Anais da Faculdade de Medicina de Olinda
Annals of Olinda Medical School

afmo.emnuvens.com.br ISSN: 2674-8487 Original article

Association between clinical factors and risk of obstructive sleep apnea syndrome evaluated by the Berlin Questionnaire

Associação entre fatores clínicos e risco de síndrome da apneia obstrutiva do sono avaliado pelo questionário de Berlim

Mário Cruz Couto[1] Fernando Augusto Pacífico[1]
Liliam de Souza Santos[1] Giovanna Sherly de Sá Guedes Marins[1]
Michelle Alves de Farias[1] Dolly Brandão Lages[1]
Eduardo Lins Paixão[1]

[1] Faculdade de Medicina de Olinda. Olinda, Pernambuco, Brazil.

Abstract

Objectives: to investigate the frequency of individuals at high risk for obstructive sleep apnea syndrome (OSAS) attending an ambulatory care of a teaching clinic in the metropolitan region of Recife/PE, and to verify the association of frequency of OSAS with clinical symptoms, such as snoring, sleepiness, fatigue, systemic arterial hypertension (SAH), and body mass index (BMI). **Methods:** This quantitative, cross-sectional, and observational study was conducted using a non-probabilistic convenience sample of 361 individuals. **Results:** Most individuals were classified as high risk for OSAS, with a higher prevalence among women. Furthermore, significant associations were identified between OSAS risk and snoring, sleepiness, fatigue, SAH, and increased BMI, highlighting the impact of these factors in identifying at-risk individuals. **Conclusion:** The findings reinforced the importance of the Berlin Questionnaire to stratify individuals at high risk for OSAS, allowing for the prioritization of diagnostic tests and proper interventions, and potentially optimizing clinical management and reducing examination costs.

Keywords: Berlin Questionnaire; Heart disease risk factors; Hypertension; Obstructive; Prevalence; Sleep apnea; Triage

How to cite: Couto **MC**, Pacífico **FA**, Santos **LS**, Marins **GSSG**, Farias **MA**, Lages **DB**, *et al*. Association between clinical factors and risk of obstructive sleep apnea syndrome assessed by the Berlin Questionnaire. An. Fac. Med. Olinda 2025; 1(13):375 doi: https://doi.org/10.56102/afmo.2025.375

Corresponding author:
Mário Cruz Couto
E-mail: m_ccouto@live.com

Funding: Programa de Desenvolvimento Institucional de Iniciação Científica - PRODIIC da Faculdade de Medicina de Olinda, FMO.
Ethics approval: 57239422.4.0000.8033
Received: 04/30/2024
Approved: 09/02/2025

Resumo

Objetivo: investigar a frequência de indivíduos com alto risco de síndrome da apneia obstrutiva do sono (SAOS) atendidos no ambulatório de uma clínica escola na região metropolitana de Recife/PE. Além disso, associou a frequência com variáveis clínicas e sintomáticas, como ronco, sonolência, fadiga, hipertensão arterial sistêmica (HAS) e índice de massa corporal (IMC). **Método:** Um estudo transversal, com amostragem do tipo não probabilística por conveniência foi conduzido com 361 pacientes. **Resultados:** A maioria dos pacientes foi classificada como de alto risco para SAOS, com maior prevalência entre as mulheres. Além disso, identificaram-se associações significativas entre o risco de SAOS e a presença de ronco, sonolência, fadiga, HAS e IMC elevado, evidenciando o impacto desses fatores na identificação de indivíduos em risco. **Conclusão:** Os achados reforçam a importância da triagem utilizando o questionário de Berlim para estratificar indivíduos com alto risco de SAOS, possibilitando a priorização de exames diagnósticos e intervenções adequadas, com potencial para otimizar o manejo clínico e reduzir custos com exames desnecessários.

Palavras-chave: Apneia obstrutiva do sono; Fatores de risco cardiovascular; Hipertensão arterial sistêmica; Prevalência; Protocolo de Berlim; Triagem

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a disorder characterized by the repetitive partial (hypopnea) or complete collapse (apnea) of the upper airway, leading to recurrent awakenings due to respiratory effort during sleep.[1] OSAS is more prevalent in men (70.2%) than in women (29.8%).[2] Studies indicate that about 3.0% of women and 10.0% of men between 30 and 49 years have OSAS, and these numbers may be underestimated.[3] Among individuals aged from 50 to 70 years, these percentages increase to 9.0% and 17.0%, respectively.[3] Furthermore, over 40.0% of individuals with a body mass index (BMI) ≥ 30 and 60.0% of those with metabolic syndrome have OSAS.[4]

OSAS is one of the causes of secondary arterial hypertension (SAH) and is associated with resistant SAH when not treated, increasing the risk of cardiovascular morbidity and mortality.[4] Despite its clinical relevance, only 10.0% of individuals with OSAS receive a correct diagnosis, evidencing a significant rate of underdiagnosis.[5] The gold standard diagnostic exam is overnight polysomnography[5]; however, due to the difficulty in performing it, screening tools are used to identify individuals at high risk for having OSAS.[6]

One of the screening tools is the Berlin Questionnaire, developed in 1996 during a conference about sleep respiratory disorders in Berlin, Germany.[7] The study by Netzer *et al*. (1999)[7] validated the questionnaire in 1999, demonstrating good performance (sensitivity of 86.0% and

specificity of 77.0%) for diagnosing mild OSAS (apnea and hypopnea index [AHI] > 5).[7] For moderate OSAS (AHI > 15), sensitivity and specificity were 54.0% and 97.0%, respectively, while for severe OSAS (AHI > 30), these values were 17.0% and 97.0%, respectively.[7]

Adeline *et al*. evaluated the performance of the Berlin Questionnaire and identified a frequency of moderate and severe OSAS of 28.1% and 10.7%, respectively.[8] To predict an AHI ≥ 15, sensitivity, specificity, negative predictive value, and positive predictive value were 58.8%, 77.6%, 82.9%, and 50.6%, respectively.[8] When used to predict an AHI ≥ 30, sensitivity increased to 76.9%, with a slight decrease in specificity to 72.7%.[8] Netzer et al. (1999) applied the questionnaire to 6,223 individuals and reported that 32.3% were at high risk for OSAS.[8] Similarly, Adeline *et al*. observed that 32.6% of individuals were classified as high risk.[8] These findings indicate that the Berlin Questionnaire may be a useful screening tool, especially due to its good sensitivity and high negative predictive value to exclude severe OSAS.

Despite the importance of OSAS, few studies evaluate its frequency in primary care services or teaching clinics, where individuals often present risk factors but may not have access to specialized diagnosis. Identifying individuals at high risk for OSAS in these environments may enable the implementation of screening and early referral strategies, reducing the negative impacts of the disease.

Thus, this study aimed to investigate the frequency of individuals at high risk for OSAS who attended the ambulatory care of a teaching clinic in the metropolitan region of Recife/PE, and to analyze their associations with clinical and symptomatic variables, such as snoring, sleepiness, fatigue, SAH, and BMI.

METHODS

This study was approved by the research ethics committee of the Faculdade de Medicina de Olinda (no. 6,214,153).

This quantitative, observational, cross-sectional study was conducted with individuals attending an ambulatory care of a teaching clinic in the metropolitan region of Recife/PE, between May 2023 and December 2023. The sample size was calculated using the Social Science Statistics calculation tool (socscistatistics.com), considering a 95% confidence level (95%CI), 5% precision, and population variability, estimating 361 individuals. A total of 375 individuals were interviewed, selected by convenience, based on their availability, and according to the inclusion criteria.

Individuals aged ≥ 30 years, of both sexes, without a previous diagnosis of OSAS or treatment with continuous positive airway pressure (CPAP), were included in the study, considering that OSAS increases significantly from this age range. Those with incomplete questionnaires were excluded.

All individuals signed the informed consent form. Two instruments were used during data collection: a questionnaire for sociodemographic data (name, address, telephone number, age, sex, weight, height, and prior diagnosis of OSAS), and the Berlin Questionnaire.

The Berlin Questionnaire comprises 10 questions, divided into three categories. Questions one to five (category one) evaluate the presence of snoring and its intensity and frequency. Questions six to eight (category two) inquire about fatigue, daytime sleepiness, and falling asleep during routine activities. Questions nine and ten (category three) evaluate whether the individual has SAH and calculate the BMI. Individuals are classified as low risk when they score positively in only one or none of the categories, or high risk when they score positively in any two of the three categories, not necessarily in order.

Categories one and two were considered positive when two or more responses were positive. Category three was positive when the response to question nine was positive or when the BMI was > 30. A total of 361 individuals were included in the analysis, respecting the inclusion criteria. Fourteen individuals were excluded due to the inability to obtain anthropometric data, name, weight, and height.

Data were organized in an Excel spreadsheet and analyzed using SPSS (version 20.0) for Windows. The analysis was performed using absolute and relative frequencies, descriptive statistics (absolute values and percentages), and statistical association tests (the Chi-square test of independence). The significance level adopted was up to 5% ($p \leq 0.05$), and the 95%CI.

A binary logistic regression analysis was performed to identify risk factors for OSAS. Furthermore, the logistic regression was adjusted for variables with confounding bias, such as potential associated factors that could interfere with the relationship between independent variables (snoring, sleepiness, fatigue, SAH, and BMI > 30) and the risk of OSAS. This adjustment is essential to ensure that the variables identified as risk factors for OSAS are indeed responsible for this association, without the influence of other factors.

RESULTS

Of the 361 individuals, 264 (73.13%) were women (Table 1). The mean age was 55.44 years (SD ± 13.67). Regarding weight and height, the mean was 74.37 kg (SD ± 16.60) and 161.84 cm (SD ± 9.07), respectively. Concerning the risk for OSAS, 44.32% (n = 160) were classified as high risk, while 55.68% (n = 201) were classified as low risk.

Analyzing individuals at high risk, 76.25% (n = 122) were women and 23.75% (n = 38) were men; among individuals at low risk, the percentages were 70.65% (n = 142) and 29.35% (n = 59). The mean age, weight, and height were 56.38 years (SD ± 12.68), 77.70 kg (SD ± 14.18), and 161.56 cm (SD ± 8.62) for individuals at high risk (respectively), and 54.70 years (SD ± 14.40), 71.71 kg (SD ± 17.89), and 162.07 cm (SD ± 9.43) for those at low risk (respectively).

Table 1. Characterization of the sample (n = 361).

Variable	Total (n = 361)	Low Risk (n = 201)	High Risk (N = 160)
Men (%)	97 (26.87 %)	59 (29.35 %)	38 (23.75 %)
Women (%)	264 (73.13 %)	142 (70.65 %)	122 (76.25 %)
Age (mean ± SD)	55.44 ± 13.67	54.70 ± 14.40	56.38 ± 12.68
Weight (mean ± SD) (kg)	74.37 ± 16.60	71.71 ± 17.89	77.70 ± 14.18
Height (mean ± SD) (cm)	161.84 ± 9.07	162.07 ± 9.43	161.56 ± 8.62
SAH (%)	189 (52.35 %)	71 (35.32 %)	118 (73.75 %)
BMI (mean ± SD) (kg/m²)	28.35 ± 5.49	27.15 ± 5.66	29.78 ± 5.15

Legend: OSAS = Obstructive sleep apnea syndrome; SAH = Systemic arterial hypertension; BMI = Body mass index; SD = Standard deviation. The variable “Total” represents the full sample before risk stratification.

Source: Prepared by the authors.

Regarding snoring-related aspects, 83.13% (n = 133) of individuals at high risk had a significantly higher positive result for this category, while only 15.42% (n = 31) of individuals at low risk were positive.

Concerning sleepiness and fatigue, individuals at high risk also presented a higher prevalence of positive results in this category, representing 53.13% (n = 85), while those at low risk showed a proportion of 10.95% (n = 22).

Analyzing the presence or absence of SAH and BMI values, individuals at high risk exhibited a considerably higher prevalence of positive results for this category, totaling 88.75% (n = 142), compared with 42.79% (n = 86) of those at low risk.

A statistically significant high risk for OSAS was found in the risk variable related to snoring [$X^2(2) = 164.709$, $p < 0.001$], sleepiness and fatigue [$X^2(2) = 76.000$, $p < 0.001$], and the presence of SAH and BMI > 30 [$X^2(2) = 80.886$, $p < 0.001$] (table 2).

Table 2. Association between clinical factors and risk of OSAS (n = 361).

Variable	Low Risk (n = 201)	High Risk (n = 160)	Chi-square (X^2)	p-value	OR (95% CI)
Snoring			164.709	< 0.001	27.013 (15.374 – 47.463)
Positive	31 (15.42 %)	133 (83.13 %)			
Negative	170 (84.58%)	27 (16.88 %)			
Sleepiness/Fatigue			76.000	< 0.001	9.221 (5.369 – 15.837)
Positive	22 (10.95 %)	85 (53.135%)			
Negative	179 (89.05 %)	75 (46.88%)			
SAH. BMI > 30, or both			80.886	< 0.001	10.549 (5.999 – 18.549)
Present	86 (42.79 %)	142 (88.75 %)			
Absent	115 (57.21 %)	18 (11.25 %)			

Legend: OSAS = Obstructive sleep apnea syndrome; SAH = Systemic arterial hypertension; BMI = Body mass index; OR = Odds Ratio; CI = Confidence interval. The chi-square test (X^2) was used to evaluate the association between categorical variables. The OR was calculated to estimate the strength of association between clinical factors and OSAS risk.

Source: Prepared by the authors.

A binary logistic regression analysis was performed to verify whether aspects related to snoring, sleepiness, fatigue, and SAH or BMI > 30 (or both) are predictors of high risk for OSAS. The results indicated that snoring-related aspects were a significant predictor (Odds ratio [OR] = 27.013; 95%CI = 15.374 to 47.463), showing that the presence of snoring significantly increased the odds of high risk for OSAS. The presence of SAH or BMI > 30 (or both) was also associated with a considerable increase in the odds of high risk for OSAS (OR = 10.549; 95%CI = 5.999 to 18.549). Additionally, individuals who reported sleepiness and fatigue had a significantly higher probability of being in the high-risk group (OR = 9.221; 95%CI = 5.369 to 15.837). The model demonstrated good fit, with all variables showing high statistical significance ($p < 0.001$), suggesting that aspects related to snoring, sleepiness, fatigue, and the presence of SAH and elevated BMI are significant predictors of the risk for OSAS.

These results suggest that snoring-related aspects, sleepiness and fatigue, SAH, and BMI, as outlined in the Berlin Questionnaire, play important roles in determining the risk of OSAS among individuals in this clinical context.

DISCUSSION

OSAS is a clinical condition associated with clinical and cardiovascular complications, including SAH, atrial fibrillation and other arrhythmias, heart failure, coronary artery disease, stroke, pulmonary hypertension, and cardiovascular mortality, highlighting the importance of early diagnosis and treatment.[1]

In this context, numerous treatments are available for OSAS, such as CPAP, autotitrating positive airway pressure (PAP), bilevel PAP, and adaptive servoventilation. Other interventions include lifestyle changes, BMI reduction, avoiding alcohol and sedatives before bedtime, surgical procedures (especially uvulopalatopharyngoplasty), oral appliances, and other devices to enlarge the nasal openings.[4]

All individuals with OSAS should be considered for treatment, including behavioral changes and weight loss.[1] Regarding the available devices, CPAP (i.e., the gold standard) should be offered to individuals at high risk for OSAS, while oral appliances may be considered for those at low risk or for those intolerant to CPAP.[1] This device maintains a continuous flow of pressurized air through the upper airway, preventing pharyngeal collapse during sleep. This mechanism reduces airway resistance, improves oxygenation, and relieves episodes of hypoxemia and sleep fragmentation, promoting better sleep quality and reducing cardiovascular complications associated with the disease.

Studies show that OSAS is more common in men, with an estimated prevalence ratio of 2:1 to 3:1 compared with women.[9] In addition, men tend to present more severe forms, with higher AHI scores.[8,11] In a study conducted in Germany, 46.9% of men had severe OSAS, compared with 35.2% of women.[8]

Our study observed that among individuals at high risk for OSAS, 76.25% (n = 122) were women and 23.75% (n = 38) were men. We recognize the potential for selection bias, especially regarding the higher demand for care among women. Thus, this limitation was included in the discussion. Since most individuals were women, this may explain the predominance of women at high risk for OSAS in our study, despite the literature suggesting a higher prevalence in men.

In the study by Margallo et al. (2014), 347 individuals (82.2%) were diagnosed, being 234 (55.5%) with moderate to severe OSAS. In individuals at high risk, moderate to severe OSAS was confirmed in 58.3%, whereas in those at low risk, it was excluded in 50.4%. The accuracy of the Berlin Questionnaire in detecting OSAS was 55.6%.[10]

In this study, 44.32% of the individuals were at high risk, and 55.68% were low risk. Polysomnography was not performed to confirm the diagnosis, given that the phase during which the study was conducted did not include diagnostic bias.

In a study conducted in South Korea, Sunwoo et al. (2018) showed that the prevalence of high risk for OSAS was 15.8% (95%CI = 14.5% to 17.2%), and a BMI ≥ 25 kg/m² (OR = 10.75) was significantly related to high risk, while regular physical activity (OR = 0.70) had a protective effect. Subjective sleep characteristics associated with high risk were perceived insufficient sleep (OR = 1.49), excessive daytime sleepiness (OR = 1.88), and insomnia (OR = 3.70). Additionally, hypertension (OR = 5.83), diabetes mellitus (OR = 2.54), hyperlipidemia (OR = 2.85), and anxiety

(OR = 1.63) were independently associated with high risk for OSAS.[11]

In this study, a BMI > 30 was also associated with an increased risk for OSAS. Individuals at high risk exhibited a considerably higher prevalence of positive results for the BMI category, totaling 88.75% (n = 142). In comparison, among individuals at low risk, only 42.79% (n = 86) were positive.

Hein et al. (2017) observed that the prevalence of moderate to severe OSAS in individuals with insomnia was 13.88%. Multivariate logistic regression analysis revealed that being men, snoring, excessive daytime sleepiness, complaint of maintenance insomnia, presence of metabolic syndrome, age between ≥ 50 and < 65 years or ≥ 65 years, BMI ≥ 25 and < 30 kg/m² or > 30 kg/m², and c-reactive protein > 7 mg/L were significant risk factors for moderate to severe OSAS in individuals with insomnia.[14]

The sleep characteristics associated with high risk for OSAS reported by Sunwoo et al. (2018) and Hein et al. (2017) corroborate our results. Aspects related to snoring, sleepiness, and fatigue played an important role in determining the risk of OSAS. For individuals positive in the sleepiness and fatigue category, 53.13% were at high risk, while those at low risk showed a proportion of 10.95%.

Among 34,727 individuals, the prevalence of self-reported habitual snoring, morning fatigue, and excessive daytime sleepiness (≥ three times per week for each) was 23.6%, 16.6%, and 19.1%, respectively. During a median follow-up of 3.1 years (interquartile range from 3.0 to 3.5), the incidence of treated SAH was 3.8%. The risk of treated SAH again was higher in individuals who reported habitual snoring (adjusted hazard ratio, 1.17 [95%CI = 1.03 to 1.32]) and excessive daytime sleepiness (adjusted hazard ratio, 1.42 [95%CI = 1.24 - 1.62]), and increased with the weekly frequency of symptoms, showing a dose-dependent relationship (trend p ≤ 0.02 for all symptoms).[15]

The literature does not provide specific anthropometric data on the mean age, weight, and height of adults classified as high or low risk. Gatt *et al*. (2024) analyzed anthropometric variables in pediatric individuals and found that higher BMI values were correlated with increased risk for OSAS.[12] Conversely, Chuang et al. (2020) did not divide groups into high and low risk, but observed that anthropometric characteristics such as increased neck circumference and higher median age are risk factors directly correlated with the determination of OSAS risk in pediatric individuals.[13]

In this study, the mean age, weight, and height were 56.38 years (SD ± 12.68), 77.70 kg (SD ± 14.18), and 161.56 cm (SD ± 8.62) respectively for individuals at high risk for OSAS, and 54.70 years (SD ± 14.40), 71.71 kg (SD ± 17.89), and 162.07 cm (SD ± 9.43) for individuals at low risk. Furthermore, anthropometric data depends on genetic, behavioral, ethnic, and racial factors,

which can vary the results depending on the sample used.

A longitudinal study analyzing data from the Wisconsin Sleep Cohort Study concluded that sleep-disordered breathing increased the risk of developing SAH by about threefold, even when confounding factors, such as age, sex, smoking, alcohol use, education, and physical activity, were present.[6] In this study, SAH was associated with the high risk for OSAS. Moreover, the results were statistically significant for this variable.

Although the present study robustly identified risk factors associated with OSAS, some limitations should be considered. While logistic regression allows identifying associations between variables, it is not possible to fully control for all variables not included in the model, which may influence the results and consequently the interpretation of associations. Additionally, the cross-sectional study design does not allow for establishing definitive causal relationships between variables. The sample may also not be representative of all populations, as the data were collected from a single center. Future studies with larger and more diverse samples and longitudinal designs could provide a more comprehensive and accurate view of the risk factors for OSAS.

CONCLUSION

Most individuals seen at the clinic-school outpatient clinic present a high risk for OSAS, with a higher prevalence among women. Individuals at high risk showed a higher frequency of symptoms, such as snoring, sleepiness, fatigue, systemic arterial hypertension, and elevated BMI. The analyses indicated significant associations between these clinical and symptomatic factors and the risk of OSAS. These results reinforce the importance of early identification of risk factors, enabling the prioritization of diagnostic exams and appropriate treatment, with the potential to reduce costs from unnecessary exams and improve the effectiveness of clinical follow-up.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

FUNDING SOURCE

Institutional Scientific Initiation Development Program, PRODIIC. Faculdade de Medicina de Olinda, FMO.

AUTHOR CONTRIBUTIONS

MCC: Writing – original draft, Writing – review and editing. **FAP:** Data curation, Formal analysis, Methodology, Supervision, Writing – original draft, Writing – review and editing. LSS: Writing – original draft, Writing – review and editing. **GSSGM:** Writing – original draft, Writing – review and editing. **MAF:** Writing – original draft, Writing – review and editing. **DBL:** Writing –

original draft, Writing – review and editing. **ELP:** Conceptualization, Data curation, Investigation, Methodology, Project administration, Resources, Supervision, Writing – original draft, Writing – review and editing.

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