

Co-morbidities of Nocturia among Adults: A Cross-sectional Study in Southern India

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ABSTRACT

Introduction: Night urination severely impacts the quality of life among adults. Coexisting factors such as age, obesity, diabetes, hypertension, cardiac diseases, UTI, asthma, anxiety, and depression are significantly related when voiding episodes exceed two per night. However, understanding its associated factors are essential aspects in the management of Nocturia.

Aim: The aim of the study was to determine the association of nocturia with selected demographic variables, co-morbidities, and the precipitating factors among adults with voiding episodes two or more times and adults who void only once at night.

Materials and Methods: A descriptive cross-sectional design was carried out among 420 adults of age 35-65 years with voiding over two times (Group I) and 206 adults of age 35-65 years who voided only once (Group II) a night. The data was collected from two selected hospitals of Mangalore between January 2018 and June 2019. The written permission was taken from the concerned authority, after obtaining the informed consent from the subjects. The baseline proforma was assessed by the researcher using structured interview schedule and the

questionnaire on co-morbidity and precipitating factors such as regular intake of alcoholism, smoking, consumption of coffee, spicy food, anxiety, urinate before bedtime, use of diuretics, day time frequency, underwent surgeries was filled by the subjects. The data was analysed using frequency, percentage, Chi-square test, and logistic regression statistics by Statistical Package for the Social Sciences (SPSS) Version 16.

Results: The study observed that the risk of nocturia was significantly higher among Group I subjects with Urinary Tract Infection (UTI), constipation, hypertension, and on medication for various diseases compared with Group II. The precipitating factors of nocturia revealed that Group I subjects who regularly took coffee, spicy food, had anxiety, daytime frequency, and had undergone various surgeries showed significant difference associated with increased risk of nocturia compared with Group II.

Conclusion: The study findings demonstrate that nocturia is strongly associated with multiple co-morbidities and precipitating factors. These results therefore provide evidence to establish the primary and secondary preventive strategies among adults with nocturia.

Keywords: Night urination, Urinary tract infection, Voiding episodes

INTRODUCTION

Nocturia is a very common Lower Urinary Tract Symptom (LUTS). It is defined as 'the ailment in which a patient has to wake up at night more than once to void, with each void preceding and followed by sleep' by the International Continence Society (ICS) [1]. It affects male and female patients of all age groups equally, and has higher incidence in the elderly [2]. Despite its prevalence, nocturia yet is a poorly reported, treated, and managed for social and medical issue [3].

The pathophysiology of nocturia is a complex one, and to date, no single direct origin has been established. Several risk factors, e.g., metabolic syndrome, aging, hypertension, congestive heart issues, Diabetes Mellitus (DM), sleep apnea, high nocturnal micturition volume, reduced bladder volume, benign prostate hypertrophy, etc., have been put forward [4,5].

Some studies have observed a significant positive correlation between nocturia and hypertension [6-8], while others have reported none at all relation between the two [9-11]. Häkkinen JT et al., observed no significant correlation between hypertension and nocturia. In their study, symptoms were evaluated twice, i.e., at baseline and five-year follow-up. So, information on the precise time of onset of symptom or deterioration was unavailable [11].

In a study by Liao CH et al., there was significant negative correlation between nocturia and the serum testosterone levels [12]. But, serum hormone levels were determined just once, and the single value is an inaccurate estimate of an individual's general hormone status and could be affected by individual and analytic errors. Kim JW et al., observed a significant association between nocturia and low testosterone levels. However, the study was a limited, open-label,

single-arm pilot research; hence both placebo and control groups were absent [13].

Rembratt A et al., observed no correlation between nocturia and ailments such as DM, angina, known and treated hypertension, or congestive heart issues [10]. However, data on the primary response variable (nightly voids per week) was missing. Furukawa S et al., observed no significant association between diabetic neuropathy/nephropathy and nocturia [14]. This is in contrast with the results of previous studies which could be because of confounding factors, e.g., gender differences, obesity, race, alcoholism, using anti-hypertensive medication, etc. Chiang GSH et al., observed a strong association between nocturia and DM. However, as a majority of the measures that gathered by self-reporting, a recall bias is suspected [15]. Moon S et al., noted that obesity was significantly associated with nocturia, and independent of gender, age, hypertension, and DM. But, though the propensity score technique was carried out for adjusting the randomization influences between control and nocturia groups, some variables were omitted [16]. In a study by Hall SA et al., the use of calcium channel blocker medication among women of age less than 55 had a significant association with nocturia. However, there is lack of data on dosage, usage duration, or even compliance [17].

Co-morbidities of nocturia comprise additional co-occurring conditions such as hypertension, DM, kidney diseases, UTI, constipation, heart diseases, etc., [18]. Multiple precipitating factors like age, BMI, alcoholism, smoking, intake of coffee, spicy food, anxiety, depression, postmenopausal status also may contribute nocturia [19,20]. However, as can be seen, there are divided opinions on their association with nocturia. Therefore, the objective of this research, conducted in South India, is to: (i) establish the

association between nocturia and demographic variables such as age, gender, education, marital status, number of children, occupation, etc., (ii) establish the association between nocturia and co-morbidities such as hypertension, DM, cardiac disease, UTI, etc., and (iii) establish the association between nocturia and precipitating factors such as alcoholism, smoking, coffee intake, spicy food intake, etc.

MATERIALS AND METHODS

A descriptive cross-sectional design was used in this study to assess the co-morbidity (hypertension, DM, cardiac disease, UTI, Kidney disease, constipation and on medication) and precipitating factors (alcoholism, smoking, consumption of coffee, spicy food, anxiety, urinate before bedtime, use of diuretics, day time frequency, underwent surgeries) associated with nocturia among adults. Institutional Ethical Clearance and permission to conduct the study were obtained from the concerned authority (FMMCIEC/CCM./320/2018, NU/CEC/2017-2018/0170). The sample size was calculated for the group I (nocturia ≥ 2 voids) based on the prevalence (47%) and the attrition rate was considered as 10%. However, the prevalence 16% was considered for the group II with one episode of nocturia. The sample size estimation was done by using the formula:

$$\frac{Z \alpha^2 \times (p) * (1-p)}{e^2}$$

The study sample size consisted of 420 adults (Group I) and 206 adults (Group II). Both groups were recruited using purposive sampling.

Inclusion criteria:

Group I:

- Age: 35-65 years
- Nocturia ≥ 2 voids
- Attending the Departments of Urology and Gynaecology of two selected hospitals in Mangaluru (India)
- Able to communicate in English, Kannada or Malayalam,
- Selected based on the symptom not by the diagnosis.

Group II:

- Age: 35-65 years
- Nocturia only once at night
- Recruited from the general population of the same hospitals.

Exclusion criteria:

- Adults who were on urinary catheter
- Pregnant women
- Those who had neurogenic bladder.

After obtaining the informed consent, the data collection was done using a questionnaire which was developed by the researcher based on the review of literature and experts' opinion. The researcher interviewed the subjects to collect the baseline proforma in terms of age, gender, education, marital status, number of children, occupation, monthly income, diet and location of the toilet. Further the self-assessment tool was filled by the subjects which has two parts: (1) Co-morbidities of subjects with nocturia such as hypertension, DM, cardiac disease, UTI, Kidney disease, constipation and on medication; (2) Precipitating factors of nocturia which includes regular intake of alcoholism, smoking, consumption of coffee, spicy food, anxiety, urinate before bedtime, use of diuretics, day time frequency, underwent surgeries.

STATISTICAL ANALYSIS

The data was analysed using frequency, percentage, chi-square test, and logistic regression statistics using Statistical Package for the Social Sciences (SPSS) version 16.

RESULTS

First the association between nocturia and demographic variables were evaluated. A total of 222 (52.9%) subjects in Group I and 100 (48.5%) subjects in Group II were in the age group of 56-65 years. Group I comprised of 264 men and 156 women, and Group II of 112 men and 94 women. The results suggested that education, marital status, occupation, and monthly income were highly significant ($p < 0.001$) and number of children were significant ($p < 0.045$) in Group I and lesser so in Group II [Table/Fig-1].

Variables	Category	(Group I) n=420		(Group II) n=206		p-value
		f	%	f	%	
Age (Years)	35-45	85	20.2	47	22.8	0.581 ^{NS}
	46-55	113	26.9	59	28.6	
	56-65	222	52.9	100	48.5	
Gender	Male	264	62.9	112	54.4	0.052 ^{NS}
	Female	156	37.1	94	45.6	
Education	Primary	212	50.5	61	29.6	0.001 ^{**}
	High school	160	38.1	69	33.5	
	Higher secondary	20	4.8	19	9.2	
	Graduate	28	6.7	57	27.7	
Marital status	Single	14	3.3	20	9.7	0.001 ^{**}
	Married	406	96.7	186	90.3	
Number of children	Nil	25	6.0	24	11.7	0.045 [*]
	1	307	73.1	141	68.4	
	≥ 2	88	21.0	41	19.9	
Occupation	Unemployed	106	25.2	57	27.7	0.001 ^{**}
	Skilled (Tailor, driver, Painter etc.)	161	38.3	81	39.3	
	Unskilled (Daily wages, sweeper, peon, farm worker etc.)	114	27.1	25	12.1	
	Professional	39	9.3	43	20.9	
Monthly income (Rs.)	≤ 5000	18	4.3	7	3.4	0.001 ^{**}
	5001-10000	260	61.9	75	36.4	
	1001-15000	77	18.3	38	18.4	
	> 15000	65	15.5	86	41.7	
Diet	Vegetarian	43	10.2	13	6.3	0.106 ^{NS}
	Mixed	377	89.8	193	93.7	
Location of the toilet	Attached to bed room	155	36.9	74	35.9	0.567 ^{NS}
	Within the house	157	37.4	71	34.5	
	Outside the house	108	25.7	61	29.6	

[Table/Fig-1]: The association between nocturia and demographic variables among Group I and Group II subjects. (Not significant^{NS}, Significant^{*}, highly significant^{**}). (N=626), <0.05 significant, 0.001^{**} highly significant

Next the association between nocturia and co-morbidities was assessed. Among co-morbid diseases, UTI and constipation were highly significant ($p < 0.001$) and Group I with UTI had 7.98 times {OR 7.98 (CI 5.08-12.58)} and with constipation had 4.01 times {OR 4.01 (CI 2.73-5.89)} the risk for nocturia than Group II. However, Group I subjects with hypertension ($p < 0.025$) {OR 1.50 (CI 1.05-2.15)} and on medication for various diseases ($p < 0.031$) [OR 1.45 (CI 1.03-2.03)] showed significant difference compared with Group II subjects [Table/Fig-2].

Subsequently, the association between nocturia and precipitating factors was evaluated. Analysis of precipitating factors of nocturia reveals that the Group I subjects who consumed coffee and spicy food regularly, had anxiety, daytime frequency, and underwent various surgeries showed significant difference ($p < 0.001$) associated with higher of nocturia {OR 2.39 (CI 1.66-3.43)}, {OR 4.97 (CI 3.47-7.12)}, {OR 3.60 (CI 2.50-5.18)}, {OR 12.19 (CI 8.02-18.52)},

Variables	Category	(Group I) n=420		(Group II) n=206		Chi-square value	p-value	Odds ratio
		f	%	f	%			
Hypertension	No	255	60.7	144	69.9	5.020	0.025*	1.50 (1.05-2.15)
	Yes	165	39.3	62	30.1			
Diabetes mellitus	No	272	64.8	146	70.9	2.320	0.127 ^{NS}	1.32 (0.92-1.90)
	Yes	148	35.2	60	29.1			
Cardiac disease	No	378	90.0	188	91.3	0.254	0.614 ^{NS}	1.16 (0.65-2.07)
	Yes	42	10.0	18	8.7			
Urinary tract infection	No	195	46.4	180	87.4	80.574	<0.001**	7.98 (5.08-12.58)
	Yes	225	53.6	26	12.6			
Kidney diseases	No	390	92.9	191	92.7	0.004	0.950 ^{NS}	0.98 (0.52-1.86)
	Yes	30	7.1	15	7.3			
Constipation	No	201	47.9	162	78.6	50.201	<0.001**	4.01 (2.73-5.89)
	Yes	219	52.1	44	21.4			
On medication	No	202	48.1	118	57.3	4.650	0.031*	1.45 (1.03-2.03)
	Yes	218	51.9	88	42.7			

[Table/Fig-2]: Association between nocturia and co-morbidities among Group I and Group II subjects (Not significant^{NS}, Significant*, Highly significant**). (N=626), <0.05 significant, 0.001** highly significant

{OR 3.22 (CI 2.16-4.81)}, respectively, compared with Group II subjects [Table/Fig-3].

DISCUSSION

The study showed statistically high significant association of nocturia with baseline characteristics such as education, marital status, occupation, monthly income and significant association with gender and number of children. This result is consistent with a study by Coyne KS et al., on prevalence of nocturia and its effect on health-related quality of life and sleep in a community sample in the USA in which a significant relationship was found between nocturia and marital status and education [21]. van Dijk L et al., observed in their study that the prevalence rate of nocturia in women was 7% higher than in men. This difference of nocturia onset between genders reduces with age [22]. They also noted that women appear to develop nocturia in a more gradual manner than do men over their lives. Another study by Coyne KS et al., on the impact of Overactive Bladder (OAB), incontinence and other LUTS on quality of life showed that OAB has significant association with marital status and education [23].

The study observed that marital status significantly associates with nocturia. In this connection, Shiri R et al., observed that widowers, divorcees, or single people are at more risk for nocturia compared to those living with their partners [24]. Johnson TM et al., concluded that married people are less likely to indulge in negative health traits, e.g., heavy smoking, drinking, physical inactivity etc., than those who are single [25]. Tudiver F et al., noted that in widowers or divorcees, disturbed sleep and psychological/psychosocial issues were more prevalent than in married males [26].

The risk of nocturia was significantly more among Group I subjects with UTI, constipation, hypertension, and those on medication for various diseases compared to Group II subjects. The finding of present study is consistent with the results of Coyne et al which identified that OAB has a high significance with high blood pressure [23].

It is seen that the hypertension is a significant co-morbidity for risk of nocturia. Hypertension and nocturia could be associated because of their influences on tubular transportation and glomerular filtration. The kidney's role in the hypertension pathogenesis has been supported by experiments indicating a positive association

Variables	Category	(Group I) n=420		(Group II) n=206		Chi-square value	p-value	Odds ratio
		f	%	f	%			
Alcoholism	No	296	70.5	157	76.2	2.267	0.131 ^{NS}	1.34 (0.92-1.97)
	Yes	124	29.5	49	23.8			
Smoking	No	305	72.6	160	77.7	1.840	0.174 ^{NS}	1.31 (0.89-1.94)
	Yes	115	27.4	46	22.3			
Coffee	No	222	52.9	150	72.8	22.255	<0.001**	2.39 (1.66-3.43)
	Yes	198	47.1	56	27.2			
Spicy food	No	95	22.6	122	59.2	76.253	<0.001**	4.97 (3.47-7.12)
	Yes	325	77.4	84	40.8			
Anxiety	No	82	19.5	96	46.6	47.283	<0.001**	3.60 (2.50-5.18)
	Yes	338	80.5	110	53.4			
Urinate before bedtime	No	76	18.1	44	21.4	0.948	0.330 ^{NS}	1.23 (0.81-1.86)
	Yes	344	81.9	162	78.6			
Use of diuretics	No	390	92.9	197	95.6	1.549	0.209 ^{NS}	1.63 (0.76-3.51)
	Yes	30	7.1	9	4.4			
Day time frequency	No	117	27.9	170	82.5	137.366	<0.001**	12.19 (8.02-18.52)
	Yes	303	72.1	36	17.5			
Underwent surgeries	No	243	57.9	168	81.6	32.537	<0.001**	3.22 (2.16-4.81)
	Yes	177	42.1	38	18.4			

[Table/Fig-3]: Association between nocturia and Precipitating factors between Group I and Group II subjects. (Not significant^{NS}, Significant*, Highly significant**). (N=626)

between blood pressure levels and renal sodium excretion [27]. Further, a few studies have noted that some younger to middle aged patients who were in the first stage of essential hypertension had issues of glomerular hyper filtration [28,29]. Hypertension might also be present along with peripheral oedema, the nocturnal re-absorption of which causes higher urine volume. Yet another association between nocturia and hypertension is obstructive sleep apnea that is linked with blood pressure elevation and obesity [30]. Those on medication, according to the results, were at significant risk for nocturia. In this regard, Asplund R observed that the use of diuretics caused a big increase in nocturia in patients of both sexes [4]. According to the study, this high prevalence may be a result of taking the medication in the mornings. In such cases, the diuretics dosage requires adjustment in accordance with its pharmacokinetics. Reynard JM et al., noted that taking diuretic medication six hours prior to bedtime substantially reduced nocturia [31]. Beta-blockers reduce the capacity of bladders and could cause nocturia when ingested just prior to bedtime [32]. Thus, inappropriate timing of medications may lead to nocturia or aggravate it.

The results on the precipitating factors of nocturia reveal that the Group I subjects who took coffee and spicy food regularly, had anxiety and daytime frequency, and had undergone various surgeries showed significant difference associated with increased risk of nocturia compared with Group II subjects. These findings are supported by a study conducted in US among men and women which observed that caffeine intake was significantly associated with urinary incontinence [33]. Another study by Gleason JL et al., assessed the relationship between the intake of caffeine and urinary incontinence among women in the US and concluded that the association was significant [34]. Contrastingly, in other studies, coffee consumption was not associated with nocturia in both male and female subjects, as observed in cohort studies [24,35]. However, a large cross-sectional research in Sweden observed that women having nocturia were less inclined to drink coffee in the evenings, which may not be the case in South India [36].

The study findings point to anxiety being a precipitating factor for nocturia. Even though the precise mechanism which explains an association between anxiety, depression, and nocturia is not known, a few shared patho-physiological pathways might be considered. Depressed individuals have more of antidiuretic hormones compared to healthy people [37]. But, these patients lack a normal increase in the level of the hormones. As a result, the loss of cycle of circulating hormones could cause nocturia [36]. This abnormality is a typical mechanism of night-time polyuria in older people, too [38].

It is, therefore, seen that nocturia is not a stand-alone symptom, but is generally combined with co-morbidities and medication use, implying that patients presenting with nocturia will perhaps be ones who are familiar to their doctor owing to their previous complaints. This is significant, since nocturia affects sleep, resulting in poorer quality of life [21]. Hence, doctors need to routinely examine patients presenting with sleep disorders for nocturia.

Limitation(s)

The study focused only on the presence or absence of the co-morbidities and precipitating factors of subjects with nocturia. It was self-reported and conducted by the hospital based survey. Community based study can be replicated. Another limitation was, the cross-sectional nature of the study limited to only two selected hospitals.

CONCLUSION(S)

The results suggested that education, marital status, occupation, and monthly income were highly significant and number of children were significantly associated with nocturia. The association of nocturia and co-morbidities UTI and constipation were highly significant,

while hypertension and taking medications were observed to be significant. The association between nocturia and precipitating factors 'regular coffee and spicy food intake', 'anxiety', 'daytime frequency', and 'various surgeries' was seen to be significant. Thus, the study observes a significant association between nocturia and many coexisting factors suggesting that multiple approaches are necessary in the management of adults with nocturia. The underlying causes of nocturia need to be addressed appropriately while deciding the treatment modalities. The awareness of these factors can help the healthcare professionals to attend to the primary prevention of nocturia.

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