

Sleep quality and obstructive sleep apnea among male patients with lower urinary tract symptoms: A prospective observational study

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ABSTRACT

Introduction: Apart from nocturia, few reports have been published on the relationship between lower urinary tract symptoms (LUTS) and sleep disturbances in patients visiting urology outpatient clinics. This study assessed the association between our population's LUTS and sleep disturbances.

Methods: This was a prospective observational study. A total of 123 male patients with a history of LUTS aged more than 40 years were recruited from urology outpatient clinic. International Prostate Symptom Score was utilized to assess LUTS. To determine the quality of sleep, the Pittsburgh Sleep Quality Index (PSQI) was used. Berlin questionnaire (BQ) was used for screening obstructive sleep apnea.

Results: A total of 123 participants were enrolled in this study. The mean age of the participants was 61 ± 11.1 years. Nocturia >3 episodes were significantly more in patients with PSQI >5 ($P < 0.05$). There was a greater prevalence of severe LUTS in patients with PSQI >5 ($P < 0.05$). The association between LUTS and BQ score showed an increased prevalence of severe symptoms in patients with high BQ. Patients with PSQI >5 had more severe LUTS (53% of patients) compared to patients with PSQI ≤ 5 (5% of patients) ($P = 0.000$). Patients with PSQI >5 had overall poorer quality of life (QOL) scores, with QOL being 5 and 6 in 18% and 4.8% of the patients, respectively.

Conclusions: There is a significant association between the prevalence of nocturia, moderate-to-severe LUTS, and the existence of sleep disorders. Therefore, screening for sleep disturbances may be performed on male patients who present with LUTS.

INTRODUCTION

The prevalence of lower urinary tract symptoms (LUTS) increases with age, with 80% of men experiencing some symptoms by age 80 years.^[1] Although pharmacological therapies for LUTS have been regarded as first-line therapy, only 29% of patients receive these medications for 1 year. The fact that most LUTS medications are designed to treat bladder outlet obstruction caused by prostatic enlargement, whereas LUTS is multifactorial and not usually concentrated on the prostate, is one

of the reasons why pharmacological therapy may not be effective for many men.^[2] It is now evident that several other factors, including ageing, diabetes, obesity, psychological or behavioral changes, and sleep disturbances, contribute to the development and progression of LUTS.^[3]

It has been demonstrated that sleep disturbances play a significant role in the development of nocturia, which is defined as more than one night-time void. The relationship

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is probably two way. Frequent nocturia is connected with sleep disturbances because men awaken more frequently to urinate at night.^[4] Alternately, sleep disturbances may awaken patients at night, prompting them to urinate more frequently.^[4] Regardless of the direction of causation, the two illnesses are connected with daytime exhaustion, a worse sense of well-being, a higher incidence of comorbidities such as depression, cardiovascular disease, and diabetes, and possibly an increased risk of death.^[4,5]

Most studies of the relationship between LUTS and sleep disturbances are done in the Western population. Few reports have been published on the relationship between LUTS and sleep disorders in patients visiting urology outpatient, except for nocturia.^[6,7] This study aimed to assess the association between LUTS and sleep disturbances in our population. We hypothesize that men with sleep disturbances are at increased risk of nocturia and other LUTSs.

MATERIALS AND METHODS

This was a prospective observational study conducted in the department of urology of a teaching center for 24 months (July 2020 to July 2022). Our institutional ethics committee approved the protocol, and it conforms to the provisions of the Declaration of Helsinki in 1995. Male patients presenting with a history of LUTS aged more than 40 years were recruited from the urology outpatient department during the study after obtaining written informed consent. However, patients who had a known case of prostate cancer, bladder cancer, prior surgery to either organ, urethral stricture disease, urinary tract infection, or patients taking medications (e.g., diuretics, dopaminergic medication, antipsychotics, and hypnotics) were excluded.

International Prostate Symptom Score (IPSS) was utilized to assess LUTS.^[8] The IPSS is a seven-item written screening instrument to detect and monitor the symptoms of benign prostatic enlargement and a variety of other disorders. Seven symptom questions pertain to the urinary system. They include symptoms of inadequate bladder emptying, frequency of urination during the day, intermittency of urination, the urge to urinate, a weak urine stream, straining, and nocturia. These questions pertained to the previous month, with each question receiving a score from 1 to 5 for up to 35 total points. The eighth question is on quality of life (QOL).^[8]

To analyze the correlation between sleep disturbances and LUTS, the patients' QOL was graded according to their current level of satisfaction (0, extremely satisfied; 1, satisfied; 2, largely satisfied; 3, uncertain; 4, slightly unhappy; 5, dissatisfied; and 6, very dissatisfied).^[8]

Pittsburgh Sleep Quality Index (PSQI) was used to assess sleep quality.^[9] It consists of 19 self-rated questions and 5-bed

partner or roommate-rated questions (if one is available). Only questions that are self-rated are included in the scoring. There are seven "component" scores ranging from 0 to 3 points and are derived from the 19 self-rated items. A number of "0" implies no difficulty, whereas a value of "3" denotes extreme difficulty. The sum of the seven component scores yields a "global" score ranging from 0 to 21 points, with 0 indicating no difficulty and 21 indicating serious difficulties in all areas.^[9] The poor and good sleep quality cutoff was taken as 5. Patients with PSQI ≤ 5 were said to have good sleep quality.^[9]

The Berlin Questionnaire (BQ) was used to screen obstructive sleep apnea.^[10] The questionnaire consists of three sections regarding sleep apnea risk. Patients can be classified as high risk or low risk based on their replies to the individual items and their total scores in the symptom categories.^[10]

After collecting demographic and clinical data, LUTS was assessed using the IPSS questionnaire. Patients were requested to fill a voiding diary for 48 h to differentiate between nocturia, nocturnal polyuria, and global polyuria. Screening of obstructive sleep apnea was done using a BQ. Sleep quality was assessed using the Hindi version of the PSQI. Patients found positive for any sleep disorders were enrolled in the sleep clinic.

Data analysis was conducted with IBM SPSS Statistics version 23 for Windows, Armonk, NY: IBM Corp, 2013.^[11] The values were expressed in mean \pm standard deviation as data had a normal distribution. Categorical variables were compared using the Chi-square analysis, and numerical variables were compared using an independent sample *t*-test. Statistical significance was considered when $P < 0.05$.

RESULTS

A total of 123 participants were enrolled in this study. The mean age of the participants was 61 ± 11.1 years. The mean body mass index was 24.16 ± 3.95 kg/m². Table 1 shows the characteristics of patients with PSQI scores below or above 5, indicating good or poor sleep quality.

Sleep quality and lower urinary tract symptoms

Patients with poor sleep quality had a significantly higher prevalence of nocturia (>3 episodes per night), nocturnal polyuria, nocturnal voided volume, and nocturnal voided volume/total voided volume (all $P < 0.05$). Table 2 and Supplementary Figure 1 show the association between sleep quality and LUTS. Patients with poor sleep quality had a significantly higher prevalence of severe LUTS than those with good sleep quality ($P < 0.05$). However, the two groups had no significant difference in quality-of-life scores.

Obstructive sleep apnea and lower urinary tract symptoms

Table 3 presents the association between various factors and low- or high-risk scores on the BQ. Patients with

Table 1: Patient characteristics and association of various factors with Pittsburgh Sleep Quality Index

| Factors | Overall | Good sleepers (PSQI ≤5) (n=40), n (%) | Poor sleepers (PSQI >5) (n=83), n (%) | P |
|------------------------|--------------|---------------------------------------|---------------------------------------|--------|
| Age (years), mean±SD | 61.06±11.11 | 59.8±11.4 | 61.6±11 | 0.40 |
| Height (cm), mean±SD | 165.05±7.14 | 165.7±8.3 | 164.7±6.5 | 0.44 |
| Weight (kg), mean±SD | 65.8±10.7 | 64.9±9.9 | 66.2±11.2 | 0.53 |
| Smoker | 26 | 10 (25) | 16 (19.3) | 0.466 |
| Alcoholic | 21 | 9 (22.5) | 12 (14.4) | 0.267 |
| ED | 11 | 3 (7.5) | 8 (9) | 0.697 |
| DM | 17 | 5 (12.5) | 12 (14.4) | 0.768 |
| HTN | 25 | 6 (15) | 19 (22.9) | 0.308 |
| COPD | 9 | 1 (2) | 8 (9) | 0.154 |
| Prostate size, mean±SD | 44.59±11.4 | 43.2±11.3 | 45.2±11.5 | 0.36 |
| PVR, mean±SD | 31.7±18.07 | 28±19 | 33.4±17.4 | 0.12 |
| Q avg, mean±SD | 7.76±3.26 | 8.3±3.3 | 7.4±3.1 | 0.16 |
| Q max, mean±SD | 14.53±4.85 | 15.4±5 | 14.1±4.7 | 0.16 |
| Voided volume, mean±SD | 235.55±83.07 | 231.7±60.4 | 237±92 | 0.72 |
| Nocturia ≤3 | 90 | 38 (95) | 52 (62.6) | <0.001 |
| Nocturia >3 | 33 | 2 (5) | 31 (37.7) | |
| Presence of NP | 22 | 1 (2) | 21 (25.3) | 0.002 |
| NVV, mean±SD | 373.66±141.2 | 286.8±102 | 415.5±138.8 | <0.001 |
| NVV/TVV, mean±SD | 22.46±8.63 | 16.6±5.8 | 25.2±8.3 | <0.001 |
| DTF | 8 (7-12) | 8 (7-10) | 8 (7-12) | 0.532 |
| Output/kg, mean±SD | 26.44±5.98 | 27.6±6.3 | 25.8±5.7 | 0.13 |
| FBC (mL), mean±SD | 258.82±42 | 260±39.4 | 258.2±43.4 | 0.83 |
| PSA (ng/mL), mean±SD | 2.09±1.30 | 1.8±1.14 | 2.23±1.36 | 0.09 |
| Storage IPSS | | 6±2 | 8±3 | 0.00 |
| Voiding IPSS | | 9±3 | 11±3 | 0.05 |

Alcoholic was defined using "At risk drinking" criteria of The National Institute on Alcohol Abuse and Alcoholism criteria (USA). ED=Erectile dysfunction, DM=Diabetes mellitus, HTN=Hypertension, COPD=Chronic obstructive pulmonary disease, PVR=Post void residue, Q avg=Average flow rate, Q max=Maximum flow rate, NP=Nocturnal polyuria, NV=Nocturnal volume, NVV/TVV=Nocturnal voided volume/total voided volume, FBC=Functional bladder capacity, PSA=Prostate-specific antigen, DTF=Day time frequency, IPSS=International Prostate Symptom Score, PAQI=Pittsburgh Sleep Quality Index, SD=Standard deviation

Table 2: Prevalence and association of lower urinary tract symptoms and quality of life score in patients with less than five and greater than five Pittsburgh Sleep Quality Index

| Factors | PSQI ≤5 (n=40), n (%) | PSQI >5 (n=83), n (%) | P |
|----------|-----------------------|-----------------------|--------|
| IPSS | | | |
| Mild | 3 (7.5) | 0 | <0.001 |
| Moderate | 35 (87.5) | 39 (46.9) | |
| Severe | 2 (5) | 44 (53) | |
| QOL | | | 0.300 |
| 1 | 0 | 1 (1.2) | |
| 2 | 6 (15) | 7 (8.4) | |
| 3 | 11 (27.5) | 18 (21.6) | |
| 4 | 20 (50) | 38 (45.7) | |
| 5 | 3 (7.5) | 15 (18) | |
| 6 | 0 | 4 (4.8) | |

IPSS=International Prostate Symptom Score, QOL=Quality of life, PAQI=Pittsburgh Sleep Quality Index

high-risk BQ scores had significantly higher nocturnal polyuria, nocturnal voided volume, and nocturnal voided volume/total voided volume ($P < 0.05$). Table 4 Supplementary Figure 2 and show the prevalence and association of LUTS and QOL score in patients with low- and high-risk BQ scores. Patients with high-risk BQ scores had a significantly higher prevalence of severe LUTS than those with low-risk BQ scores ($P < 0.05$). However, the two groups had no significant difference in quality-of-life scores.

International Prostate Symptom Score and quality of life

A total of 53% of patients in the poor sleep quality group (PSQI >5) had severe category IPSS scores compared to 5% of patients in the good sleep quality group (PSQI ≤5) ($P = 0.000$). Patients with poor sleep quality also had overall poorer QOL scores, with 18% and 4.8% of patients reporting QOL scores of 5 and 6, respectively. In contrast, there were no cases of QOL score 6 in patients with good sleep quality. Patients with high-risk BQ scores had significantly higher IPSS scores and a much higher prevalence of moderate-to-severe LUTS compared to those with low-risk BQ scores ($P < 0.05$). Although there was no significant difference in quality-of-life scores, a higher proportion of patients with high-risk BQ scores reported a QOL score of 6 compared to those with low-risk BQ scores (4.7% vs. 0).

The IPSS subscores were also analyzed, as given in Tables 1 and 3. Poor sleepers had higher storage and voiding LUTS ($P = 0.05$). Patients with high-risk BQ scores also had higher storage and voiding IPSS ($P = 0.00$).

Our findings suggest that poor sleep quality and obstructive sleep apnea are associated with a higher prevalence of LUTS, particularly nocturia, and poorer QOL among male patients.

| Factors | Low risk BQ (n=39), n (%) | High risk BQ (n=84), n (%) | P |
|------------------------|---------------------------|----------------------------|-------|
| Age (years), mean±SD | 60.9±11.6 | 61.1±10.9 | 0.92 |
| Height (cm), mean±SD | 164.7±8 | 165.1±6.7 | 0.75 |
| Weight (kg), mean±SD | 65.2±9.7 | 66.1±11.2 | 0.68 |
| Smoker | 11 (42.3) | 15 (57.7) | 0.466 |
| Alcoholic | 9 (42.9) | 12 (57.1) | 0.228 |
| ED | 2 (18.2) | 9 (81.8) | 0.312 |
| DM | 5 (29.4) | 12 (70.6) | 0.827 |
| HTN | 6 (24) | 19 (76) | 0.354 |
| COPD | 1 (11.1) | 8 (88.9) | 0.168 |
| Prostate size, mean±SD | 43.7±10.6 | 44.9±11.8 | 0.58 |
| PVR, mean±SD | 29.6±20.2 | 32.6±17 | 0.40 |
| Q avg, mean±SD | 8±3.2 | 7.6±3.2 | 0.51 |
| Q max, mean±SD | 15.2±4.9 | 14.1±4.7 | 0.25 |
| Voided volume, mean±SD | 247.4±94.4 | 230±77.2 | 0.27 |
| Nocturia >3 | 3 (9.1) | 30 (90.9) | 0.001 |
| Presence of NP | 3 (13.6) | 19 (86.4) | 0.044 |
| NVV, mean±SD | 317.4±127.6 | 399.7±140.2 | 0.02 |
| NVV/TVV, mean±SD | 18.6±7.7 | 24.2±8.5 | 0.01 |
| DTF | 8 (7-12) | 8 (7-12) | 0.58 |
| Output/kg, mean±SD | 27±5.2 | 26.1±6.3 | 0.43 |
| FBC (mL), mean±SD | 258.7±44 | 258.8±41 | 0.98 |
| PSA (ng/mL), mean±SD | 1.88±1.23 | 2.19±1.33 | 0.22 |
| Storage IPSS, mean±SD | 6±3 | 8±3 | 0.01 |
| Voiding IPSS, mean±SD | 9±3 | 11±3 | 0.01 |

Alcoholic was defined using "At risk drinking" criteria of The National Institute on Alcohol Abuse and Alcoholism criteria (USA). ED=Erectile dysfunction, DM=Diabetes mellitus, HTN=Hypertension, COPD=Chronic obstructive pulmonary disease, PVR=Post void residue, Q avg=Average flow rate, Q max=Maximum flow rate, NP=Nocturnal polyuria, NV=Nocturnal volume, NVV/TVV=Nocturnal voided volume/total voided volume, FBC=Functional bladder capacity, PSA=Prostate-specific antigen, DTF=Day time frequency, IPSS=International Prostate Symptom Score, PAQI=Pittsburgh Sleep Quality Index, SD=Standard deviation

Table 4: Prevalence and association of lower urinary tract symptoms and quality of life score in patients with low and high risk in Berlin questionnaire

| Factors | BQ - low risk (n=39), n (%) | BQ - high risk (n=84), n (%) | P |
|----------|-----------------------------|------------------------------|--------|
| IPSS | | | |
| Mild | 3 (7.6) | 0 | <0.001 |
| Moderate | 30 (76.9) | 44 (52.3) | |
| Severe | 6 (15.3) | 40 (47.6) | |
| QOL | | | |
| 1 | 0 | 1 (1.1) | 0.605 |
| 2 | 3 (7.6) | 10 (11.9) | |
| 3 | 11 (28.2) | 18 (21.4) | |
| 4 | 20 (51.2) | 38 (45.2) | |
| 5 | 5 (12.8) | 13 (15.4) | |
| 6 | 0 | 4 (4.7) | |

IPSS=International Prostate Symptom Score, QOL=Quality of life, BQ=Berlin questionnaire

DISCUSSION

Historically, LUTS treatment in males has focused primarily on the prostate. However, current evidence suggests that LUTS are multifactorial. Evaluation for LUTS must also consider nonurological factors. The objective of this study was to help highlight the link between LUTS and sleep difficulties among men with LUTS.

This study showed that 67.4% of the patients with LUTS had poor sleep quality, and 68.2% had a high risk of obstructive sleep apnea. Results from previous Western studies showed

that 8.8% of men aged 40 years and more had a sleep disorder.^[5] A significant association between severe LUTS was seen in our patients having poor sleep quality and a high risk of obstructive sleep apnea. This shows that a higher incidence of sleep disturbances is associated with more severe cases of LUTS.

This study showed a significantly higher rate of nocturia episodes, nocturnal polyuria, and nocturnal voided volumes associated with patients with poor sleep quality. A higher rate of nocturnal voided volume was also associated with patients having higher BQ scores. Numerous studies have found an association between nocturnal voids and various sleep disturbances.^[6,7,12] Bliwise *et al.* showed in a survey of 1424 elderly aged 55–84 years that nocturia was a predictor of self-reported insomnia (75% increased risk) and decreased sleep quality (71% increased risk).^[13] Prostatic hyperplasia results in increased nocturia episodes and these men are known to have a poor sleep, which can lead to sleep disorders.^[14,15]

Nocturia is one of the LUTS conditions that has conventionally been one of the most challenging to treat pharmacologically and surgically.^[16] Studies have shown that the prostate's transurethral resection reduces nocturia episodes by <20%.^[17] It is generally known that sleep problems can contribute to nocturia. Obstructive sleep apnea has been considered one of the paradigmatic sleep disorders that leads to nocturia. It has been seen that

treatment of sleep apnea by positive pressure or surgical correction leads to improvement in LUTS.^[18,19]

It is plausible that sleep disturbances have been found in more significant percentages of patients treated at urology departments across all age groups because these patients have some LUTS. This is the case regardless of whether the patients are male or female. However, the current study did not address the problem of medical issues, which may also cause sleep difficulties; hence, future investigations are necessary to address it.^[20]

Imbalances in steroid hormone action, sympathetic system activity, and immune dysfunction may all be involved in developing such sleep disorders. These factors have all been considered to potentially contribute to the development of bladder outlet obstruction and symptomatic benign prostatic enlargement.^[21] Disruption of circadian rhythm may also contribute to sleep disorders. The body's internal biological clock is responsible for regulating bladder function and the volume of urine that will be stored over 24 hours. This is a critical factor in ensuring a person can get quality sleep and stay asleep throughout the night. As a result, this mechanism may be implicated in the relationship between LUTS and sleep disturbances.^[22] If these underlying physiological problems are not treated, the quality of sleep may suffer, which will have a substantial adverse influence on energy levels, mood, and overall QOL.

Patients visiting urology outpatient can be screened for sleep disturbances and quality of sleep. If needed, a specialist consultation should be taken with the goal of multidisciplinary management of LUTS. The treatment of these sleep disorders, on the other hand, will assist patients in maintaining their level of activity while also improving their QOL. It is also likely that decreasing LUTS will help in reducing the severity of sleep disturbances. To gain a deeper understanding of the connection between LUTS and sleep disturbances, a therapeutic intervention involving many patients is required.

Further research is required to determine whether sleep problems and LUTS share a common pathway, as the processes that underlie both conditions have only been partially investigated. There is a lack of research on sleep disturbances even though they are widespread among patients who are being treated in urology outpatient.

CONCLUSIONS

This study highlights the significant link between LUTS and sleep difficulties among men with LUTS. There is an increased prevalence of moderate and severe symptoms in patients with a high risk of sleep apnea. Patients with poor sleep had overall poorer QOL scores. There is an increased risk of nocturia and nocturnal polyuria with sleep

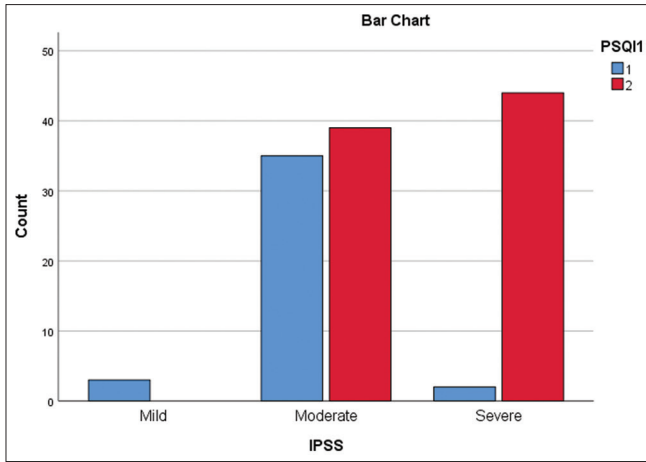
disorders. Therefore, screening for sleep disturbances can be considered on male patients with LUTS and vice versa.

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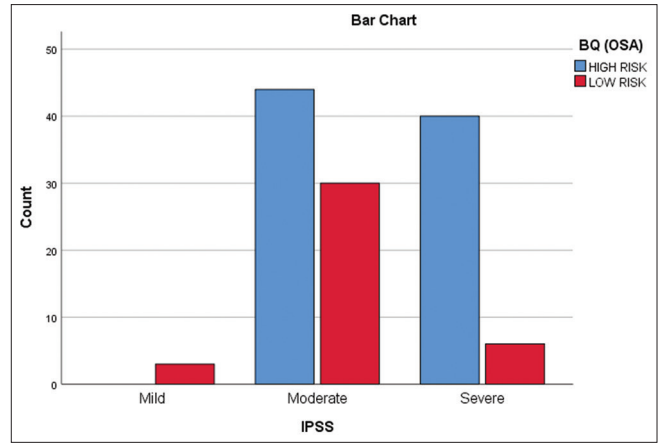
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Supplementary Figure 1: Association of lower urinary tract symptoms in patients with <5 and >5 Pittsburgh Sleep Quality Index. PSQI = Pittsburgh Sleep Quality Index, IPSS = International Prostate Symptom Score



Supplementary Figure 2: Association of lower urinary tract symptoms in patients with low and high risk in Berlin Questionnaire. BQ = Berlin Questionnaire, IPSS = International Prostate Symptom Score, OSA = Obstructive Sleep Apnea