

# The Etiologic Classification of Nocturia among 133 Thai Patients in a Tertiary Teaching Hospital

Supanat Sirikulchayanonta, Sompol Permpongkosol\*

Division of Urology, Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand  
Email: \*sompolpermpong@gmail.com

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## ABSTRACT

**Introduction:** Nocturia is categorized into many categories. Each category requires different approaches and treatment. We aimed to obtain data regarding nocturia, classified into categories according to its pathogenesis, in Thai patients. **Methods:** We reviewed 133 medical records and voiding diaries of the patients who attended a urologic clinic in a tertiary teaching hospital during year 2009-2010 with nocturia problems. Those data were analyzed to sort these nocturia patients into the appropriate categories. **Results:** There were a total of 133 patients, consisting of 94 males (70.1%) and 39 females (29.9%). Overall mean age was  $64.74 \pm 25.85$  years. There was no statistically difference between the two genders (Male  $65.94 \pm 24.56$  years vs Female  $61.87 \pm 28.24$  years,  $p = 0.10$ ). Among these, 71 patients (53.4%) had nocturnal polyuria. Almost all patients (132 patients, 99.2%) met the criteria for diminished global/nocturnal bladder capacity. The younger patients (less than 40 years) were found to have more severe clinical symptoms than the older patients (6 from 8 or 75% vs 46 from 125 or 36%,  $p = 0.032$ ). Seventy patients (52.6%) met the criteria of Mixed NP and Diminished. There were 32 patients (24.1%) found in the group of Global polyuria. Only one patient was classified as isolated nocturnal polyuria and none as isolated global polyuria. **Conclusion:** Nocturnal polyuria and global polyuria are not uncommon conditions and most of these patients might have concomitant diminished bladder capacity for which investigation or simultaneous treatment may be needed to gain the best treatment result.

**Keywords:** Nocturia; Prevalence; Etiology; Classification; Sleep Disorders

## 1. Introduction

Nocturia, according to International continence society 2002, was defined as the complaint forcing an individual to wake at night one or more times to void [1]. It is one of the most common complaints in urological practice [2, 3]. With overall prevalence 11% - 33.5% in various population studies [4-8] and 58.5% among older adults, [9] patients are affected by worsening health, sleep deprivation, poor quality of life, dissatisfaction with work and even unexpected accidents [5,10-15]. In the past, most patients who presented with nocturia were diagnosed and treated for bladder outlet obstruction (BOO) and overactive bladder (OAB); some of them did not respond to the treatment. Later on, after the pathogenesis of nocturia was better clarified, nocturia was then classified into 4 main categories [1,16,17]: 1) Nocturnal polyuria, 2) Diminished nocturnal and/or global bladder capacity, 3) Global polyuria 4) Mixed nocturnal polyuria and diminished nocturnal and/or global bladder capacity [1,16]. However, for individual cases, more than one of these etiologies might be involved [17]. This classification

helped urologists to precisely diagnose nocturia and delineate it according to its pathogenesis which should lead to more appropriate treatment.

There are some prevalent studies in nocturia in Asian countries using questionnaires but these did not represent data according to the classifications listed above [4,18, 19]. At present, in Thailand, as well as in other South East Asian countries, to the best of our knowledge, there has been no specific data regarding nocturia. It seemed that the previous researchers focused on the diseases related to nocturia such as OAB or BPH rather than the nocturia per se. This particular study aimed to obtain data regarding nocturia in Thai patients. This may be helpful in making precise diagnosis of nocturia and providing rational treatment as well as minimizing the unnecessary or overtreatment for BOO, OAB.

## 2. Materials and Methods

We reviewed 133 medical records and voiding diaries of the patients who attended a urologic clinic in the Faculty of Medicine, Ramathibodi Hospital, Mahidol University during the years 2009-2010 with pure nocturia problems regardless the duration of their nocturia. All patients were

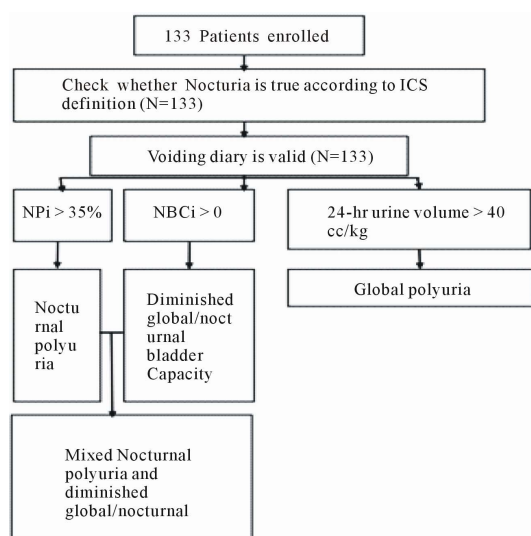
\*Corresponding author.

checked as to whether their complaints were true nocturia according to the ICS 2002 definition [1] which was mentioned earlier. The inclusion criteria were that each participant had at least a 3-day valid voiding record. No specific age group was intended to be excluded from our study. Patients who had other significant urologic complaints beside nocturia (e.g. pyuria, gross hematuria, dysuria) or previously known pathology (e.g. stone, recurrent UTI, urothelial carcinoma) were excluded from the study. Then, 24 h-void volume (24 h.V), maximal void volume (MVV), night voids and nocturnal urine volume (NUV) were recorded. Arithmetic means of these data were calculated using the formulae in **Table 1**. Each nocturia category was determined according to the flowchart in **Figure 1**. All values are presented as means  $\pm$  standard deviation. Independent t-test was used to compare the two groups. Pearson's Chi-square test was used as a test of independence between two groups. All tests were 2-sided, and p values  $< 0.05$  were considered statistically significant. All obtained data were statistically analyzed using IBM®SPSS® statistics version 20.

**Table 1. Formula used for categorize the patients.**

Formula	Analysis
$N_i = NUV/MVV$	If $N_i$ is $>1$ , nocturia is due to NUV exceeding MVV
$NP_i = NUV/24\text{ h.V}$	If $NP_i$ is $>25\%$ , the diagnosis is nocturnal polyuria
$NBC_i = ANV - PNV$ ( $PNV = N_i - 1$ )	If $NBC_i$ is $>0$ , nocturia occurs at volumes $<MVV$

24 h.V = 24 hour urine volume; ANV = actual number of nightly voids; MVV = maximum voided volume;  $NBC_i$  = nocturnal bladder capacity index;  $N_i$  = nocturnal index;  $NP_i$  = nocturnal polyuria index; NUV = nocturnal urine volume; PNV = predicted number of nightly voids; Adapted from New aspects of the classification of nocturia and polyuria [27].



**Figure 1. Flow chart showing processes starting from enrollment of cases and algorithm for categorization of cases according to etiologic groups.**

### 3. Results

All of the 133 reviewed cases fulfilled the inclusion criteria. There were a total of 133 patients, consisting of 94 males (70.1%) and 39 females (29.9%). Overall mean age was  $64.74 \pm 25.85$  years. There was no statistically significant difference between the two genders. (Male  $65.94 \pm 24.56$  years vs. Female  $61.87 \pm 28.24$  years,  $p = 0.10$ ). Overall mean weight was  $62.86 \pm 20.66$  kg. Male weight was significantly greater (Male  $64.73 \pm 19.62$  kg vs. Female  $58.33 \pm 20.52$  kg,  $p = 0.001$ ).

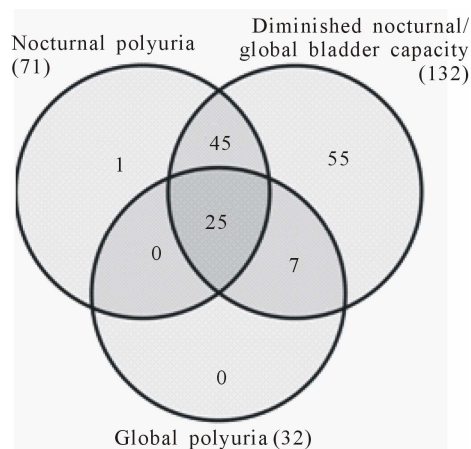
Among these, 71 patients (53.4%) met the criteria for nocturnal polyuria and there were no statistically significant differences between any age groups or the two genders [Male 54.3% vs female 51.3% ( $p = 0.754$ )].

There were 132 patients (99.2%) who met the criteria for diminished global/nocturnal bladder capacity. No differences between gender or age groups were noted but the proportion of younger patients (less than 40 years) was found to be significantly greater than the that of older patients among the severe group (6 from 8 or 75% vs. 46 from 125 or 36%,  $p = 0.032$ ). Seventy patients (52.6%) met the criteria of Mixed NP and Diminished NBC and showed no significant differences between sex and age groups. **Tables 2 and 3** show a comparison of the data between groups. **Figure 2** represents overlapping between the nocturia categories.

There were 32 patients (24.1%) classified in the group for Global polyuria; no significant sex difference was found [22.3% vs 28.2% ( $p = 0.471$ )]. But a significant number of cases were found in the younger group (less than 40 years old) compared to the older group (5 from 8 vs 27 from 125,  $p = 0.009$ ). Only one patient was classified as suffering from isolated nocturnal polyuria and none as isolated global polyuria.

### 4. Discussion

Nocturia is one of the most common urologic complaints.



**Figure 2. Overlapping between the nocturia categories.**

**Table 2. Comparison among each category of nocturia and gender.**

Categories of Nocturia	Male	Female	Total
Nocturnal polyuria	51 (54.3%)	20 (51.3%)	71 (53.4%, p = 0.75)
Diminished global/nocturnal bladder capacity	93 (98.9%)	39 (100%)	132 (99.2%, p = 0.52)
Severe (NBCi > 2)	37 (61.3%)	15 (38.5%)	52 (39.4%, p = 0.92)
Global polyuria	21 (22.3%)	11 (28.2%)	32 (24.1%, p = 0.47)
Mixed Nocturnal polyuria and Diminished global/nocturnal bladder capacity	50 (53.2%)	20 (51.3%)	70 (52.6%, p = 0.84)
Total patients	94 (70.7%)	39 (29.3%)	133 (100%)

**Table 3. Comparison among each category of nocturia and the age group.**

Categories of Nocturia	Age group					
	<40	40 - 50	51 - 60	61 - 70	71 - 80	>80
Nocturnal polyuria (71)	6 (75%)	4 (50%)	17 (52%)	14 (45.2%)	23 (59%)	7 (50%)
Diminished global/ nocturnal bladder capacity (132)	8 (100%)	8 (100%)	33 (100%)	31 (100%)	39 (100%)	13 (92.8%)
Severe (NBCi > 2) (52)	6 (75%)	1 (12.5%)	15 (45.5%)	11 (35.5%)	13 (33.3%)	6 (42.9%)
Global polyuria (32)	5 (62.5%)	0 (0%)	10 (30.3%)	3 (9.7%)	13 (33.3%)	1 (7.2%)
Mixed Nocturnal polyuria and Diminished global/nocturnal bladder capacity (70)	6 (75%)	4 (50%)	17 (51.5%)	14 (45.2%)	23 (59%)	6 (42.9%)
Total patients (133)	8	8	33	31	39	14

It leads to many adverse sequelae including daytime fatigue, attention deficit, emotional disorder, memory problems, etc. [4-9]. According to many studies, there is greater prevalence of nocturia in elderly patients [20-23]. That is consistent with our study; only 12% of the nocturia patients in this study were less than 50 years of age. Most nocturia patients (99.2%) had diminished global/nocturnal bladder capacity. This indicates nocturnal urine volume that exceeds maximal function capacity of the bladder. It may represent some bladder pathology including bladder outlet obstruction, stones, tumors, OAB, etc. The urologist should keep in mind when any nocturia treatment is given and the condition is not improved, further investigation should be considered [1]. Also, from our study, it may be assumed that treatment of nocturnal polyuria by using only antidiuretics may not be adequate because most of these patients also had concomitant diminished global/nocturnal bladder capacity for which simultaneous treatment of the latter may be needed. On the other hand, nocturia patients for whom bladder outlet obstruction or OAB treatment is initiated may not be fully improved because of occult nocturnal polyuria.

Nocturia is a condition thought to be due to the impairment of the ADH secretion circadian pattern during sleep. Elderly plasma ADH decrease during sleep [24] leads us to hypothesize that nocturnal polyuria is commonly found

in the elderly. Since our study did not show any difference among age groups this might imply that there might be other factors besides nocturnal ADH secretion impairment that play a role in nocturnal polyuria pathogenesis.

In 1998, Weiss *et al.* studied 200 nocturia patients and found 7% were categorized as isolated nocturnal polyuria whereas our study found only 0.75%. They also reported 36% of those patients were categorized as Mixed Nocturnal polyuria and diminished global/nocturnal bladder capacity while this category amounted to 52.6% in our present study [25]. The discrepancies might be due to the differences in inclusion criteria of nocturia. Most researchers choose to define nocturia in their study as 2 or more nocturnal voids. In view of evidence that most people with less than 2 voids nightly generally experience only minimal bother from the condition [17], but we decided to use a single nocturnal void as our nocturia definition because we believe these patients certainly face the problem of nocturia, otherwise, they would not come to see a urologist. Study methodology [26], and probably race and socioeconomic factors may also have contributed to the different results.

Moreover, focusing on the patients who had NBCi > 2, which indicates severe diminished global/nocturnal bladder capacity [16], there were 39.4%. And a more significant proportion was shown in younger patients (less

than 40 years old). These data might suggest that urologists should treat conditions that may cause diminished global/nocturnal bladder capacity in young patients prior to treating for existing nocturnal polyuria, because it could be the primary component of their nocturia.

Global polyuria is considered when patient's urine output exceeds 40-ml/kg bodyweight during a 24-hour period, which is mostly due to non-urologic condition. Medical workup needs to be done for diagnosis and medical referral is necessary [27]. There were 24.1% of our patients who met such criteria and this was comparable to Weiss' study which found 23% [25].

None of patients who met the criteria of global polyuria had isolated polyuria. This might indicate that only medical referral is inadequate in the treatment of polyuria because these patients always have concomitant urologic conditions. Data from the present study might not represent the prevalence of nocturia in the general population since it was obtained from cases who presented to our clinic with problems of nocturia, which more or less affected their quality of life. From Chen's study, only 13% of nocturia patients come to see a physician [28]. There could be many more patients whose qualities of life were not disturbed and so were not included.

Collecting data from overall population would be significantly beneficial to urologists, in terms of both the statistical and clinical aspects. But it is difficult to practically achieve. However, the data from the present study might represent patients who should receive treatment and we may be able to use these data to make presumptive diagnoses, suggest guidelines for investigations and provide appropriate treatment.

For our future project, we intend to conduct a prospective multicenter study to find reliable data on the prevalence of each classification of nocturia in Thailand. We believe that the reliable prevalence of each category of nocturia should have major impact upon the change of the nocturia treatment paradigm and lead to minimize unnecessary treatment.

#### 4. Conclusion

Nocturia is classified into many categories according to its pathogenesis. Each category has different approaches and treatment. Among them, nocturnal polyuria and global polyuria are not uncommon conditions, and most of these patients might have concomitant diminished bladder capacity, for which investigation or simultaneous treatment may be needed to gain the best treatment result.

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