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The Relationship between Idiopathic Intracranial Hypertension and Obstructive Sleep Apnea: Is Obesity the Only Mediating Factor between the Two?

İdiyopatik İntrakraniyal Hipertansiyon ve Obstrüktif Uyku Apnesi Arasındaki İlişki: İkisi Arasındaki Tek Aracı Faktör Obezite mi?

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ABSTRACT

Aim: This study aimed to investigate the possible reciprocal relationship between idiopathic intracranial hypertension (IIH) and obstructive sleep apnea (OSA).
Material and Methods: This cross-sectional study was conducted from October 2023 to February 2024. Patients with IIH and age and gender-matched controls without IIH were included. Information on age, gender, comorbidities, smoking, and alcohol consumption was recorded. Body mass index (BMI) was calculated, and a BMI ≥30 was considered obese. Berlin questionnaire and STOP-BANG questionnaire were administered to all participants. High risk for OSA was determined if participants responded affirmatively to at least three out of the eight questions on the STOP-BANG questionnaire, or if two out of the three categories showed positive results on the Berlin questionnaire.
Results: Sixty patients with IIH and 120 controls participated. There were no significant differences between groups regarding age (p=0.437) and gender distribution (p=0.716). The percentage of obese subjects was significantly higher in the IIH group (p<0.001). The Berlin and STOP-BANG results showed that the IIH group had higher risks for OSA than the control group. Multivariate logistic regression analysis revealed obesity as the only factor independently associated with high-risk classification with the Berlin questionnaire. In the STOP-BANG survey, higher age, male gender, obesity, and hyperlipidemia were independently related to high-risk classification.
Conclusion: Obesity is a common risk factor for both OSA and IIH. The coexistence of OSA and IIH may cause increased morbidity and mortality rates in both diseases. Therefore, we recommend that patients with IIH be screened for OSA risk.
Keywords: Pseudotumor cerebri; obstructive sleep apnea; body mass index; obesity.

ÖZ

Amaç: Bu çalışmanın amacı idiyopatik intrakraniyal hipertansiyon (İİH) ve obstrüktif uyku apnesi (OSA) arasındaki olası karşılıklı ilişkiyi araştırmaktır.
Gereç ve Yöntemler: Bu kesitsel çalışma Ekim 2023 ile Şubat 2024 tarihleri arasında gerçekleştirilmiştir. İİH'li hastalar ve İİH'si olmayan yaş ve cinsiyet uyumlu kontroller çalışmaya dahil edilmiştir. Yaş, cinsiyet, komorbiditeler, sigara içme ve alkol tüketimine ilişkin bilgiler kaydedilmiştir. Vücut kitle indeksi (VKİ) hesaplanmış ve VKİ ≥30 olanlar obez olarak kabul edilmiştir. Tüm katılımcılara Berlin anketi ve STOP-BANG anketi uygulanmıştır. Katılımcılar STOP-BANG anketindeki sekiz sorudan en az üçüne olumlu yanıt verdiğinde veya Berlin anketinde üç kategoriden ikisi olumlu sonuç verdiğinde OUA için yüksek risk belirlenmiştir.
Bulgular: Altmış İİH hastası ve 120 kontrol grubu katılmıştır. Gruplar arasında yaş (p=0.437) ve cinsiyet dağılımı (p=0.716) açısından anlamlı fark yoktu. Obez bireylerin yüzdesi İİH grubunda anlamlı derecede yüksekti (p<0.001). Berlin ve STOP-BANG sonuçları, İİH grubunun kontrol grubuna göre OUA için daha yüksek risk taşıdığını göstermiştir. Çok değişkenli lojistik regresyon analizi, Berlin anketinde yüksek risk sınıflandırması ile bağımsız olarak ilişkili tek faktörün obezite olduğunu ortaya koymuştur. STOP-BANG anketinde ise yüksek yaş, erkek cinsiyet, obezite ve hiperlipidemi bağımsız olarak yüksek risk sınıflandırması ile ilişkili bulunmuştur.
Sonuç: Obezite hem OSA hem de İİH için ortak risk faktörüdür. OSA ve İİH birlikteliği her iki hastalıkta da artmış morbidite ve mortalite oranlarına neden olabilir. Bu nedenle, İİH'li hastaların OSA riski açısından taranmasını öneriyoruz.
Anahtar kelimeler: Psödotümör serebri; obstrüktif uyku apnesi; vücut kitle indeksi; obezite.

INTRODUCTION

Idiopathic intracranial hypertension (IIH), commonly recognized as pseudotumor cerebri, is a pathological state characterized by the symptomatic elevation of intracranial pressure devoid of discernible causative factors (1,2). IIH is rare but has a markedly higher frequency among obese individuals and middle-aged females (1,3,4), and thus, there is a rising incidence in parallel with increasing global obesity (5). IIH manifests with characteristic clinical indicators of elevated intracranial pressure (6) and is linked to diminished quality of life and heightened cardiovascular risk.

Obstructive sleep apnea (OSA) is a prevalent disorder characterized by total or partial upper airway obstruction during sleep, leading to various associated symptoms (7). It is related to obesity and older age and is more common in men (4). OSA similarly correlates with diminished quality of life and elevated susceptibilities to type 2 diabetes, cardiovascular diseases, hypertension, and heightened mortality rates (8). Recent studies have reported a relationship between OSA and papilledema (9-11). Perhaps more interestingly, the pathophysiology of OSA has been associated with cerebral venous dilatation and increased intracranial pressure due to hypoxia and hypercapnia episodes during sleep (12).

Despite affecting different demographics, obesity appears to be a shared characteristic of patients with OSA and IIH, potentially suggesting shared pathophysiology and other common risk factors (4,13,14). Although some cross-sectional studies have made notable findings suggesting a relationship between IIH and OSA (15), there is no definitive evidence about the effect of OSA on IIH or vice versa. However, considering that both diseases are independent risk factors for increased risk of morbidity, especially cardiovascular morbidity, the coexistence of these diseases may cause a synergistic effect. Therefore, it will be essential to determine the risks and relationships between OSA and IIH to understand pathophysiology or diagnostic approaches which can be complicated. It is widely acknowledged within the academic sphere that polysomnography is the definitive diagnostic tool for identifying OSA; however, its customary application in screening procedures presents certain inherent complexities (16). In the context of OSA, the Berlin and STOP-BANG questionnaires serve as validated screening instruments to evaluate the likelihood of disease onset (17).

This study aimed to explore the potential bidirectional association between IIH and OSA, a correlation that remains inadequately elucidated. This investigation is conducted by employing the Berlin and STOP-BANG questionnaires among patients clinically diagnosed with IIH. It was also a secondary aim to investigate other factors associated with IIH and increased OSA risk.

MATERIAL AND METHODS

Study Design and Participants

A cross-sectional investigation was conducted within the Neurology Department of our institution, spanning from October 2023 to February 2024. Patients who were followed up with a diagnosis of IIH in our hospital's neurology inpatient or outpatient clinic and a control group matched with these patients in terms of age and gender were included in the study. IIH diagnoses were made according to the revised diagnostic criteria (modified Dandy criteria) for IIH (18). The IIH criteria were briefly as follows: (i) presence of signs and symptoms of increased intracranial pressure, (ii) absence of localizing findings other than abducens nerve palsy, (iii) cerebrospinal fluid opening pressure ≥25 cmH_2O, (iv) normal cerebrospinal fluid composition, and (v) normal neuroimaging, exclusion of venous sinus thrombosis (18). Volunteers for the control group were recruited from individuals attending the neurology outpatient clinic whose clinical evaluations did not indicate elevated intracranial pressure. The healthy control group was matched to the patient group in terms of sex and age.

The shared exclusion criteria for both cohorts encompassed individuals under 18, those lacking the cognitive capacity to respond to the questionnaire, pregnant or breastfeeding individuals, those diagnosed with sleep disorders, and individuals unwilling to volunteer for the study. Patients with secondary causes of increased pressure such as intracranial mass, cerebral venous thrombosis, etc., and those with complaints suggestive of these pathologies were excluded from both patient and control groups. The research protocol was comprehensively delineated to the participants, and their written consent, signifying their informed acknowledgment and agreement, was obtained. The study protocol was structured to adhere to anticipated ethical considerations, aligning with the principles outlined in the Declaration of Helsinki and subsequent revisions, and received approval from the pertinent local ethics committee (Başakşehir Çam and Sakura City Hospital, dated 13.09.2023, and numbered 422).

Data Collection, Definitions, and Tools

The IIH diagnosis-related information of the patients was obtained by retrospective scanning of our hospital's digital records. All data of the participants (including healthy controls) who volunteered to participate in the study were obtained by examining their information at first admission during the study period. After written consent was obtained, we recorded age, sex, comorbidity information, smoking and alcohol consumption status. Only those who actively smoked tobacco products and consumed alcohol were defined as users of tobacco or alcohol. Presenting symptoms for patients with IIH were recorded. The height and weight measurements of the participants were taken and body mass index (BMI) was calculated as weight/height^2 (kg/m^2). Participants were grouped according to their BMI <18.5 as underweight, 18.5-24.9 as normal weight, 25.0-29.9 as overweight, and ≤30 as obese (19). The Berlin and STOP-BANG questionnaires were administered to all participants.

Berlin Questionnaire

The Berlin questionnaire contains ten questions in 3 categories and one measurement (BMI). The first six questions concern snoring (first dimension), and questions 7 to 9 concern daytime sleepiness (second dimension). High blood pressure was questioned in the third dimension, and BMI was measured. The patient's family members verified answers to questions about snoring. In the first and second dimensions, two or more positive responses indicating recurrent symptoms (>3-4

times/week) were considered to show positivity. A history of high blood pressure or a BMI of more than 30 kg/m^2 was considered positive for the third dimension. Patients who were positive for two or more categories were considered to have a high risk for OSA (16,20). The validity of the Berlin questionnaire in Turkish was confirmed by Karakoc et al. (21).

STOP-BANG Questionnaire

The STOP-BANG questionnaire encompasses a set of inquiries consisting of eight binary (affirmative/negative) interrogatives and four supplementary demographic inquiries about sleep apnea symptoms. Moreover, it incorporates four queries constituting the STOP segment, which assesses variables such as snoring, fatigue, witnessed apnea events, hypertension, BMI, age, neck circumference, and male gender. Each affirmative response to the questionnaire prompts an allocation of 1 point, while each negative response warrants 0 points, resulting in a cumulative score ranging from 0 to 8. If 3 out of the 8 questions in the STOP-BANG survey received affirmative answers, the individual was considered to be at high risk for OSA (22).

Outcome Measures

The principal aim of the investigation was to examine the autonomous correlations between the occurrence of IIH and a heightened probability of OSA. The secondary outcomes of the study were to investigate other variables associated with IIH and increased OSA risk.

Statistical Analysis

Statistical analysis was conducted using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). Statistical significance was defined as $p<0.05$. Histograms and Q-Q plots were employed to assess the normal distribution of variables. Descriptive statistics were reported as mean ± standard deviation for normally distributed continuous variables, median (25th percentile - 75th percentile) for non-normally distributed continuous variables, and frequency (percentage) for categorical variables. Normally distributed continuous variables underwent analysis via Student's t-test, while non-normally distributed continuous variables were analyzed using the Mann-Whitney U test. Categorical variables were subjected to chi-square, Fisher's exact, or Fisher-Freeman-Halton tests. Logistic regression analyses were conducted to identify significant factors independently associated with high risk on the Berlin and STOP-BANG questionnaires. Variables were initially assessed via univariate regression analysis, with statistically significant variables subsequently included in multivariate analysis.

RESULTS

The study comprised 60 individuals diagnosed with IIH and 120 healthy participants. The IIH group exhibited a median age of 33 (interquartile range (IQR), 27-43.5) years whereas the control group had a median age of 31 (IQR, 27-40) years. Females represented 86.67% (n=52) of the IIH group and 83.33% (n=100) of the control group. No statistically significant differences were observed among the groups concerning age (p=0.437) and gender distribution (p=0.716). The proportion of individuals with normal weight was notably greater within the control group, while the prevalence of obesity was markedly elevated among participants in the IIH group ($p<0.001$). The prevalence of diabetes mellitus (p=0.007) and respiratory diseases (p=0.043) exhibited statistically significant elevation within the IIH group compared to the control group. According to the Berlin questionnaire results, the percentage of patients with positivity for dimension 1 (p=0.008), dimension 2 ($p<0.001$), and dimension 3 ($p<0.001$) was higher among IIH patients. Furthermore, patients categorized as having high risk for OSA were statistically significantly more common among those with IIH, based on the Berlin ($p<0.001$) and the STOP-BANG (p=0.004) questionnaires (Table 1).

Subsequently, multivariate logistic regression analysis was conducted, indicating that obesity emerged as the sole factor exhibiting an independent association with the

Table 1. Comparison of demographics, symptoms, and questionnaire results with regard to groups

	IIH (n=60)	Control (n=120)	p
Age (years)	33 (27 - 43.5)	31 (27 - 40)	0.437†
Gender, n (%)			
Female	52 (86.67)	100 (83.33)	0.716§
Male	8 (13.33)	20 (16.67)	
BMI (kg/m^2)	32.64±6.32	26.63±5.10	**<0.001**‡
BMI Groups, n (%)			
Underweight	0 (0.00)	3 (2.50)	**<0.001**¶
Normal weight	8 (13.33)	50 (41.67)	
Overweight	11 (18.33)	28 (23.33)	
Obese	41 (68.33)	39 (32.50)	
Comorbidities, n (%)			
Diabetes mellitus	8 (13.33)	3 (2.50)	**0.007**$^{\#}$
Hypertension	6 (10.00)	7 (5.83)	0.363$^{\#}$
Hyperlipidemia	3 (5.00)	7 (5.83)	1.000$^{\#}$
Heart diseases	3 (5.00)	2 (1.67)	0.335$^{\#}$
Respiratory diseases	4 (6.67)	1 (0.83)	**0.043**$^{\#}$
Thyroid diseases	1 (1.67)	4 (3.33)	0.666$^{\#}$
Epilepsy	1 (1.67)	0 (0.00)	0.333$^{\#}$
Smoking, n (%)	16 (26.67)	34 (28.33)	0.953§
Alcohol use, n (%)	4 (6.67)	8 (6.67)	1.000$^{\#}$
Symptoms, n (%)			
Headache	55 (91.67)	-	-
Dizziness	15 (25.00)	-	-
Tinnitus	39 (65.00)	-	-
Visual problems	46 (76.67)	-	-
Berlin Q., n (%)			
Dimension 1 positive	29 (48.33)	34 (28.33)	**0.008**§
Dimension 2 positive	35 (58.33)	28 (23.33)	**<0.001**§
Dimension 3 positive	39 (65.00)	38 (31.67)	**<0.001**§
High risk	35 (58.33)	33 (27.50)	**<0.001**§
STOP-BANG Q., n (%)			
High risk	27 (45.00)	29 (24.17)	**0.004**§

IIH: idiopathic intracranial hypertension, BMI: body mass index, Q: questionnaire, †: Mann-Whitney U test, ‡: Student's t-test, §: chi-square test, $^{\#}$: Fisher's exact test, ¶: Fisher-Freeman-Halton test, descriptive statistics were presented as mean ± standard deviation for normally distributed continuous variables, median (25th - 75th percentile) for non-normally distributed continuous variables, and frequency (percentage) for categorical variables

attainment of a "high risk" outcome based on the Berlin questionnaire (odds ratio (OR): 9.366, 95% confidence interval (CI): 4.222-20.776, p<0.001). IIH (OR: 2.148, 95% CI: 0.985-4.684, p=0.055) was not found to be significant (Table 2).

High age (OR: 1.047, 95% CI: 1.002-1.094, p=0.042), male sex (OR: 5.692, 95% CI: 1.992-16.263, p=0.001), obesity (OR: 9.934, 95% CI: 3.948-24.996, p<0.001) and hyperlipidemia (OR: 17.905, 95% CI: 1.576-203.424, p=0.020) were found independently associated with being designated as "high risk" by the STOP-BANG questionnaire. Again, IIH (OR: 1.734, 95% CI: 0.743-4.048, p=0.203) was not independently associated with high-risk results from the STOP-BANG questionnaire (Table 3).

DISCUSSION

Idiopathic intracranial hypertension is a rare condition that occurs mainly in obese patients, and its etiology is unknown. Diagnostic criteria and treatment guidelines for IIH are still being modified (23). While the precise pathophysiological mechanisms underlying IIH remain elusive, obesity, hormonal irregularities, and OSA have been posited as potential risk factors contributing to the onset of IIH (9-11). On the contrary, studies on IIH as a risk factor for increased OSA risk are quite limited. This study aimed to examine the interconnection between IIH and OSA. Consequently, our findings revealed an increased likelihood of OSA among patients diagnosed with IIH compared to those without the condition.

Additionally, the IIH group had a higher BMI, percentage of obese patients, and percentage of patients with diabetes mellitus and respiratory diseases. Nonetheless, IIH did not emerge as an autonomous factor predisposing individuals to a heightened risk of OSA as per the evaluations derived from the Berlin and STOP-BANG questionnaires. As per the Berlin questionnaire, obesity was identified as the sole autonomous predictor associated with a heightened risk of OSA. As indicated by the STOP-BANG questionnaire, advanced age, male gender, obesity, and hyperlipidemia emerged as independent predictors correlating with an elevated risk of OSA. Although IIH is more prevalent among young individuals and women, OSA is more common in older individuals and men. However, several investigations have indicated an increased likelihood of IHH

Table 2. Logistic regression analysis results for high risk of Berlin questionnaire

	Univariate		Multivariate	
	OR (95% CI)	**p**	**OR (95% CI)**	**p**
Age	1.057 (1.024 - 1.091)	**0.001**	1.040 (0.997 - 1.085)	0.071
Gender (male)	2.155 (0.955 - 4.865)	0.065		
Obesity	12.758 (6.127 - 26.566)	**<0.001**	9.366 (4.222 - 20.776)	**<0.001**
Hypertension	10.614 (2.275 - 49.521)	**0.003**	1.268 (0.171 - 9.426)	0.817
Hyperlipidemia	4.169 (1.040 - 16.712)	**0.044**	1.463 (0.203 - 10.566)	0.706
Heart diseases	1.101 (0.179 - 6.762)	0.917		
Respiratory diseases	2.538 (0.413 - 15.593)	0.315		
Thyroid diseases	6.937 (0.759 - 63.417)	0.086		
Smoking	1.013 (0.517 - 1.984)	0.970		
Alcohol use	0.813 (0.235 - 2.808)	0.743		
IIH	3.691 (1.925 - 7.078)	**<0.001**	2.148 (0.985 - 4.684)	0.055

OR: odds ratio, CI: confidence interval, IIH: idiopathic intracranial hypertension, Nagelkerke R^2: 0.422

Table 3. Logistic regression analysis results for high risk of STOP-BANG questionnaire

	Univariate		Multivariate	
	OR (95% CI)	**p**	**OR (95% CI)**	**p**
Age	1.065 (1.031 - 1.101)	**<0.001**	1.047 (1.002 - 1.094)	**0.042**
Gender (male)	4.478 (1.931 - 10.385)	**<0.001**	5.692 (1.992 - 16.263)	**0.001**
Obesity	10.403 (4.833 - 22.388)	**<0.001**	9.934 (3.948 - 24.996)	**<0.001**
Diabetes mellitus	6.722 (1.711 - 26.411)	**0.006**	0.901 (0.131 - 6.213)	0.916
Hypertension	8.768 (2.309 - 33.290)	**0.001**	0.477 (0.062 - 3.692)	0.478
Hyperlipidemia	23.553 (2.904 - 191.025)	**0.003**	17.905 (1.576 - 203.424)	**0.020**
Heart diseases	1.494 (0.243 - 9.199)	0.665		
Respiratory diseases	3.453 (0.561 - 21.268)	0.182		
Thyroid diseases	1.494 (0.243 - 9.199)	0.665		
Smoking	0.617 (0.293 - 1.299)	0.204		
Alcohol use	1.639 (0.497 - 5.407)	0.417		
IIH	2.567 (1.329 - 4.959)	**0.005**	1.734 (0.743 - 4.048)	0.203

OR: odds ratio, CI: confidence interval, IIH: idiopathic intracranial hypertension, Nagelkerke R^2: 0.470

in individuals with OSA, and conversely. It is noteworthy that IIH alone leads to a twofold increase in the risk of cardiovascular morbidity (8). It is widely recognized that OSA represents a notable predisposing factor for the onset of type 2 diabetes, cardiovascular diseases, hypertension, and mortality (5). The concurrent occurrence of OSA in individuals diagnosed with IIH, or conversely, may be associated with an increased susceptibility to adverse health outcomes and mortality, potentially demonstrating a synergistic effect. Thus, assessing the potential coexistence of OSA in individuals with IIH, or vice versa, examining the likelihood of IIH in patients at elevated risk for OSA may mitigate individual or synergistic risks associated with morbidity and mortality linked to these respective conditions. Moreover, identifying additional risk factors contributing to these associations and implementing preventive measures against these factors could help prevent potential increases in adverse outcomes.

Although polysomnography stands as the primary diagnostic modality for OSA, its utilization is often deemed impractical (16). Alternative diagnostic tools have been developed to address these challenges. The Berlin and STOP-BANG questionnaires represent readily deployable screening instruments that have exhibited sensitivity in discerning the propensity for OSA (13). We therefore evaluated the increased risk of OSA with these two questionnaires. The IIH group had significantly higher positivity for the dimensions and overall results with these tests. In addition, the percentage of patients with diabetes mellitus and respiratory diseases was significantly higher in the IIH group compared to those without IIH. In a prospective study, BMI exhibited a statistically significant elevation in the cohort diagnosed with IIH compared to the control group. The percentage of patients with positive results for Berlin questionnaire dimensions 1 and 2 was significantly higher in the IIH group compared with the control group (13). In another study, the Berlin questionnaire was applied simultaneously with polysomnography in patients with IIH. While 75% of those with a high-risk Berlin questionnaire score had polysomnography-confirmed OSA, 70% of those with a low-risk Berlin questionnaire score did not have OSA (16). Another investigation demonstrated that following adjustments for BMI, males diagnosed with IIH exhibited a notably higher likelihood of presenting with a positive Berlin questionnaire or a documented history of OSA (19). A comprehensive retrospective cohort study showed that individuals with untreated sleep apnea had a twofold more significant risk of developing IIH. Moreover, following adjustments for age, gender, BMI, and concurrent medical conditions, continuous positive airway pressure therapy for OSA seemed to lower the likelihood of developing IIH (24). Yiangou et al. (4) demonstrated that individuals diagnosed with IIH who also presented with OSA exhibited poorer papilledema severity and visual field recovery after 12 months compared to those without OSA, notwithstanding similar alterations in intracranial pressure. This observation implies that OSA might worsen papilledema and visual dysfunction through shared or potentially synergistic pathways with IIH. Moreover, numerous prior investigations have indicated a heightened incidence of OSA among individuals diagnosed with IIH (10,11,15,25). However, some studies claim the opposite and report no connection between OSA and IIH. In a recent prospective study, no association was observed between OSA and IIH in terms of opening pressure and the severity of papilledema (26). Another investigation determined that the frequency and intensity of OSA among individuals diagnosed with IIH did not exceed anticipated levels relative to factors such as age, gender, ethnicity, BMI, and menopausal status (15). Youssef et al. (27) indicated that IIH did not constitute a predisposing factor for the occurrence or severity of OSA. While the majority of research aims have posited that individuals diagnosed with IIH encounter a heightened susceptibility to OSA, findings from the present study corroborate these assertions. However, the available evidence is insufficient to assert that IIH alone is an autonomous risk factor contributing to an elevated likelihood of developing OSA. Given that obesity, a significant confounding variable, represents a prevalent risk factor shared by both OSA and IIH.

The most important known common risk factor for both OSA and IIH is obesity. The frequency of IIH and OSA is escalating in tandem with the growing prevalence of obesity on a global scale (4,25,28). In the current study, mean BMI and percentage of obese patients were significantly higher in the IIH group compared to those without IIH. Although IIH did not emerge as an autonomous variable associated with a heightened risk of OSA based on the outcomes of multivariate analysis, obesity independently stood out as a risk factor contributing to elevated susceptibility to OSA across both survey methodologies. Several studies have illustrated bariatric surgery's clinical and economic efficacy in managing IIH (4,14,29,30). Yiangou et al. (4) investigated the effects of bariatric surgery on intracranial pressure, papilledema, OSA prevalence, and severity in women with IIH. They showed that bariatric surgery improved all of these characteristics in patients with IIH. In a 5-year randomized clinical trial, changes in the intracranial pressure of women diagnosed with IIH were investigated 12 months after bariatric surgery, showing significant decreases in post-operative data collection (14). It is essential at this point to note that high BMI is recognized as the strongest predictor of OSA, regardless of IIH (25). Our study showed that high BMI is a significant risk factor for both OSA and IIH, supporting previous studies. However, no definitive evidence links IIH as a risk factor to OSA. The link between IIH and OSA may be based on BMI value, possibly as a causative risk factor or a mediating parameter. However, it remains uncertain whether the existence or management of OSA influences the clinical trajectory of IIH. This issue needs to be investigated in more detail with more comprehensive, multicenter studies involving a large number of subjects.

Just as the frequency relationship between IIH and OSA is unclear, the pathophysiological connection mechanisms are also unclear (4). While the causal relationship between OSA and IIH remains ambiguous, pathophysiological and clinical associations probably exist between IIH, OSA, and obesity. Measurements of cerebrospinal fluid pressures reaching as high as 750 mm H_2O have been documented in individuals experiencing OSA during episodes of nocturnal apnea, indicating a potential correlation between OSA and elevated intracranial pressure (9,31). It is speculated that OSA and obesity may cause an increase in

the number of retinol-binding proteins that transport vitamin A or retinol in the blood, resulting in increased cerebrospinal fluid production and possibly decreased absorption. Another possible mechanism is that increased intra-abdominal pressure due to obesity and OSA leads to increased central venous pressure, preventing the absorption of cerebrospinal fluid. Hypoxia and hypercapnia induced by OSA can lead to cerebral vasodilation and augmented cerebral blood flow, thereby contributing to heightened intracranial pressure. Cerebral edema arising from hypoxia due to OSA could instigate a rise in intracranial pressure via the apneic stress response, liberation of excitatory neurotransmitters, or compromise of the blood-brain barrier, particularly in susceptible individuals (4,13,16,30,32-34). Additionally, it is already well known that OSA can negatively affect visual functions by causing microangiopathic complications (35,36). Intermittent nocturnal hypoxia as a result of OSA is thought to worsen the visual consequences of IIH by causing exacerbation of optic nerve ischemia. Based on these data, we recommend that all patients diagnosed with IIH be screened for the risk of OSA. However, for this screening purpose, using polysomnography, the gold standard in diagnosing OSA, has some difficulties, as mentioned above. The high-risk classification derived from the Berlin questionnaire demonstrates a sensitivity of 86% and specificity of 77% in identifying OSA compared to results obtained from sleep studies (20). Specific references have cited the STOP-BANG questionnaire as possessing the greatest sensitivity (84%) among screening assessments for identifying OSA in contrast to the Epworth Sleepiness Scale (69%) and the Berlin questionnaire (68%). However, it exhibits lower specificity (38%) compared to the Epworth Sleepiness Scale (74%) (4). According to the results of these two surveys in our study, findings indicating a high risk of OSA in patients with IIH were obtained. Nevertheless, the present investigation did not permit the examination of the accuracy of the Berlin and STOP-BANG questionnaires in diagnosing OSA, as polysomnography was not conducted on the study participants. Therefore, more data is needed regarding the usability of these questionnaires in detecting OSA risk in patients with IIH.

The current study was conducted in a single center, limiting its external validity. The number of participants in the IIH group was relatively small because IIH is not a common disease. OSA evaluation was made through surveys. Polysomnography was not applied because it was not compatible with study practice. Significant differences in comorbidity and BMI between IIH and control groups have made it difficult to evaluate the pure OSA risk in patients with IIH. A possible longitudinal relationship between IIH and OSA has been ignored because the time to diagnosis of patients with IIH is not available. Longitudinal studies tracking improvement in IIH after treatment of OSA or obesity are required to definitively comment on the cause-and-effect relationship between IIH, OSA, and obesity. This study was not designed to investigate which morbidities OSA causes to increase the risk in patients with IIH. Examining these factors will substantially enhance comprehension of the synergistic impacts of these two conditions on concurrent medical conditions.

CONCLUSION

Patients with IIH showed higher rates of obesity and a higher risk of OSA compared to the control group. However, IIH was not an independent predictor of high OSA risk. Male sex, older age, obesity, and hyperlipidemia are independent factors associated with a high risk of OSA. Obesity represents a prevalent risk factor shared by both OSA and IIH. The coexistence of OSA and IIH may cause a synergistic effect on increased morbidity and mortality rates in both diseases. Henceforth, individuals diagnosed with IIH should undergo screening for OSA risk utilizing the Berlin and STOP-BANG questionnaires or other validated screening methodologies.

Ethics Committee Approval: The study was approved by the Clinical Research Ethics Committee of Başakşehir Çam and Sakura City Hospital (13.09.2023, 422).

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REFERENCES

1. Elsaid N, Ahmed O, Belal T, Razek A, Azab A. Pathogenesis and evaluation of the effects of idiopathic intracranial hypertension on the optic nerves. Neuroophthalmology. 2020;44(5):281-9.
2. Akçakaya NH, Akçakaya MO, Sencer A, Yapıcı Z. Idiopathic intracranial hypertension: diagnosis and therapeutic approach. Turk J Neurol. 2017;23(2):43-50.
3. Wakerley BR, Mollan SP, Sinclair AJ. Idiopathic intracranial hypertension: Update on diagnosis and management. Clin Med (Lond). 2020;20(4):384-8.
4. Yiangou A, Mitchell JL, Nicholls M, Chong YJ, Vijay V, Wakerley BR, et al. Obstructive sleep apnoea in women with idiopathic intracranial hypertension: a sub-study of the idiopathic intracranial hypertension weight randomised controlled trial (IIH: WT). J Neurol. 2022;269(4):1945-56.
5. Adderley NJ, Subramanian A, Nirantharakumar K, Yiangou A, Gokhale KM, Mollan SP, et al. Association between idiopathic intracranial hypertension and risk of cardiovascular diseases in women in the United Kingdom. JAMA Neurol. 2019;76(9):1088-98.
6. Jensen RH, Radojicic A, Yri H. The diagnosis and management of idiopathic intracranial hypertension and the associated headache. Ther Adv Neurol Disord. 2016;9(4):317-26.
7. Maurer JT. Early diagnosis of sleep related breathing disorders. GMS Curr Top Otorhinolaryngol Head Neck Surg. 2008;7:Doc03.
8. Adderley NJ, Subramanian A, Toulis K, Gokhale K, Taverner T, Hanif W, et al. Obstructive sleep apnea, a risk factor for cardiovascular and microvascular disease in patients with type 2 diabetes: Findings from a population-based cohort study. Diabetes Care. 2020;43(8):1868-77.

9. Purvin VA, Kawasaki A, Yee RD. Papilledema and obstructive sleep apnea syndrome. Arch Ophthalmol. 2000;118(12):1626-30.
10. Marcus DM, Lynn J, Miller JJ, Chaudhary O, Thomas D, Chaudhary B. Sleep disorders: a risk factor for pseudotumor cerebri? J Neuroophthalmol. 2001;21(2):121-3.
11. Lee AG, Golnik K, Kardon R, Wall M, Eggenberger E, Yedavally S. Sleep apnea and intracranial hypertension in men. Ophthalmology. 2002;109(3):482-5.
12. Fraser CL, Bliwise DL, Newman NJ, Lamirel C, Collop NA, Rye DB, et al. A prospective photographic study of the ocular fundus in obstructive sleep apnea. J Neuroophthalmol. 2013;33(3):241-6.
13. Elsaid N, Mosa AAH, Saied A. Screening for obstructive sleep apnea in a sample of Egyptian idiopathic intracranial hypertension female patients using the Berlin questionnaire. Mansoura Med J. 2023;52(1):15-19.
14. Mollan SP, Mitchell JL, Ottridge RS, Aguiar M, Yiangou A, Alimajstorovic Z, et al. Effectiveness of bariatric surgery vs community weight management intervention for the treatment of idiopathic intracranial hypertension: a randomized clinical trial. JAMA Neurol. 2021;78(6):678-86.
15. Thurtell MJ, Trotti LM, Bixler EO, Rye DB, Bliwise DL, Newman NJ, et al. Obstructive sleep apnea in idiopathic intracranial hypertension: comparison with matched population data. J Neurol. 2013;260(7):1748-51.
16. Thurtell MJ, Bruce BB, Rye DB, Newman NJ, Biousse V. The Berlin questionnaire screens for obstructive sleep apnea in idiopathic intracranial hypertension. J Neuroophthalmol. 2011;31(4):316-9.
17. Chung F, Abdullah HR, Liao P. STOP-Bang questionnaire: A practical approach to screen for obstructive sleep apnea. Chest. 2016;149(3):631-8.
18. Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology. 2013;81(13):1159-65.
19. Fraser JA, Bruce BB, Rucker J, Fraser LA, Atkins EJ, Newman NJ, et al. Risk factors for idiopathic intracranial hypertension in men: a case-control study. J Neurol Sci. 2010;290(1-2):86-9.
20. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Intern Med. 1999;131(7):485-91.
21. Karakoc O, Akcam T, Genc H, Yetkin S, Piskin B, Gerek M. Use of the Berlin questionnaire to screen at-risk patients for obstructive sleep apnea. B-ENT. 2014;10(1):21-5.
22. Ulukavak Çiftçi T, Çiftçi B; Turkish Thoracic Society Sleep Breathing Disorders Study Group. Turkish Thoracic Society obstructive sleep apnea syndrome diagnosis and treatment consensus report. Turk Thorac J. 2012;13(Suppl 1):1-66. Turkish.
23. Ziemska-Gorczyca M, Woźniak, M, Dżaman K. Otoneurological symptoms in idiopathic intracranial hypertension. Pol Otorhino Rev. 2023;12(1):35-41.
24. Stein JD, Kim DS, Mundy KM, Talwar N, Nan B, Chervin RD, et al. The association between glaucomatous and other causes of optic neuropathy and sleep apnea. Am J Ophthalmol. 2011;152(6):989-98.e3.
25. Kabanovski A, Chan A, Shapiro C, Margolin E. Obstructive sleep apnea in men with idiopathic intracranial hypertension: a prospective case-control study. J Neuroophthalmol. 2023;43(4):531-4.
26. Ajjeya MT, Sudhakar P. Role of obstructive sleep apnea in idiopathic intracranial hypertension. Neurology; 2023;100(17 Suppl 2):P10-4.004.
27. Youssef M, Sundaram ANE, Veitch M, Aziz A, Gurges P, Bingeliene A, et al. Obstructive sleep apnea in those with idiopathic intracranial hypertension undergoing diagnostic in-laboratory polysomnography. Sleep Med. 2024;114:279-89.
28. Senaratna CV, Perret JL, Lodge CJ, Lowe AJ, Campbell BE, Matheson MC, et al. Prevalence of obstructive sleep apnea in the general population: A systematic review. Sleep Med Rev. 2017;34:70-81.
29. Aguiar M, Frew E, Mollan SP, Mitchell JL, Ottridge RS, Alimajstorovic Z, et al. The health economic evaluation of bariatric surgery versus a community weight management intervention analysis from the Idiopathic Intracranial Hypertension Weight Trial (IIH:WT). Life (Basel). 2021;11(5):409.
30. Elliot L, Frew E, Mollan SP, Mitchell JL, Yiangou A, Alimajstorovic Z, et al. Cost-effectiveness of bariatric surgery versus community weight management to treat obesity-related idiopathic intracranial hypertension: evidence from a single-payer healthcare system. Surg Obes Relat Dis. 2021;17(7):1310-6.
31. Sugita Y, Iijima S, Teshima Y, Shimizu T, Nishimura N, Tsutsumi T, et al. Marked episodic elevation of cerebrospinal fluid pressure during nocturnal sleep in patients with sleep apnea hypersomnia syndrome. Electroencephalogr Clin Neurophysiol. 1985;60(3):214-9.
32. Baronio D, Martinez D, Fiori CZ, Bambini-Junior V, Forgiarini LF, Pase da Rosa D, et al. Altered aquaporins in the brains of mice submitted to intermittent hypoxia model of sleep apnea. Respir Physiol Neurobiol. 2013;185(2):217-21.
33. Fung SJ, Xi MC, Zhang JH, Sampogna S, Yamuy J, Morales FR, et al. Apnea promotes glutamate-induced excitotoxicity in hippocampal neurons. Brain Res. 2007;1179:42-50.
34. Lim DC, Pack AI. Obstructive sleep apnea and cognitive impairment: addressing the blood-brain barrier. Sleep Med Rev. 2014;18(1):35-48.
35. Shiba T, Maeno T, Saishin Y, Hori Y, Takahashi M. Nocturnal intermittent serious hypoxia and reoxygenation in proliferative diabetic retinopathy cases. Am J Ophthalmol. 2010;149(6):959-63.
36. Mojon DS, Hedges TR 3rd, Ehrenberg B, Karam EZ, Goldblum D, Abou-Chebl A, et al. Association between sleep apnea syndrome and nonarteritic anterior ischemic optic neuropathy. Arch Ophthalmol. 2002;120(5):601-5.