (61.1%)	113 (58.0%)	239 (60.5%)	170 (64.0%)	0.2709
White/Caucasian	305 (35.7%)	76 (39.0%)	145 (37.0%)	84 (32.0%)	
American Indian/Alaskan Native	3 (0.4%)	0 (0%)	1 (0.25%)	2 (1.0%)	**
Native Hawaiian/Other/Pacific Islander	2 (0.2%)	1 (0.5%)	1 (0.25%)	0 (0%)	**
Asian	22 (2.6%)	5 (2.5%)	9 (2.0%)	8 (3.0%)	**
Nocturia Medication	N = 896	N = 203	N = 414	N = 275	
Yes	79 (8.8%)	4 (2.0%)	26 (6.3%)	49 (17.8%)	<0.0001
Co-morbidities	N = 794	N = 187	N = 370	N = 237	
None	275 (34.6%)	82 (43.9%)	123 (33.2%)	70 (29.5%)	
1	213 (26.8%)	48 (25.7%)	110 (29.7%)	55 (23.2%)	0.0019
≥2	306 (38.5%)	57 (30.5%)	137 (37.0%)	112 (47.3%)	

*Tukey's multiple comparison: No nocturia vs. 1×/night ($p = 0.0014$); No nocturia vs. ≥2/night ($p < 0.0001$); 1×/night vs. ≥2/night ($p < 0.0001$). **Values too low to include in statistical analysis. SD: Standard Deviation

more, the prevalence of participants with a family history of myocardial infarction exhibited a significant association with nocturia, with the highest prevalence observed in the group experiencing nocturia once per night.

In our study population, hypertension (HTN) prevalence increased considerably with a higher frequency of nocturnal voids. At the same time, the prevalence of participants with a family history of HTN who did not have HTN themselves decreased with increasing frequency of nocturnal voids. Combining these findings suggests that nocturia may be a direct consequence of hypertension, as patients with HTN and ≥2 nocturia were less likely to have a family history of HTN. Although the relationship between hypertension and nocturia is not completely understood, several mechanisms, such as altered glomerular filtration rate and tubular transport, increased release of atrial natriuretic peptide secondary to chronic hypertension, and reduced antidiuretic hormone from isolated increases in systolic blood pressure may play a role [10].

Non-insulin-dependent diabetes also exhibited a higher prevalence with increasing frequency of nocturnal voids. One proposed mechanism for this relationship is hyperglycemia-induced osmotic diuresis, which increases urine output [9]. Bladder dysfunction secondary to diabetic neuropathy,

atherosclerosis, and chronic systemic bladder urothelial inflammation may also play a role in developing diabetes-associated overactive bladder, resulting in nocturia [11, 12]. Each of these factors could be investigated further.

In addition, we identified a significant increase in anxiety among participants with higher numbers of nocturnal voids. Several studies have explored the connection between anxiety and nocturia and have suggested a bidirectional relationship. In the EpiLuts study, an analysis of 14,107 men, the prevalence of anxiety was shown to positively correlated with the number of nocturnal voids [7]. This same study demonstrated an association between men with chronic anxiety and the prevalence of >2 nocturnal voids [6]. Lower urinary tract symptoms have also been associated with decreased self-esteem, embarrassment and social anxiety [13]. Nocturia has also been shown to diminish sleep quality and quantity, leading to impaired daytime cognitive functioning, productivity, ability to concentrate and subsequent anxiety [14]. Additionally, studies have shown that the stress related to conditions such as anxiety may contribute to or prolong lower urinary tract symptoms such as nocturia and overactive bladder [15]. Furthermore, anxiety is known to cause insomnia, which could also affect the number of voids reported each night [16]. Clearly, the links between nocturia and anxiety are deeply intertwined and compound

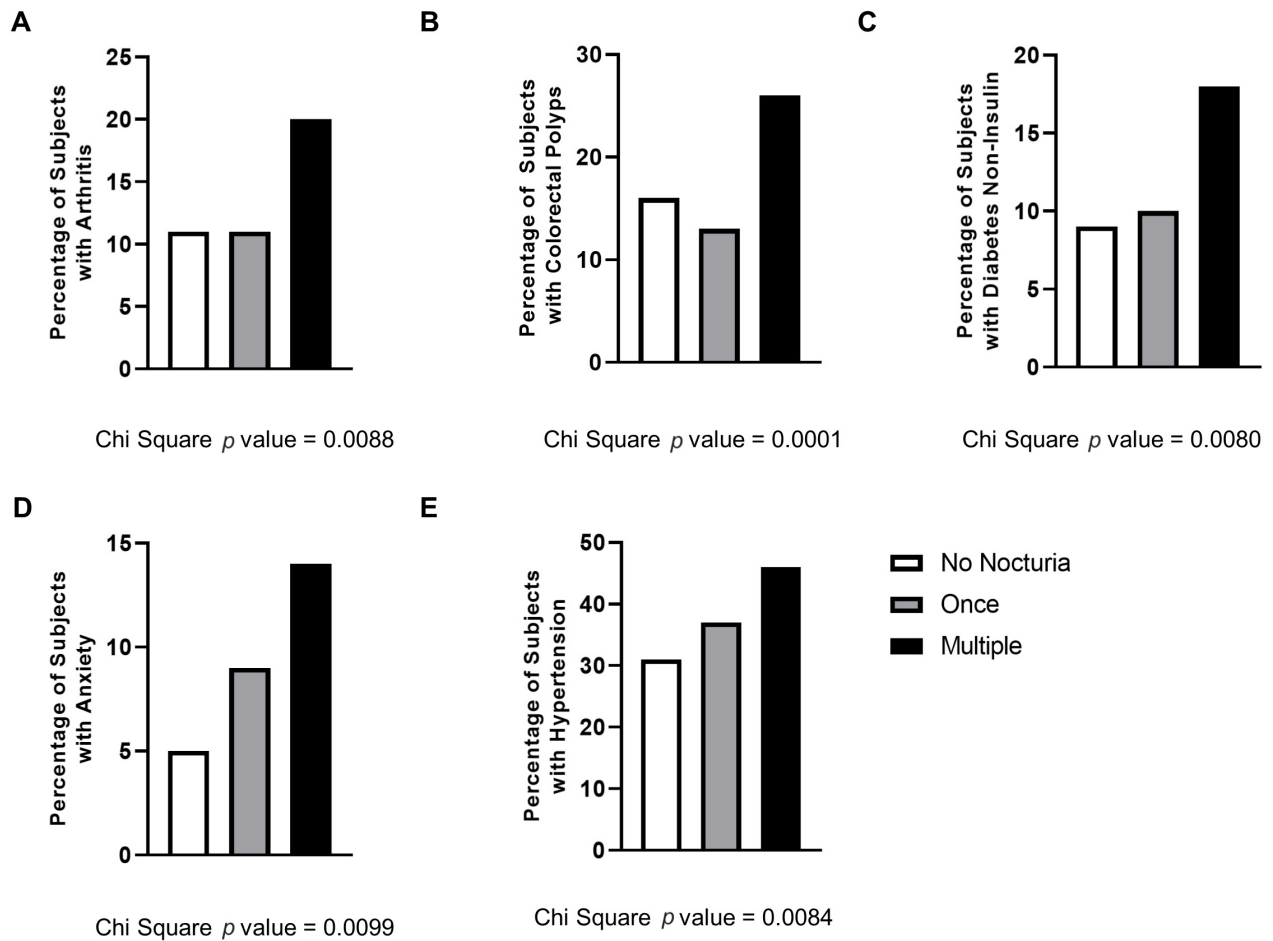


FIGURE 1. Severity of nocturia is associated with numerous comorbidities. Prevalence of (A) Arthritis (B) Colorectal polyps (C) Non-insulin dependent diabetes (D) Anxiety and (E) Hypertension, showed statistically significant change with varying frequency of nocturia. Statistical analysis done with Chi-square test.

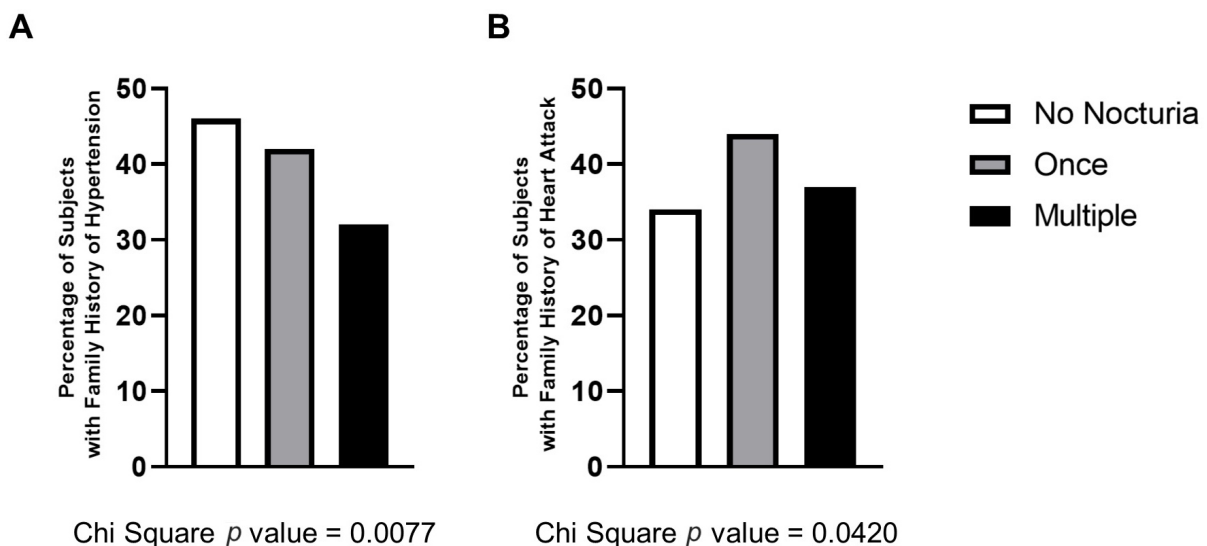


FIGURE 2. Severity of nocturia is associated with family history of comorbidities. Prevalence of (A) patients with only a family history of hypertension and (B) myocardial infarction, showed statistically significant change with varying frequency of nocturia. The participants themselves do not have the specified conditions. Statistical analysis done with Chi-square test.

detrimental effects on quality of life, indicating the importance of bringing these comorbidities to light.

Arthritis was another comorbid condition that showed a significant increase in prevalence in the ≥ 2 nocturia category. Although our study did not distinguish the specific type of arthritis, several studies have demonstrated significant associations between lower urinary tract symptoms, including nocturia, in patients with rheumatoid and osteoarthritis [6]. However, this relationship is not entirely understood. There has been some evidence to suggest that conditions such as overactive bladder and interstitial cystitis may stem from an autoimmune etiology, and both of these conditions can present with nocturia [17]. This may explain the increased correlation between rheumatoid arthritis and nocturia that has been demonstrated in prior studies [18]. It is also plausible that patients with chronic arthritis may awaken more frequently due to pain or discomfort and subsequently choose to void rather than awaken from the actual urge to void itself. This may then be misconstrued in patient-reported responses and result in falsely elevated rates of true nocturia in this specific patient group. Regardless, further investigation into this relationship is needed to determine if there is an underlying causality.

Our study also found that the prevalence of participants with colorectal polyps was significantly increased in the ≥ 2 nocturia cohort. Although colorectal polyps may be related to an increased risk of colorectal cancer, which can present with various urinary symptoms, this is typically evident late in the disease process when there is a locally invasive disease and would be unlikely to show such significance in our study population [19]. Thus, the exact mechanism of this relationship is unclear and would benefit from further exploration to possibly identify an underlying systemic link.

Lastly, our study observed a higher prevalence of family history of myocardial infarction in the nocturia cohorts, with the highest percentage in the $1 \times$ nocturia group. Common risk factors for MI include hypertension, diabetes and obesity, which have been shown to be associated with nocturia in several studies [5, 6]. Several risk factors for MI, including those mentioned, are also known to have genetic components involved in their inheritance [20]. Therefore, it is plausible that participants with a family history of MI may also have comorbid conditions themselves that may predispose them to higher odds of developing nocturia.

This study has several limitations. Firstly, the data were obtained through a retrospective analysis of self-reported answers to our Men's Health questionnaire, rather than relying on objective measures or medical charts. Consequently, there may be some inaccuracies in the reported data. These inaccuracies are particularly noteworthy since the study design precluded the utilization of voiding diaries or further assessment of lower urinary tract symptoms among our participants. Secondly, the study population consisted exclusively of male participants, limiting the generalizability of the findings to the female population. Thirdly, our questionnaire did not collect information on medication usage, such as diuretics, thereby impeding our ability to consider the possibility of pharmacologically-induced nocturnal voiding. Lastly, due to the design of the questionnaire, we did not have access to information regarding the medical management or severity of

comorbidities among our participants.

5. Conclusions

Nocturia is a common condition among men in Southeast Michigan and is associated with numerous comorbidities. While some mechanisms can be postulated to explain these associations, a causality cannot be assumed. Further research is needed to explore the relationship between nocturia and the identified comorbidities, potentially unveiling underlying pathophysiological mechanisms and opportunities to improve health outcomes.

ABBREVIATIONS

ICS, International Continence Society; MIU, Michigan Institute of Urology's; COPD, Chronic Obstructive Pulmonary Disease; HTN, Hypertension; MI, Myocardial Infarction.

AVAILABILITY OF DATA AND MATERIALS

All data available from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

MDL, BMMZ and DF—conceived and designed this study. MDL and DF—curated study data. DF, BMMZ and PS—analyzed data and prepared figures. MDL and BMMZ—provided project administration and supervision. DF and PS—wrote the manuscript. MDL, BMMZ, AG and PS—reviewed and edited the manuscript. All authors approved the manuscript for submission.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was conducted with full approval and oversight from Beaumont Internal Review Board (IRB# 2012-293). Samples collected through Men's Health event participation were completed through an information sheet, so no written consent was obtained. Completing the survey was taken as full consent to participation.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at <https://oss.jomh.org/files/article/1718877468153004032/attachment/Supplementary%20material.pdf>.

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