

Relation between Obstructive Sleep Apnea-Hypopnea Syndrome and Glaucoma in a Sub-Saharan African Population

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Abstract

Introduction: Obstructive sleep apnea-hypopnea syndrome (OSAHS) is a frequent pathology worldwide whose main mechanism is a complete or partial obstruction of the upper airway. One of the pathophysiological mechanisms described in primary open-angle glaucoma is that hypoxia in the optic nerve progressively destroys the retinal cells leading to the onset and/or aggravation of glaucoma. The aim of the study was to evaluate the risk of OSA in patients with primary open-angle glaucoma. **Methodology:** An analytical study was conducted from January to May 2020 at the UHC. After obtaining ethical clearance, 112 patients including 50 glaucoma patients (44.64%) and 62 in the control group were enrolled. Sociodemographic and clinical data were collected from the medical records of the participants, with or without glaucoma, and a questionnaire was administered and a clinical examination performed. The STOP BANG score was used to determine the risk level of OSAHS. Statistical analyses were performed using Epi Info version 7.2. **Results:** A female predominance was found (60%) in the glaucoma group with a mean age of 55 ± 17 years against 49 ± 18 years in the control group. The high risk of OSAHS was more associated with glaucoma patients. In glaucoma patients, an association was found between high risk of OSAHS and snoring (OR = [1.43 - 849.53]; $p = 0.029$) as well as insomnia (OR = [1.36 - 482.86]; $p = 0.030$). **Conclusion:** High risk of OSAHS was found in participants with chronic open-angle glaucoma. Signs of OSAHS should be sought in chronic open-angle glaucoma as it may be a factor in its progression.

Keywords

Obstructive Sleep Apnea-Hypopnea Syndrome, Glaucoma, Risk Factor,

1. Introduction

Glaucoma is a major cause of blindness worldwide [1], with the Primary chronic open angle glaucoma being the predominant form in Africa [2]. In Cameroon, the prevalence of glaucoma is between 4.5% and 8.2% according to the authors [3] [4]. Its exact origin remains unknown. However, many risk factors have been incriminated in its pathogenesis among which are vascular factors [5] [6] [7]. An association between glaucoma and obstructive sleep apnea and hypopnea syndrome (OSAHS) has been previously described in literatures [8] [9] [10]. OSAHS has also been implicated as a risk factor in glaucoma [8] [9] [11]. In OSAHS, microangiopathy, hypoxia, and vascular dysregulation have been implicated in optic nerve head damage in glaucoma [12] [13]. OSAHS is a common condition worldwide [14] which first reports dated back to 1976, according to Guillemault [15]. At the beginning, it was described as Pickwick's syndrome in obese people [16]. Studies have been conducted on OSAHS in sub-Saharan Africa and mostly conducted on hospitalized patients [17] [18] [19] [20]. These studies report that OSAHS is a common condition in Cameroon whose presence is associated with arterial hypertension [21] [22]. Given the prevalence of primary open angle glaucoma in our context, we went out to investigate its relationship with OSAHS. The aim of the present study was to evaluate the level of risk of OSAHS in patients with chronic open-angle glaucoma in Yaoundé.

2. Materials and Method

Type and context of the study

This cross-sectional study, conducted over a period of 5 months from January to May 2020, was carried out in the University Teaching Hospital Center in Yaoundé. All patients aged 21 years and older were eligible for the study. The study population consisted of patients seen in eye unit with confirmed chronic open-angle glaucoma for the case group while the controls had no form of glaucoma. Patients with other forms of glaucoma or participants unable to complete the questionnaires were excluded. Participants were recruited consecutively during the inclusion period.

Procedure

Patients meeting the eligibility criteria were included in the study after consent was obtained. Sociodemographic, anthropometric, and clinical data were collected on a data sheet created for this purpose. A review of the medical records provided additional information, particularly concerning the various investigations undertaken to confirm glaucoma. The diagnosis of open angle glaucoma was confirmed for any patient presenting in one or both eyes, papillary alterations associated with visual field defects, as well as an opened iridocorneal angle

according to the Shaffer classification [23], independent of the intraocular pressure. The visual field was considered as pathologic according to the criteria proposed by the American Academy of Ophthalmology [24] when the loss of sensitivity was greater than 5 dB with changes in global indices.

Analysis of the risk of OSAHS

The STOP BANG score was used for risk assessment of OSAHS [19] [25] [26]. For its interpretation, low risk of OSAHS corresponded to a positive response to 0 - 2 questions of the score. Medium risk was defined as a positive response to 3 - 4 questions, and high risk as a positive response to 5 - 8 questions or at least 2 of the first 4 questions for male participants or at least 2 of the first 4 questions with a BMI > 35 kg/m² or at least 2 of the first 4 questions with a neck circumference greater than 43 cm in men and 41 cm in women. To facilitate analysis of the variables, we considered 02 modalities: low risk and high risk (moderate and advanced) (See **Table 1**).

Data collection

The sociodemographic variables recorded were: age and gender. The comorbidity investigated was hypertension. Anthropometric parameters collected were weight, height, abdominal circumference; and the calculation of the body mass index was performed. Concerning the ophthalmological variables, the measurement of papillary excavation (Cup/Disc ratio) and the parameters of the automatic visual field (MD: median deviation, LV: loss variance) were obtained. For the OSAHS symptoms, insomnia, snoring, morning headaches were investigated through a questionnaire administered to the participant and a relative.

Ethical considerations

The study was approved by the Institutional Ethics Committee of Université des Montagnes, Cameroon. The study received administrative approval from the University Hospital of Yaoundé and free and informed consent from all participants.

Statistical analysis

The collected data were analyzed using Epi Info version 7.2. Central trend (mean, mode, median) and dispersion (standard deviation, interquartile range) parameters were used to report continuous variables. Categorical variables were represented as percentages, proportions, and/or frequency. The chi² test was

Table 1. Questionnaire STOP BANG [19].

Has anyone ever told you that you snore?
Are you tired or drowsy during the day?
Has anyone observed you stop breathing or suffocate while sleeping?
Do you have high blood pressure
Body mass index > 35 Kg/m ²
Age > 50years
abdominal circumference > 94 cm for men (>80 cm for women)

used to compare proportions and odds ratios to measure the strength of an association between two variables. A p value of less than 5% was considered statistically significant. For variables that were considered significant in univariate analysis, we performed a multivariate analysis using logistic regression to eliminate confounding factors.

3. Results

Sociodemographic and clinical data

A total of 112 participants, 50 in the glaucoma group and 62 in the control group. The glaucoma group was predominantly female, consisting of 30 (60%) women and 20 (40%) men, for a sex ratio of 0.67.

The mean age of the study population was 55 ± 17 years in the glaucoma patients and 49 ± 18 years in the control group. In the glaucomatous participants, the predominant age range was 50 to 60 years. There was no statistically significant difference in age ($p = 0.081$) and sex ($p = 0.70$) between the 2 groups [Table 2].

Ophthalmological findings

The median of the visual field values found was for the median deviation (MD) at 2.1 dB [Interquartiles: 0.7 - 5.2; extremes: 0.06 - 23.50] in the right eye and 2.7 dB [Interquartiles: 0.9 - 8.6; extremes: 0.13 - 29.05] in the left eye. For the LV (Loss Variance), the value was 5.25 dB [Interquartiles: 3.6 - 7.6; Extremes: 1.70 - 68.90] in the right eye and 5.3 dB [Interquartiles: 3.2 - 9.2; Extremes: 1.50 - 62.10] in the left eye. For the papillae, the mean cup/disc ratio was 0.66 ± 0.18 [0.3 - 1] and 0.71 ± 0.15 [0.3 - 1] in the right and left eyes, respectively,

Table 2. Description of the study population.

	Glaucomatous patients [N = 50]	Controls [n = 62]	P value
Men [women]	20 [30]	27 [35]	0.84
Age (years) [Minimum - maximum]	55 + 17 [18 - 83]	48 + 19 [17 - 83]	
Age > 40 years	40 [80%]	42 [68%]	0.006
Presence of Arterial Hypertension	15 [30%]	15 [24.59%]	<0.001
Abdominal circumference (cm) [Minimum - maximum]	88.42 + 11.05 [71 - 119]	83.06 + 10.17 [69 - 124]	
Abdominal circumference > 80 cm	41 [82%]	36 [58%]	0.035
BMI (kg/m ²) [Minimum - maximum]	27.79 + 4.61 [21 - 40.46]	26.87 + 4.08 [14.76 - 38.70]	
BMI > 26 kg/m ²	24 [53%]	28 [51%]	0.04
Snoring [%]	29 [58]	25 [40.32]	<0.001
Insomnia [%]	22 [44]	22 [35.48]	0.0005
Morning headache [%]	08 [16]	10 [16.13]	0.05

BMI: body mass Index.

in glaucoma patients.

Risk analysis of OSAHS in glaucomatous participants.

A significant difference was found between the two groups ($p = 0.0148$), notably a low risk in the majority of the control group with a proportion of 66.15%. The medium (62.50%) and high (57.14%) risks were found mostly in the glaucoma group.

Figure 1 shows the level of risk of OSAHS in the different groups according to the STOP BANG evaluation score.

Figure 2 depicts the distribution of OSAHS in the two populations according to high (medium and advanced) risk and low risk. In this figure, there is an association between high risk OSAHS and glaucoma patients with the linear regression curve decreasing from glaucoma patients to controls. Indeed, glaucoma patients are three times more at risk of belonging to the high-risk group for OSAHS. In contrast, low-risk patients are more likely to be in the control group.

Factors associated with OSAHS in the glaucoma population.

Table 3 represents the association between the risk level of OSAHS in glaucoma patients and abdominal circumference and body mass index (BMI). There is a correlation between the increase in anthropometric parameters and the risk level of OSAHS.

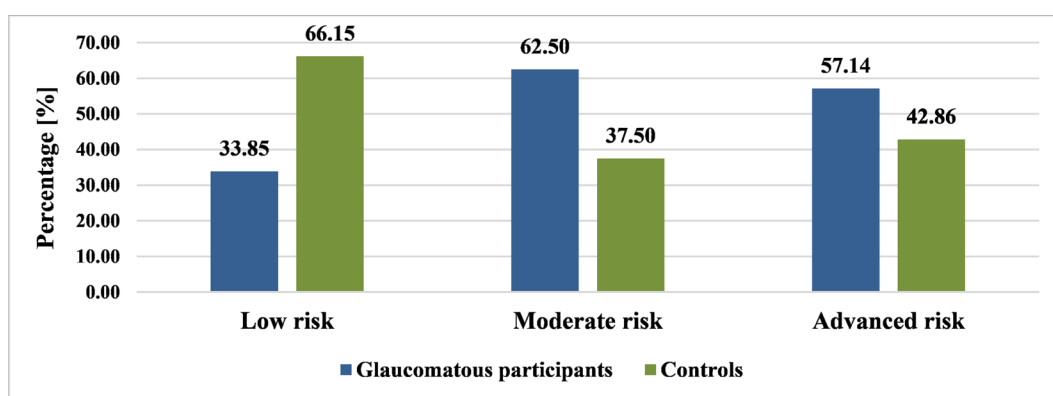


Figure 1. Risk level of OSAHS in glaucoma and control participants.

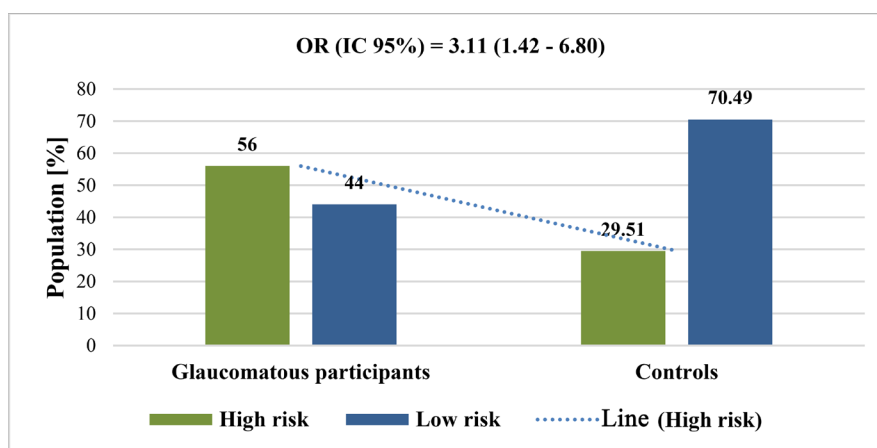


Figure 2. Comparison of the risk of OSAHS between glaucoma patients and controls.

It was found that there was a strong significance ($P < 0.001$) between the increased risk of OSA and the increase in abdominal circumference. The same is true for BMI ($P = 0.00001$). Thus, it can be seen from **Table 3** that as abdominal circumference and body mass index increase, the level of risk increases.

After eliminating confounding factors by logistic regression, it appears that snoring and insomnia are independent factors associated with high risk of OSAHS in glaucoma patients (**Table 4**). Indeed, the presence of snoring multiplies the risk by 35, whereas insomnia multiplies it by 26.

The independent factors associated with high risk of OSAHS in controls are represented in **Table 5**.

Table 3. Association between the level of OSAHS and anthropometric parameters in glaucoma patients.

Variables (mean + Standard deviation)	OSAHS			P value	Coefficient of correlation
	low	Medium	advanced		
AC (cm)	83 ± 7	87 ± 9	106 ± 9	<0.001	0.51
BMI (Kg/m ²)	26 ± 3	27 ± 4	34 ± 5	0.00001	0.28

AC: Abdominal circumference; BMI: body mass index.

Table 4. Independent factors associated with OSAHS after adjustment for confounding factors in glaucoma patients.

Variables	Adjusted odds ratio	Adjusted p value
Age > 40 years (yes/no)	3.14	0.199
Snoring (yes/no)	34.85	0.029
Insomnia (yes/no)	25.64	0.030
Arterial Hypertension (yes/no)	1,100,741.42	0.960
Abdominal circumference > 80 cm	0.67	0.790
BMI > 26 kg/m ² (yes/no)	1.42	0.4641
Morning headache	2.05	0.599

BMI: Body mass index.

Table 5. Independent factors associated with OSAHS in the control group.

Variables	Adjusted odds ratio	Adjusted p value
Age > 40 years (yes/no)	4.52	0.185
Snoring (yes/no)	23.26	<0.001
Insomnia (yes/no)	9.07	0.115
HTA (yes/no)	16.80	<0.001
Abdominal Circumference > 80 cm	1.88	0.458
BMI > 26 Kg/m ² (yes/no)	1.91	0.462
Morning headache	7.52	0.020

BMI: Body mass index.

In the previous table, the independent factors associated with high risk of OSAHS in control participants are snoring, hypertension, and morning headache. Indeed, snoring increased the risk by 23-folds, whereas hypertension increased it by 17-folds and headache by 8-folds.

4. Discussion

The objective of this study was to assess the risk level of OSAHS in glaucoma patients. In the present study, 112 patients, including 50 glaucoma patients and 62 in the control group, were selected.

In sub-Saharan Africa, glaucoma is predominantly detected in people over 40 years of age [2], with age over 40 years recognized as a risk factor for glaucoma. In the present series, the mean age for glaucoma participants was 55 ± 17 years, whereas it was 49 ± 18 years for controls. The most represented age group was 50 - 60 years. In Cameroon, the average age of glaucoma is over 50 years. In the study by Ellong *et al.*, the mean age of glaucoma patients was 53 ± 17 years and that reported by Eballé *et al.* was 62 ± 13 years [4] [27]. An African study (Cote d'Ivoire) on the association of OSAHS with primary open-angle glaucoma reported an age group of 40 to 50 years [28].

In the present series, glaucoma was predominant in female patients; 60% of cases. This female predominance was also found by Balbay *et al.* in Turkey [29] and Onen *et al.* in France [30], 54.3% and 57.1% respectively. On the other hand, there is a male predominance in the study conducted by Wozniak *et al.* [31]. Our results could be justified by the fact that women are more numerically represented and more health conscious hence their high participation in the study.

Regarding the structural evaluation, the mean cup/disc ratio at 0.66 ± 0.18 and 0.71 ± 0.15 on the right and left, respectively. These results are similar to those found by Ellong *et al.* where the mean cup/disc ratio was 0.7 ± 0.2 in both eyes in glaucoma patients [4]. This may be explained by the fact that glaucoma is an asymptomatic disease in its early stages and the majority of patients were detected at an advanced stage of the disease.

In the present series, the low risk of OSAHS was predominantly found in the control group (66.15%). In glaucoma patients, the medium (62.50%) and advanced (57.14%) risks were more frequent. Moreover, it appears from this study that high risk of OSAHS was multiplied by 3 in participants with chronic open angle glaucoma. Studies have shown that OSAHS is more frequent in glaucoma patients than in the control group. Indeed, Wozniak *et al.* [31] reported that among patients with moderate and severe forms of OSAHS, glaucoma patients accounted for 22% compared to 16% among controls. It can also be noted that the high risk of OSAHS is prevalent in glaucoma patients compared to the low risk. Moreover, the high risk of OSAHS decreased in the control group while the low risk predominated in this group as illustrated in the present study. These results are similar to those found by Lin *et al.* (2013) who had reported in a cohort study that OSAHS increases the 5-year risk of glaucoma [9]. In addition,

Mojon *et al.* in 2000 also found that glaucoma patients had more cases of OSAHS and that it could be considered a risk factor for chronic open angle glaucoma [32]. This can be explained by the fact that pathophysiologically, OSAHS, due to the hypoxia it induces, will lead to chronic papillary hypoperfusion. The chronic hypoperfusion will lead to cell apoptosis with progressive destruction of the optic nerve head fibers and therefore to glaucoma by an ischemic mechanism [9] [32].

The study of factors associated with high risk of OSAHS in the present series shows that snoring ($P < 0.001$) is found to be the predominant sign in the high risk group of OSAHS. It multiplies the risk by 20 in glaucoma patients and 31 in controls. According to the work of Onen *et al.*, snoring was found in 47.6% of cases in glaucoma patients with a significant difference compared to controls ($p = 0.04$) [30]. Balbay *et al.*, reported that snoring was present in all glaucoma participants with OSA [29]. Koffi *et al.* also reported that snoring predominated in glaucomatous participants (63.3%) compared to controls (36.7%) [28]. Massongo *et al.* also found snoring to be a symptom associated with OSAHS [18]. This can be explained by the fact that in OSAHS, snoring is related to the vibration of the muscles and mucosae of the throat relaxed by sleep following the passage of respiratory air. The same is true for abdominal circumference and body mass index, whose increase was significantly related to the increased risk of OSAHS in glaucoma patients. The present study also shows that high blood pressure is not associated with OSAHS in glaucoma patients in contrast to participants in the control group. Intermittent hypoxia would lead to oxidative stress which results in vascular and systemic inflammation favoring the development of arterial hypertension [33]. On the other hand, Wozniak *et al.* in 2019 reported that arterial hypertension is more common in glaucoma patients (107) compared to controls [31].

In control participants, morning headaches were associated with high risk of OSAHS. This may be explained by the fact that OSAHS generates nocturnal micro awakenings thus participating in the fragmentation of sleep at night, hence the appearance of headaches early in the morning. These results are superimposed on those of Agrebi *et al.* (2017) who stated that OSAHS is associated with morning headaches [34]. Insomnia ($p < 0.001$) was significantly associated with the high risk of OSAHS in the glaucoma group, this being explained by the apneas and hypopneas that occur during OSAHS and which generate episodes of nocturnal awakenings. In a study conducted by Omarjee *et al.* (2019), insomnia was also found in 53% of cases in patients with glaucoma [35]. Daytime sleepiness has also been reported as a symptom more frequently associated with primary open angle glaucoma [28]. This justifies the search of OSAHS in patients with glaucoma and its multidisciplinary management to prevent the progression of glaucoma.

Limitations of the Study

Throughout this study, an association between glaucoma and high risk of

OSAHS was found. Confirmation with polysomnography of OSAHS would have provided a diagnosis of certainty. However, the tool used for risk assessment of OSAHS whose validity on African populations has been reported, was relevant to this work [Bassogbag, 2017].

5. Conclusion

In the present study, chronic open-angle glaucoma was diagnosed at an advanced stage and with a 3-fold increase in risk for high risk of OSAHS in this population. OSAHS in glaucoma patients was associated with snoring and insomnia. However, it was not associated with arterial hypertension as found in control patients. Signs of OSAHS should be investigated in glaucoma patients because it could be a factor involved in the progression of glaucoma.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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