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Evaluation of Sleep Quality in Patients With Genital and Non-Genital Cutaneous Warts: a Prospective Controlled Study

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ABSTRACT

Introduction: Diseases affect sleep quality, and sleep quality may also affect diseases by affecting the immune system. Depending on the immune status of patients with cutaneous warts, the extent of the disease and the response to treatment may vary.

Objectives: This study aimed to characterize the association between cutaneous warts and sleep quality.

Methods: A prospective controlled study was conducted. Patients over 18 years with cutaneous warts were enrolled. The control subjects were healthy, age- and sex- matched people. Demographic and clinical data on the participants were gathered. The sleep quality of participants was evaluated with the Pittsburgh Sleep Quality Index (PSQI).

Results: A total of 138 patients with genital or non-genital cutaneous warts (N = 59, N = 79, respectively) and 83 controls were interviewed. The average global PSQI score of the group with cutaneous warts was significantly higher than that of the control group (1.292 95% confidence interval 1.174-1.422). The rate of poor sleep quality in the patient group was higher than in the control group (odds ratio 3.835). Patients with genital warts had a significantly higher average global PSQI score than patients with non-genital warts (8.61 ± 3.63 versus. 6.98 ± 3.32). Female patients with genital warts had a significantly higher average global PSQI score than male patients with genital warts.

Conclusions: Evaluation of sleep quality in patients with warts, especially in patients with genital warts, may be suggested. The management of sleep disturbances associated with cutaneous warts may help increase the quality of life of patients and may affect disease control.

Introduction

Sleep is an active, restorative, physiological, and neurobiological state that occupies approximately one third of our lives. It is mainly regulated by the homeostatic sleep drive and the circadian system, often called the "central clock," controlled particularly by the cortisol and melatonin hormones [1,2]. Sleep disruption associated with skin diseases may impair quality of life. Poor sleep quality also has a significant effect on the nervous and immune systems. Moreover, poor sleep quality may induce and/or aggravate skin disease by affecting the regional immune function [3].

Skin also plays a major role in convenient sleep activity by regulating body temperature, peripheral circadian oscillators, ultraviolet (UV)-induced fluctuations in melatonin levels, and cortisol [1]. It has been reported that only one night of sleep deprivation may hinder the recovery of the skin barrier. Natural killer cells and some proinflammatory cytokines (interleukin-1beta/tumor necrosis factor-alfa), which play an important role in the regulation of non-rapid eye movement (NREM) sleep, may increase after sleep disruption [4].

Especially chronic inflammatory skin conditions (eg atopic dermatitis, psoriasis vulgaris, and chronic urticaria) may affect sleep quality [5–7]. Recently, rosacea, lichen planus, hidradenitis suppurativa, acne vulgaris, and Behçet disease have been shown to negatively affect sleep quality [8–12].

Cutaneous warts are a common infectious skin disease caused by human papillomavirus (HPV). Depending on a patient immune status, common warts may appear anywhere on the skin; moreover, spontaneous remission and treatment-resistant lesions may be seen, and it is thought that the immune system is effective in the response to treatment [13]. Although diseases themselves affect the quality of sleep, sleep quality can also affect diseases by affecting the immune system.

Objectives: The aim of this study was to better characterize the association between cutaneous warts and sleep quality.

Methods

Study Participants

A prospective, controlled study was conducted between January and July 2021. The study included patients over 18 years old who were enrolled from tertiary referral dermatology outpatient clinics and diagnosed with cutaneous warts. The control subjects were healthy, age- and sex-matched people.

Exclusion Criteria for Patient Group

Patients aged < 18 years, patients known to have sleep disorders, patients with other chronic and/or any inflammatory systemic and/or dermatologic disorders that may affect sleep quality, and pregnant and lactating women were excluded from the patient group.

Exclusion Criteria for Control Group

Patients aged < 18 years, patients with other chronic and/or any inflammatory systemic and/or dermatologic disorders that may affect sleep quality, and pregnant and lactating women were excluded from the control group.

Ethical Considerations

All participants signed the written consent form before the questionnaire, provided information, and gave permission to use that information in the study regarding the survey. Ethics committee approval was received from the University Scientific Research and Publication Ethics Board.

Survey

In the first section, the demographic and clinical data of the participants were queried. The questions included age, sex, and presence of systemic, autoimmune, and dermatological diseases. The type of warts (genital/non-genital), number of warts (single, 1–5 warts, >5 warts), localization of warts (if non-genital), and duration of the disease were recorded.

The sleep quality of participants was evaluated with the Pittsburgh Sleep Quality Index (PSQI). It is a self-rated questionnaire evaluating sleep quality and sleep disturbances over an interval of the previous month. The questionnaire included 11 questions about subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping medication, and daytime dysfunction. Each domain was scored with 0–3 points. PSQI scores range from 0–21 points. A global PSQI score of 5 or higher reflects poor sleep quality.

Statistical Analysis

SPSS 22.0 package program was used to evaluate the data. The descriptive statistics were the number and percentage for categorical variables and numerical variables as mean, standard deviation, minimum, maximum, and median. The rates in groups were compared using the Chi-squared test, Mann–Whitney U test, and Kruskal–Wallis test. The distribution of variables was measured by the Kolmogorov–Smirnov test. Since the numerical variable did not meet the normal distribution condition, the Mann–Whitney U and Kruskal–Wallis tests were used for comparison. Statistical alpha significance level was accepted as $P < 0.05$.

Results

Demographic and Clinical Characteristics

A total of 138 patients with genital and non-genital cutaneous warts (N = 59, N = 79, respectively) and 83 healthy, sex- and age-matched controls were interviewed. General characteristics of the participants are shown in Table 1. The majority of patients with genital warts were male (89.8%). The sex distribution in patients with non-genital warts was similar. The most frequent localizations of non-genital warts were plantar and palmar (40.5% and 39.2%, respectively).

Comparison of Sleep Quality Between Patient and Control Groups

Patients with cutaneous warts had a significantly higher average global PSQI score than the control group with an odds ratio [OR] of 1.292, 95% confidence interval (CI) 1.174-1.422, with a significantly higher score in all components of the PSQI excluding use of sleeping medication.

Poor sleep quality was observed in 79.7% of the patient group and in 50.6% of the control group (P < 0.05). It was determined that the rate of poor sleep quality in the patient group was higher than in the control group (OR: 3.835; 95% CI: 2.110-6.972) (Table 2).

Table 1. General Characteristics of Participants and Association Between Sleep Quality and Demographic Characteristics.

	Nongenital (N = 79) mean ± SD		Genital (N = 59) mean ± SD		Control (N = 83) mean ± SD
Age (years)	27.94±10.23		31.54±10.01		30.20±9.57
Disease duration (years)	1.08±1.55		1.20±1.39		
	N (%)		N (%)		N (%)
Sex Male Female	39(49.4) 40(50.6)		53(89.8) 6(10.2)		47(56.6) 36(43.4)
Number of warts 1 1-5 >5	36(45.6) 28(35.4) 15(19.0)		1(1.7) 16(27.1) 42(71.2)		
Localization – Hand – Plantar – Facial – Palmoplantar – Others	31(39.2) 32(40.5) 9(11.4) 4(5.1) 3(3.8)				
	Non-genital (N = 79)		Genital (N = 59)		z/P
	N	mean ± SD	N	mean ± SD	
Age ≤ 30 years >30 years	 56 23	 6.76±3.09 7.52±3.83	 33 26	 8.33±3.72 8.96±3.56	 -1.898/0.058 -1.327/0.184
z/P	-0.786/0.432		-0,797/0.425		
Sex Male Female	 39 40	 6.87±3.18 7.10±3.48	 53 6	 8.30±3.65 11.33±2.06	 -1.737/0.082 -2.621/0.009*
z/P	-0.015/0.988		-2.102/0.036*		
Disease duration ≤ 1 year >1 year	 65 14	 6.87±3.40 7,.0±2.95	 42 17	 8.66±3.88 8.47±3.04	 -2.278/0.023* -0.979/0.327
z/P	-0.574/0.566		-0.109/0.913		

SD = standard deviation; z = Mann Whitney U test.
* P < 0.05.

Table 2. Comparison of Sleep Quality Between Patient and Control Group.

Pittsburgh Sleep Quality Index (PSQI) and PSQI domains	Patients (N = 138) mean ± SD	Control (N = 83) mean ± SD	z/P	Odds Ratio [a] (95% confidence interval)
Global PSQI	7.68±3.53	4.92±2.91	-5.549/0.000*	1.292 (1.174-1.422)
Subjective sleep quality	1.42±0.64	1.18±0.68	-2.498/0.012*	1.764 (1.152-2.701)
Sleep latency	1.55±0.88	1.03±0.86	-4.127/0.000*	1.955 (1.405-2.720)
Sleep duration	1.18±1.06	0.77±0.83	-2.738/0.006*	1.541 (1.153-2.060)
Habitual sleep efficiency	0.55±0.74	0.12±0.32	-4.813/0.000*	4.587 (2.299-9.154)
Sleep disturbance	1.23±0.63	0.74±0.55	-5.460/0.000*	3.936 (2.316-6.690)
Use of sleeping medication	0.47±0.91	0.27±0.70	-1.648/0.099	1.363 (0.952-1.950)
Daytime dysfunction	1.25±1.01	0.79±0.77	-3.210/0.001*	1.704 (1.251-2.321)
Sleep quality	N (%)	N (%)	x^2/P	
Poor sleep quality	110 (79.7)	42 (50.6)	20.449/0.000*	3.835 (2.110-6.972)
Good sleep quality	28 (20.3)	41 (49.4)		

SD = standard deviation; z = Mann Whitney U test; x^2 = Xi square test.
* P < 0.05; , [a] Logistic regression analysis.

Table 3. Comparison of Sleep Quality Between Patients With Genital and Non-genital Warts.

Pittsburgh Sleep Quality Index (PSQI) and PSQI domains	Non-genital (a) (N = 79) mean ± SD	Genital (b) (N = 59) mean ± SD	Control (c) (N = 83) mean ± SD	KW/p
Global PSQI	6.98±3.32	8.61±3.63	4.92±2.91	36.79/0.000* b>a>c [a]
Subjective sleep quality	1.39±0.70	1.47±0,56	1.18±0.68	6.904/0.032* b>a=c [a]
Sleep latency	1.46±0.85	1.66±0.90	1.03±0.86	18.222/0.000* a=b>c [a]
Sleep duration	1.06±1.01	1.33±1.10	0.77±0.83	9.666/0.008* b>a=c [a]
Habitual sleep efficiency	0.54±0.81	0.55±0.65	0.12±0.32	23.997/0.000* a=b>c [a]
Sleep disturbance	1.13±0,61	1.37±0.64	0.74±0.55	33.497/0.000* a=b>c [a]
Use of sleeping medication	0.36±0.78	0.62±1.04	0.27±0.70	4.411/0.110
Daytime dysfunction	1.01±0.98	1.57±0.98	0.79±0.77	21.785/0.000* b>a>c [a]

KW = Kruskal Wallis test.
* P < 0.05; [a] Bonferroni's correction: P < 0.0167.

Comparison of Sleep Quality Between Patients With Genital and Non-genital warts

Patients with genital warts had a significantly higher average global PSQI score than patients with non-genital warts (8.61 ± 3.63 versus 6.98 ± 3.32), with a significantly higher score in 2 components of the PSQI, ie sleep disturbance and daytime dysfunction (Table 3; Figure 1).

Association Between Sleep Quality and Demographic Characteristics

Female patients with genital warts had a significantly higher average global PSQI score than male patients with genital warts (11.33 ± 2.06 versus 8.30 ± 3.65). There was no significant difference in sleep quality regarding age, number of warts, or disease duration (Table 1).

Conclusions

Although the reason cannot be fully clarified, chronic inflammatory skin diseases (eg atopic dermatitis, psoriasis vulgaris, chronic urticaria) and rosacea, lichen planus, hidradenitis suppurativa, acne vulgaris and Behçet disease are shown to have a negative effect on sleep quality [5–12]. Apart from symptoms such as pain and itching caused by diseases, the

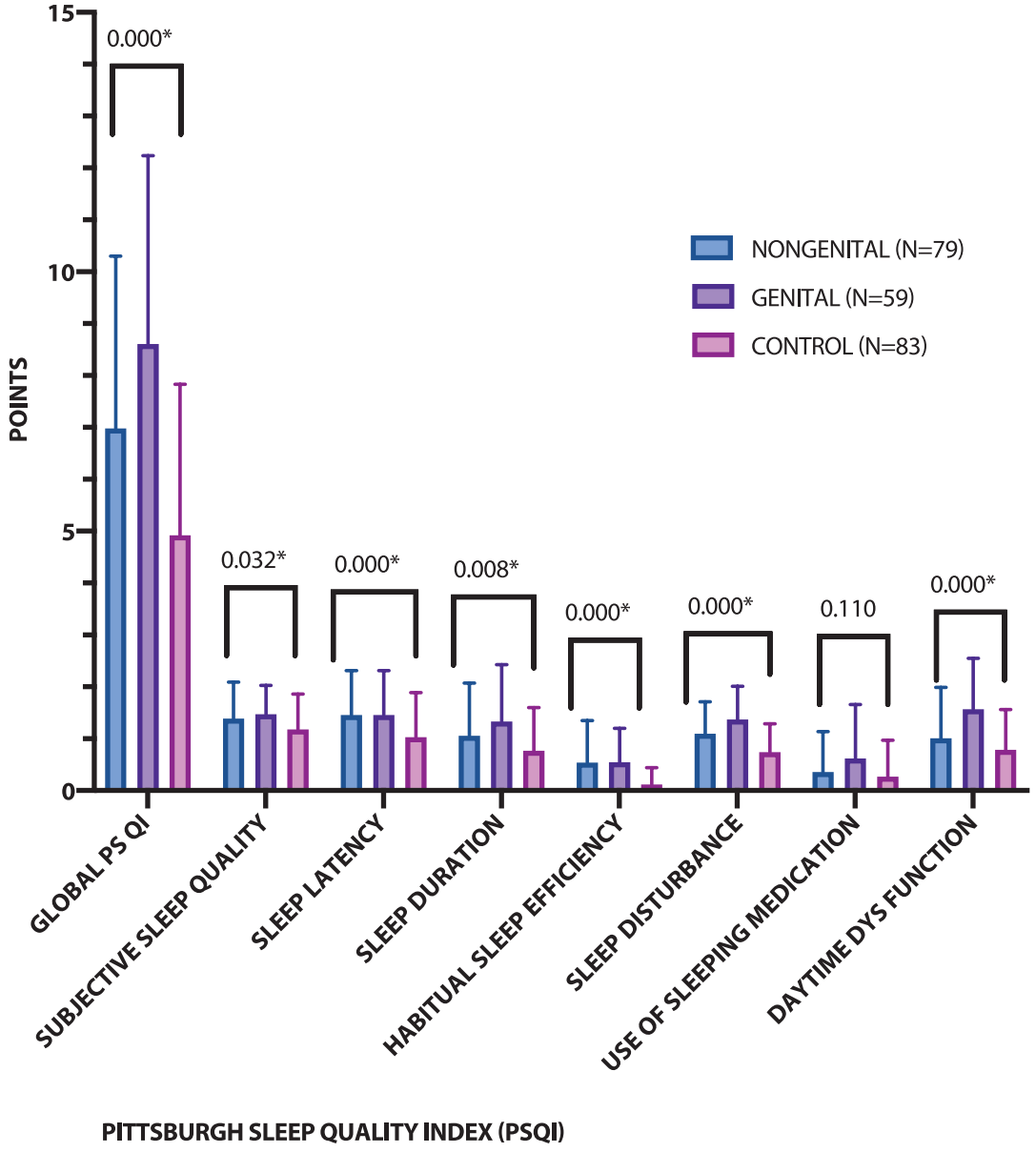

Figure 1. Comparison of sleep quality among patients with genital and non-genital warts and controls.
*P < 0.05.
Non-genital: a. Genital: b. Control: c.
Global PSQI b>a>c**
subjective sleep quality b>a=c**
sleep latency a=b>c**
sleep duration b>a=c**
habitual sleep efficiency a=b>c**
sleep disturbance a=b>c**
use of sleeping medication -
daytime dysfunction b>a>c**
**Bonferroni correction: P < 0.0167.

psychosocial effects of dermatological diseases cannot be denied. Sleep quality is also one of the most important of these psychosocial effects. For this reason, the effects of dermatological diseases on sleep quality have been frequently investigated in recent studies.

In fact, although diseases themselves affect sleep quality, sleep quality may also affect diseases by affecting the immune system. Sleep disorders may result in some changes in immune system functions. In accordance with the association between cytokines, host immune function, and the sleep-wake cycle, sleep disturbance may play a role in the inflammatory cascade that can result in a chronic inflammatory state [1].

Cutaneous warts are a common disease, and depending on the immune status of the person, the extent of the disease and the response to treatment may vary [14]. In the literature, only one study has mentioned the effect of cutaneous warts on sleep quality [15]. In the study of Liu et al,

in which 215 patients with palmoplantar warts were evaluated, 11.0% of the patients reported poor sleep quality; however, this study was conducted without questionnaires or a control group. Although the reason is not mentioned, it was observed that the treatment response was low in those with poor sleep quality [15]. Our study is significant in that it is the first controlled study in this respect and that patients with genital warts (ie as opposed to only non-genital warts) were also evaluated.

In our study, patients with cutaneous warts had a significantly higher average global PSQI score than that of the control group. Here, the disease itself, treatment processes, and response or non-response to treatment may affect sleep quality. However, the sleep quality of the patients may also affect their immune status, thus affecting the elimination of the virus or the extent of the virus and the response to treatment. Sleep is actually an immunological activity. Human sleep consists of two phases: REM (rapid eye movement) and NREM (non-REM) sleep. Natural killer cells and some proinflammatory cytokines (interleukin-1beta/tumor necrosis factor-alfa), which play an important role in the regulation of NREM sleep, may increase after sleep disruption [4]. However, slow-wave sleep (deep sleep) plays a role in reducing immune system activation, while sleep deprivation can activate the immune system, leading to an increase in IL-1, IL-6, TNF a, leukocytes, NK, and monocyte cells. hypothalamic-pituitary-adrenal (HPA) activation reduces the sleep-enhancing effects of cytokines, decreases non-REM sleep, and increases wakefulness in the advanced stages of inflammation [16].

Patients with genital warts had a significantly higher average global PSQI score than patients with non-genital warts and controls in this study. The transmission of genital warts by sexual contact and the feeling of guilt and shame caused by it, relapses during treatment, and the risk of malignancy are the most important causes of psychological damage in patients. In addition, the sexual life of patients may be affected [17]. The degree of this impact on quality of life may also affect sleep quality.

Female patients with genital warts showed a significantly higher average global PSQI score than male patients with genital warts in this study. Evaluating the literature, it has been shown that the quality of life of female patients with genital warts is more affected than that of male patients [17,18]. This suggests that the anxiety and stress caused by the disease in women are more intense and that women are more sensitive to changes in their quality of life. However, genital warts remind women of cervical cancer, and thanks to preventive medicine, women's awareness of cervical cancer has increased in recent times. For all these reasons, it was thought that the sleep quality of women might be more affected.

The shortcoming of the study is that concurrent quality of life was not evaluated. In addition, since the treatment options were not standard in all patients, it was not evaluated whether the sleep quality of the patients had an effect on the response to treatment.

Our study reveals the association between poor sleep and cutaneous warts. Cutaneous warts seem to have an effect on sleep, but perhaps the reverse direction is also true. Evaluation of sleep quality in patients with warts, especially in patients with genital warts, may be suggested. The management of sleep disturbances in cutaneous warts may help increase the quality of life of patients and may affect disease control.

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