ORIGINAL ARTICLE

Association of Obstructive Sleep Apnoea Risk and Severity of Psoriasis Vulgaris in Adults

Wei Hsi Chang, Ting Guan Ng

Hospital Tengku Ampuan Rahimah, Jalan Langat, 41200 Klang, Selangor, Malaysia

ABSTRACT

Introduction: Psoriasis vulgaris has a significant association with obstructive sleep apnoea (OSA). The study intended to explore the relation between the severity of psoriasis vulgaris and OSA risk, and to identify the factors that are attributed to increased risk of OSA. **Methods:** A cross sectional, observational study was carried out from October 2020 until April 2021 at the dermatology clinic of Hospital Tengku Ampuan Rahimah, Malaysia. All study participants were evaluated for OSA risk using the STOP-Bang and Epworth Sleepiness Scale questionnaires. **Results:** Our study recruited 237 participants and the results revealed a higher percentage of moderate to severe psoriasis participants with intermediate to high risk of OSA than participants with mild psoriasis (35.3% versus 17.7%, respectively). There was also a 2.3 times higher incidence of daytime sleepiness among participants with moderate to severe psoriasis as opposed to participants with mild psoriasis (44.1% versus 19.2%, respectively). We have also detected a significantly higher probability for OSA in psoriasis patients with diabetes mellitus versus those without (odds ratio: 2.09). We also noticed that for every unit rise in body mass index (BMI), there seemed to be a 1.06 times higher risk of OSA. Furthermore, patients with moderate to severe psoriasis were found to possess 3.32 times increased odds to have OSA. **Conclusion:** Our results suggest that psoriasis severity and the existence of comorbidities i.e. diabetes mellitus and high BMI are linked with an enhanced risk of OSA in adults with psoriasis.
Malaysian Journal of Medicine and Health Sciences (2023) 19(1):158-164. doi:10.47836/mjmhs19.1.22

Keywords: Psoriasis, Obstructive sleep apnoea, Obesity, Diabetes mellitus

Corresponding Author:
Wei Hsi Chang, MRCP
Email: elizzchang@gmail.com
Tel: +60172582864

INTRODUCTION

Psoriasis, which affects 0.51 to 11.43% of the adult population in the world, is an immune-mediated, chronic disease whereby the patients suffer from skin and joints inflammation (1–3). Proinflammatory cytokines including interleukins (IL) especially IL-1 and IL-17, and tumour necrosis factor-α (TNF-α) are responsible for the multisystemic effects of psoriasis (1,4–6). One of the common clinical variants of psoriasis is psoriasis vulgaris, impacting about 85 to 90% of all patients with psoriasis and is characterised by red, scaly, raised plaques (5,6). Comorbidities commonly aligned with psoriasis include psoriasis arthritis, inflammatory bowel disease, psychological/psychiatric disorders, Crohn's disease, and uveitis (1,3,7). Recent studies have also shown the link between psoriasis and metabolic syndrome (including its components such as obesity, dyslipidaemia, diabetes mellitus, hypertension and cardiovascular diseases) (3,7).

Obstructive sleep apnoea (OSA) is presented by frequent collapse of the upper airway while sleeping, contributing to recurrent hypoxia (1,7). People with OSA often have night snoring, recurrent sleep arousals as well as excessive daytime sleepiness due to sleep disruption (1,7,8). Previous studies have discovered that individuals with OSA carry a high probability of developing serious diseases for example cardiovascular disease, stroke, hypertension, myocardial infarction, insulin resistance, type 2 diabetes mellitus, metabolic syndrome and obesity (1,7,8). Moreover, these patients also display a tendency towards upper airway and systemic inflammation along with oxidative stress, as shown by increased amounts of inflammatory biomarkers such as IL-6, C-reactive protein and TNF-α (7,8).

Since both OSA and psoriasis are affiliated with chronic, systemic inflammation as well as an overactive immune response, the potential link between both of these diseases has been extensively studied in the last few years (1,8). It is noteworthy that psoriasis is able to increase the occurrence of sleep apnoea and snoring (7). The cases of OSA in individuals with psoriasis range between 2.7 to 81.8% (9). In a study by Shalom et al., people with psoriasis appeared to exhibit a higher

incidence of OSA in comparison to healthy individuals (2.7% and 1.5%, respectively, odds ratio [OR] 1.74, 95% confidence interval [CI] 1.50–2.03, p < 0.001) (8). A study of 2,258 patients with OSA by Yang et al. stated that the hazard ratio of psoriasis or psoriatic arthritis was 2.3 times greater (95% CI 1.13–4.69, p = 0.022) among those with OSA in contrast to control individuals (10). A meta-analysis of multiple studies consisting of 5,544,674 participants also found a substantial correlation of OSA and psoriasis (pooled incidence rate ratios [IRR] = 2.52; 95% CI, 1.89–3.36) (1). Another study by Egeberg et al. on 5,522,190 Danish participants discovered a bidirectional connection between OSA and psoriasis i.e. psoriasis was linked to high chance of developing OSA, and similarly OSA was linked to high risk of psoriasis (11). In participants with mild psoriasis, severe psoriasis and psoriatic arthritis, the IRRs (95% CI) for OSA were 1.30 (1.17–1.44), 1.65 (1.23–2.22) and 1.75 (1.35–2.26), respectively (11).

In-laboratory polysomnography (PSG), a night-time sleep study, continues to be the gold standard in OSA diagnosis (1,8,12–17). The study records the number of apnoeic and hypopneic events (12,16). The apnoea-hypopnea index (AHI) is used as the main measurement to assess the seriousness of OSA (12,18). A person with an AHI of > 5 events/hour of sleep is interpreted as having OSA syndrome (18). Although PSG is accurate with low failure rates, it is a long and time-consuming process, relatively expensive and requires the knowledge and skills of a sleep medicine specialist to interpret the results (13–17). Hence, several prediction models and screening questionnaires were created to assist in detecting individuals with OSA (15). The STOP-Bang questionnaire and Epworth Sleepiness Scale (ESS) are among the most popular, easy-to-use and widely accepted instruments for identification of high risk patients of OSA (16,17).

As far as we know, there are not many studies that specifically explore the association of the severity of psoriasis with OSA risk. Thus, their relationship remains unclear. To help answer this question, we used STOP-Bang questionnaire and ESS to investigate the correlation of OSA risk with the intensity of psoriasis vulgaris as rated by Psoriasis Severity and Area Index (PASI). This study also aimed to evaluate the relation of obesity with OSA risk in adults with psoriasis vulgaris.

MATERIALS AND METHODS

Study design and protocol

This is a cross-sectional, questionnaire-based, observational study conducted on adults (≥ 18 years) with a clinical diagnosis of psoriasis vulgaris who attended the dermatology clinic of Hospital Tengku Ampuan Rahimah (HTAR). Every consecutive patient from October 2020 to April 2021 were evaluated for eligibility into the study. Inclusion criteria consist of the following: ≥ 18 years of age, good understanding of written English or Malay language, and personal agreement and willingness to take part in the study. Patients with known craniofacial structural abnormalities, chronic sinusitis, bronchial asthma requiring rescue inhaler more than twice a week in the last three months, chronic obstructive airway disease, thyroid disorder, depression-anxiety disorders, congestive heart failure, alcoholism, pregnancy (or breastfeeding mothers), on narcoleptics, on sedative antihistamines, patients who are mentally challenged or unable to understand written English or Malay language are excluded. We have obtained written consent from all participants prior to their inclusion in this study.

A clinical evaluation of psoriasis has been conducted whereby information was collected from the participants according to the data collection form which included: details of psoriasis vulgaris like disease duration, mode of treatment (topical/systemic/phototherapy/biologics), and presence of concurrent psoriasis arthropathy. The main investigator also performed the PASI assessment to evaluate the severity of psoriasis vulgaris for each participant. PASI is a validated measurement tool designed to assess the severity of psoriasis (19). PASI measurements comprise of mean erythema (redness), induration (thickness) and desquamation of lesion (0 to 4 scale), and the area of involvement (19,20). Total PASI scores extend from 0 (disease free) to 72 (maximum) (19,20). Based on the PASI scores, patients were categorised as mild (PASI ≤ 10) and moderate to severe (PASI > 10) psoriasis at the time of assessment.

After a thorough clinical examination, all study patients were evaluated for the risk of OSA using two validated questionnaires: the STOP-Bang screening tool and self-administered ESS questionnaires. Participants were given some time to answer the STOP-Bang and ESS questionnaires on their own in the presence of an investigator. STOP-Bang questionnaire involves subjective items (i.e. STOP: snoring, tiredness, observed apnoea and high blood pressure) as well as demographic items (i.e. BANG: body mass index [BMI], age, neck circumference and gender) (17,21). One point will be given for each 'yes' answer; 0 for 'no' answers (17,21). A STOP-Bang results of ≥ 3 (total: 8) is classified as having greater probability for OSA (17,21). Meanwhile, ESS questionnaire is a validated method for daytime sleepiness measurement (21). It requires the participants to grade their possibility of falling asleep (scale: 0 to 3) in eight situations, with a score of < 11 (out of a possible total score of 24) indicating low/mild risk for daytime sleepiness, while ≥ 11 as high risk (21).

Information on their comorbidities (namely hypertension, diabetes mellitus, ischemic heart disease, inflammatory bowel disease, bronchial asthma, malignancy or human immunodeficiency virus infection) was subsequently obtained from the participants. Anthropometric parameters like BMI and waist, hip and neck

circumference were determined by the investigator to minimise interrater bias. Obesity is measured by BMI (based on the data on Asian Indian populations; normal BMI: 18.0–22.9 kg/m^2, overweight: 23.0–24.9 kg/m^2, obesity: > 25 kg/m^2) (22).

Statistical analysis

In this study, data was analysed using the SPSS version 26.0. Continuous variables were recorded as mean ± standard deviation (SD), and one-way analysis of variance (ANOVA) was utilised to analyse and compare three groups means. Categorical data was analysed using Chi-square test to compare between groups. Univariate analysis was used to measure statistically significant confounders. Logistic regression was employed to identify the relation of severity of psoriasis and the risk of OSA after confounder adjustment. A p-value of < 0.05 is interpreted as statistically significant.

Ethical clearance

We performed this study in accordance with the ethical standards and principles of the Declaration of Helsinki and Malaysian Guideline for Good Clinical Practice. This study was validated and approved by the Medical Research and Ethics Committee, Ministry of Health Malaysia [NMRR-20-2213-55858 (IIR)].

RESULTS

Demographics study

From October 2020 to April 2021, a total of 237 study participants were recruited in our study. Among the participants, there were 135 (57.0%) males and 102 (43.0%) females, with a mean age of 44.0 ± 25.5 years. About 203 (85.6%) participants were classified with mild psoriasis and 34 (14.3%) participants with moderate to severe psoriasis, assessed based upon PASI classification. In terms of additional diseases, 40 (19.7%) patients with mild psoriasis and 8 (25.0%) with moderate to severe psoriasis had a diagnosis of diabetes mellitus, while 49 (24.1%) patients with mild psoriasis and 8 (23.5%) with moderate to severe psoriasis had hypertension. Majority of the patients were obese (mean BMI of 27.12 kg/m2 among those with mild psoriasis and 27.81 kg/m2 among those with moderate to severe psoriasis). The median duration of psoriasis was 10 years in participants with mild psoriasis and 11 years for those with moderate to severe psoriasis. Demographic characteristics according to quantitative and qualitative parameters were reported in Table I.

Risk of OSA and daytime sleepiness in patients with psoriasis

Our data demonstrated an enhanced risk of OSA in participants with moderate to severe psoriasis. As illustrated in Fig. 1, the percentage of moderate to severe psoriasis participants with intermediate to high risk of OSA (STOP-Bang assessment score of ≥ 3) was higher than participants with mild psoriasis (35.3% versus 17.7%, respectively). In terms of daytime sleepiness (Fig. 2), participants with moderate to severe psoriasis presented 2.3 times higher incidence as compared to mild psoriasis group (44.1% versus 19.2%, respectively).

Table I: Clinical characteristics of the study participants stratified by the severity of psoriasis

Characteristics	Mild psoriasis (n = 203)	Moderate-severe psoriasis (n = 34)	p value*
Median (SD) age, in years	45.32 (15.64)	39.59 (11.92)	0.043[a]
Gender, n (%)			
Male	115 (56.7)	20 (58.8)	0.813[b]
Female	88 (43.3)	14 (41.2)	
Ethnic group, n (%)			
Malay	100 (49.3)	22 (64.7)	0.047[b]
Chinese	17 (8.4)	5 (14.7)	
Indian & others	86 (42.4)	7 (20.6)	
BMI, mean (SD) in kg/m^2	27.12 (5.53)	27.81 (11.33)	0.577[a]
Neck circumference, mean (SD) in cm	37.50 (5.0)	38.00 (4.8)	0.522[a]
Presence of hypertension, n (%)	49 (24.1)	8 (23.5)	0.939[b]
Presence of diabetes mellitus, n (%)	40 (19.7)	8 (25.0)	0.608[b]
Current smoker, n (%)	38 (18.7)	8 (27.4)	0.732[b]
Duration of psoriasis, median (IQR) in years	10.00 (14.00)	11.00 (8.50)	0.487[c]
Presence of psoriatic anthropathy, n (%)	45 (22.2)	8 (23.5)	0.860[b]
Patients who received systemic therapy past 6 months, n (%)	24 (11.8)	9 (26.5)	0.032[b]

[a] Independent T-test; [b] Chi-Square test; [c] Mann Whitney test; * p value < 0.025 is considered statistically significant.
SD: standard deviation; BMI: body mass index; IQR: interquartile range.

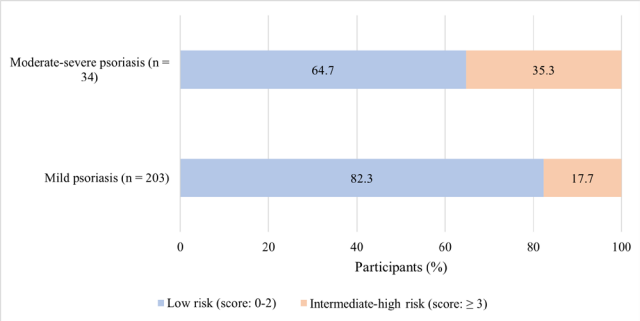

Figure 1: Results from STOP-Bang assessment p = 0.018 (Chi-Square test).

OSA risk factors in patients with psoriasis

As demonstrated in Table II, univariate analysis showed several factors and characteristics that were significantly associated with ESS score; including having family members with OSA, diabetes mellitus, BMI, hip circumference, body surface area involvement and moderate to severe psoriasis.

Following the univariate analysis, a multiple logistic regression analysis was performed, and the results are illustrated in Table III. We found at least three factors

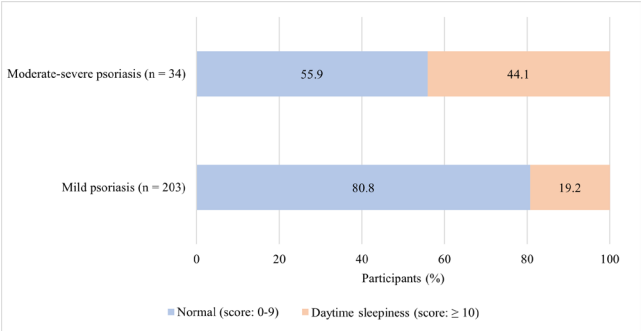

Figure 2: Results from ESS questionnaire response
ESS: Epworth Sleepiness Scale. p = 0.001 (Chi-Square test).

known to be significantly associated with sleep apnoea among participants with psoriasis, namely diabetes mellitus, high BMI and severity of psoriasis. Our results revealed that psoriasis patients with diabetes mellitus have higher OSA risk compared to those without (OR: 2.09, p = 0.045). Of the patients studied, many were found to be obese with mean BMI values of 27.12 kg/m^2 (± 5.53) and 27.81 kg/m^2 (± 11.33) for mild and moderate to severe psoriasis patients, respectively (Table I). Further statistical analysis determined that for every 1 unit increase of BMI, the risk of developing OSA increases by 1.06 times among these patients (p = 0.025, Table III). Our results also showed a heightened probability of having OSA in patients with psoriasis. Patients with moderate to severe psoriasis were found to be at 3.32 higher odds of having OSA (p = 0.003) after adjusting for confounding variables.

DISCUSSION

The main findings of this study were as follows: (i) psoriasis patients with diabetes mellitus have higher OSA risk compared to those without diabetes mellitus (OR: 2.09), (ii) for each unit increase in BMI, there is a 1.06 times higher risk of OSA, and (iii) patients with moderate to severe psoriasis possess 3.32 times higher odds to experience OSA.

In the current study, we found that OSA risk was significantly greater in moderate to severe psoriasis participants as opposed to that of mild psoriasis group. This is in accordance to previous research by Karagьn et al., which uncovered a heightened occurrence of OSA symptoms including snoring (56.1%), excessive daytime sleepiness (25.6%) and witnessed apnoea (15.9%) in patients with severe psoriasis (23). Similarly, Karaca et al. reported a 54.5% prevalence of OSA symptoms among 33 adult patients with more than five years duration of moderate psoriasis (24). According to the literature, the inflammatory activity and overactive immune response in psoriasis may prominently contribute to the higher risk of OSA (8,18,25).

Table II: Univariate study of factors associated with ESS score

Factors/Characteristics	Simple Logistic Regression	
	Crude Odd Ratio (95% CI)	p value
Age when psoriasis vulgaris diagnosed	1.00 (0.97, 1.02)	0.629
Duration of psoriasis	0.98 (0.94, 1.01)	0.148
Family members with psoriasis		
No	1	-
Yes	0.64 (0.31, 1.35)	0.242
Family members with sleep apnoea		
No	1	-
Yes	1.86 (1.00, 3.45)	0.050
Co morbidities		
No	1	-
Yes	1.29 (0.69, 2.38)	0.427
Ischemic heart disease	-	-
Stroke	1.71 (0.15, 19.20)	0.665
Diabetes mellitus	2.25 (1.13, 4.50)	0.021
Hypertension	0.88 (0.43, 1.81)	0.721
Hypercholesterolemia	1.75 (0.77, 4.00)	0.181
Depression	1.37 (0.26, 7.26)	0.712
Bronchial asthma	0.56 (0.07, 4.73)	0.591
Irritable bowel syndrome	-	-
Malignancy	-	-
Cigarette smoking		
No	1	-
Ex-smoker	0.33 (0.04, 2.61)	0.291
Current smoker	0.79 (0.35, 1.76)	0.563
Number of sticks/day	1.04 (0.93, 1.15)	0.520
Substance abuse		
No	1	-
Yes	1.38 (0.42, 4.60)	0.696
Amount of substance taken in unit/week	1.15 (0.97, 1.38)	0.114
BMI	1.06 (1.01, 1.11)	0.011
Waist circumferences	1.02 (1.00, 1.04)	0.061
Hip circumferences	1.03 (1.01, 1.06)	0.011
Neck circumferences	1.00 (0.98, 1.03)	0.809
Percentages of BSA involvement	1.03 (1.01, 1.04)	0.002
PASI severity		
Mild	1	-
Moderate-severe	3.32 (1.55, 7.11)	0.002
Psoriatic Anthropathy		
No	1	-
Yes	1.47 (0.73, 2.94)	0.279
Nail involvement	1.29 (0.70, 2.38)	0.411
Special sites		
No	1	-
Yes	1.59 (0.66,3.81)	0.301
Treatment received		
Topicals	1	-
Topical + Systemic therapy	1.10 (0.47, 2.60)	0.830

ESS: Epworth Sleepiness Scale; CI: confidence interval; BMI: body mass index; BSA: body surface area; PASI: Psoriasis Severity and Area Index.

Table III: Multiple logistic regression analysis of independent clinical factors associated with high OSA risk

Predictive factors	Adjusted OR (95% CI)	p value
Diabetes mellitus	2.09 (1.02, 4.30)	0.045
BMI	1.06 (1.01, 1.11)	0.025
Moderate-severe PASI	3.32 (1.49, 7.41)	0.003

OSA: obstructive sleep apnoea; OR: odd ratio; CI: confidence interval; BMI: body mass index; PASI: Psoriasis Severity and Area Index.

Earlier studies have suggested that psoriasis is linked to a variety of medical comorbidities, for example obesity, cardiovascular disease, hypertension, cancer, autoimmune disease, diabetes mellitus and other metabolic syndromes (24,26–28). With regards to their similarity in the pathogenesis with inflammatory mediators, both psoriasis and OSA may also share the same common links to these diseases (24). Our observation on the link between OSA and diabetes mellitus among patients with psoriasis was in line with the findings from a large case-control study which incorporated 253 patients with OSA and 104 healthy participants. The study demonstrated that more patients with OSA and psoriasis had diabetes mellitus versus patients with OSA but without psoriasis (29.2% versus 13.1%, p = 0.03) (18).

We have shown that high BMI was associated with high OSA incidence among patients with psoriasis. Our results were in concordance with Kobeloglu Ilbay et al. study which described a significant correlation between BMI and the development of OSA symptoms ($p < 0.005$) among patients with psoriasis who were obese (mean BMI of 30.44 ± 5.02 kg/m2) (29). Another published study of 35 patients from Greece also discovered that BMI was related to an enhanced probability of OSA and hypopnea syndrome in patients with psoriasis adjusting for age and gender (adjusted OR of 1.32, 95% CI 1.07–1.63) (26). High BMI or obesity can be both a risk factor and a potential outcome of the abnormal immune system in chronic inflammatory diseases such as psoriasis and OSA (11). We are in agreement with Papadavid et al. study which suggested that obese patients with psoriasis must be assessed for OSA and hypopnea syndrome regardless of the intensity or duration of psoriasis, or the existence of metabolic syndromes and comorbidities (26).

The current study has disclosed that the incidence of OSA is closely related to the intensity of psoriasis. We noticed an increased risk of OSA in patients with moderate to severe psoriasis in contrast to mild psoriasis. Egeberg et al. also reported similar findings, whereby the incidence rate of sleep apnoea was greater in severe psoriasis than mild psoriasis patients (incidence rates of 6.48 [95% CI 6.41–6.55], 12.18 [95% CI 10.79–13.53] and 18.23 [95% CI 13.82–24.05] per 10,000 person-years for the control group, mild psoriasis and severe psoriasis patients, respectively) (11).

As the link between psoriasis and OSA is medically significant (8), managing psoriasis may be an important instrument to prevent OSA and other cardiovascular mortality related to OSA and psoriasis. Healthcare professionals attending to individuals with psoriasis should be mindful of the association between these two diseases (8). In addition, initial OSA screening using appropriate self-administered questionnaires, such as STOP-Bang and ESS, should be employed so that physicians can make immediate and appropriate assessment of the disease, and better selection of treatment (8,24,30).

The strength of this study includes its comprehensive OSA evaluation given low resource setting. There was no selection bias as the study was designed based on consecutive sampling whereby we recruited every patient who meets the selection criteria within the specified time period. The limitation of our work was that we performed the assessment of OSA using only self-reported questionnaires, without PSG as the reference test as it is not readily available in most medical centres in Malaysia, including the one where this study took place. Therefore, we used the ESS questionnaire, which is a validated and feasible initial screening tool, with sensitivity and specificity of 73% and 75% respectively (31), to evaluate the OSA risk in our cohort of psoriasis patients. We took further initiative of referring our patients who showed high OSA risk to centres with PSG for definitive diagnosis and management. A follow-up study using objective assessment i.e. PSG in adults with psoriasis versus healthy control group would be of great value.

CONCLUSION

In conclusion, our study has demonstrated an increased likelihood of OSA among those with moderate to severe psoriasis. We also discovered that psoriasis patients with diabetes mellitus and high BMI have an increased chance of developing OSA.

ACKNOWLEDGEMENTS

We wish to express our appreciation to the Director General of Health, Malaysia for giving us the permission to publish this manuscript. We would also like to thank all dermatology clinic staffs from HTAR for their contribution in this study.

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