

Obstructive Sleep Apnea and Floppy Eyelid Syndrome: An Eye Opener

Nileena NKM¹, Nagarajan Ramakrishnan², Mary I Charles³, Hema Deenadayalan⁴, Lakshmi Ranganathan⁵

ABSTRACT

Aim and objective: Obstructive sleep apnea (OSA) is a common yet underdiagnosed sleep disorder associated with partial or complete obstruction of upper airway during sleep. Floppy eyelid syndrome (FES) is another frequently overlooked diagnosis associated with lax upper eyelids, a soft and foldable tarsus, and a chronic papillary conjunctivitis of the upper palpebral conjunctiva. There has been growing literature to support the association between the two, and this study explores the same and also the clinical implications.

Materials and methods: Retrospective study from 2015 to 2018 at a freestanding sleep clinic, India. Patients who were diagnosed with FES at an ophthalmic care hospital, and referred for evaluation of suspected OSA based on symptoms of snoring and daytime hypersomnolence were included in the study. Subjects underwent clinical evaluation and polysomnography, if required.

Results: All the referrals were males and the mean age was 49.8 ± 13.4 . Of 51 patients, 13 (25.4%) were not willing to undergo sleep study as they were unwilling to accept the possible association of OSA and FES and/or could not afford additional testing. Thirty-six of the 38 patients with FES were diagnosed of OSA (94.8%) and 20 of 38 had severe OSA (55.5%). Of the 38 patients diagnosed with OSA, only one patient accepted continuous positive airway pressure (CPAP) therapy.

Conclusions: Ophthalmologists were able to effectively screen patients for OSA with simple screening questions about snoring and daytime hypersomnolence. The association between OSA and FES was significant but a large proportion of patients were not ready to undergo sleep study or commence treatment despite being diagnosed and explained the consequences of untreated severe OSA.

Keywords: Floppy eyelid, Obstructive sleep apnea, Snoring.

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INTRODUCTION

Obstructive sleep apnea (OSA) is characterized by periodic, partial, or complete obstruction in the upper airway during sleep resulting in intermittent hypoxia and hypercapnea which further triggers repetitive arousal from sleep in order to reestablish airway patency.¹ Our understanding of the pathophysiology and clinical implications of OSA has come a long way since its discovery in 1965.¹ A meta-analysis by Franklin and Lindberg² inferred that the prevalence of OSA is about 22% (4–50%) and has been increasing over the years due to improved diagnostic modalities and changes in the criteria and grading of severity of the illness. The diagnosis of OSA is ascertained by polysomnography which aims at identifying nocturnal obstructive events and the subsequent changes in blood oxygen. The severity of OSA is primarily based on apnea-hypopnea index (AHI), calculated as the number of obstructive events per hour of sleep.¹ Treatment modalities for OSA include lifestyle modifications, positive airway pressure (PAP) therapy, oral appliances, and palate-pharyngeal surgeries. OSA is noted to be frequently associated with various other diseases.³ Most commonly observed associations comprise of cardiovascular diseases like systemic hypertension, coronary artery disease, arrhythmias, and ischemic stroke; respiratory diseases, such as chronic obstructive pulmonary disease (COPD) and bronchial asthma; metabolic disorders including diabetes mellitus, dyslipidemia, gout, and obesity; gastrointestinal disorders (gastroesophageal reflux disorders and chronic liver disease); psychiatric disturbances including depression, anxiety, and insomnia; and ophthalmologic conditions like glaucoma, floppy eyelid syndrome (FES), and keratoconus.^{2–5}

Recent studies have suggested that OSA can be suspected based on presence of ocular disorders.⁶ First discovered in 1981,

^{1–5}Nithra Institute of Sleep Sciences, Chennai, Tamil Nadu, India

Corresponding Author: Nagarajan Ramakrishnan, Nithra Institute of Sleep Sciences, Chennai, Tamil Nadu, India, Phone: +91 44 4350 2252, e-mail: ram@nithra.com

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FES is one such ophthalmic disorder which has been found to be associated with OSA. FES is characterized by lax upper eyelids that evert effortlessly on elevation, a soft and foldable tarsus, and a chronic papillary reaction (conjunctivitis) of the upper palpebral conjunctiva.⁶ There is growing literature to suggest that OSA is the most frequently associated systemic disease with FES. Various theories have been put forward to explain the underlying pathophysiology linking the two disorders, like repeated mechanical trauma due to pressure from sleeping on one side and chronic inflammation attributed to hypoxia further exacerbated by reperfusion injury causing connective tissue weakness.⁷

Studies have been conducted to look into the prevalence of OSA in FES and vice versa. The prevalence of OSA in patients with FES was observed to be as high as 96% and the prevalence of FES in patients with OSA has been reported to be anywhere between 2% and 33%.⁷ An Indian study by Tyagi et al.⁸ identified that among 81 patients with FES, 60 (74.1%) had significant values

on Berlin questionnaire; 24.1% of these patients were confirmed on polysomnography.

In the current study, we aimed at evaluating the prevalence of OSA in patients with a confirmed diagnosis of FES. We also explored the willingness for further evaluation and management of OSA.

MATERIALS AND METHODS

This is a retrospective cross-sectional study conducted in a freestanding sleep clinic in Chennai from 2015 to 2018. Patients who were diagnosed with FES at an ophthalmic care hospital and referred to the sleep clinic for evaluation of suspected OSA were included in the study.

Preassessment at the Ophthalmic Center

- Diagnosis of FES was made at the ophthalmic center, based on the following clinical criteria:
 - Lax, distensible tarsal plate.
 - Papillary changes of the conjunctiva.
 - Ready eversion of tarsal plates in classical cases on superior traction of the eyebrow.
- Patients who were diagnosed with FES were further screened for presence of OSA. Patients were asked if they had snoring or excessive daytime somnolence. If they screened positive for possible OSA, they were referred to the sleep clinic for further evaluation by the sleep physician.

Assessment at the Sleep Center

- Level III cardiorespiratory sleep study was advised if there was a high pretest probability of OSA based on sleep clinic evaluation.
- Level I polysomnography and multiple sleep latency test (MSLT) were conducted if there was a suspicion of other sleep disorders like insomnia, restless leg syndrome, or narcolepsy.
- The severity of OSA was graded using AHI as per American Academy of Sleep Medicine (AASM) criteria,⁹ as normal <5, mild—5–15, moderate >15–30, and severe >30.

Inclusion Criteria

All the patients with FES who were referred from the ophthalmic center for evaluation of OSA were included in the study, with no exclusions. As this was a retrospective observational study, patients' details were de-identified before data analysis and ethical conflicts were thereby eliminated.

Statistical Analysis

Data were summarized by routine descriptive statistics to describe the demographic and clinical characteristics including age, gender, clinical diagnosis, comorbidities, and severity of OSA. Mean values for AHI and percentage of patients belonging to each category of OSA were estimated and follow up status of patients were analyzed.

RESULTS

The study was conducted from January 2015 to December 2018. During this period, 51 patients with FES were referred consecutively to the sleep clinic and all of them were included in the study. All the referrals were males and the mean age was 49.8 ± 13.4 . One of the patients had ENT related complaints and was referred to otolaryngorhinologist, and excluded from analysis. Two patients had their polysomnography done elsewhere before presenting to our clinic. Based on clinical assessment of the remaining 48 patients,

Table 1: Severity of obstructive sleep apnea (OSA) based on apnea-hypopnea index

| Severity of OSA | Number of patients (%) |
|-----------------|------------------------|
| Normal | 2 (5.2) |
| Mild | 9 (23.6) |
| Moderate | 7 (18.4) |
| Severe | 20 (52.6) |
| Total | 38 (100) |

all of them required sleep studies (46 patients required Level III polysomnography, one patient required level I polysomnography, and one required level I polysomnography with MSLT). Of these 48 patients who were prescribed PSGs, 12 (24%) were unwilling to undergo sleep study as they were disinclined to accept the possible association of OSA and FES and/or could not afford additional testing. Risk factors such as weight gain (15.7%) and comorbidities including hypertension (13.7%) and diabetes mellitus (11.8%) were addressed and reinforced.

Of the 38 patients who underwent polysomnography, 36 (94.8%) were found to have OSA (Table 1). Only one of these patients followed up and accepted continuous positive airway pressure (CPAP) therapy (Flowchart 1). The patient is not a resident of Chennai and had not come for a follow up thereafter. The patient had not responded to our attempts of communication.

DISCUSSION

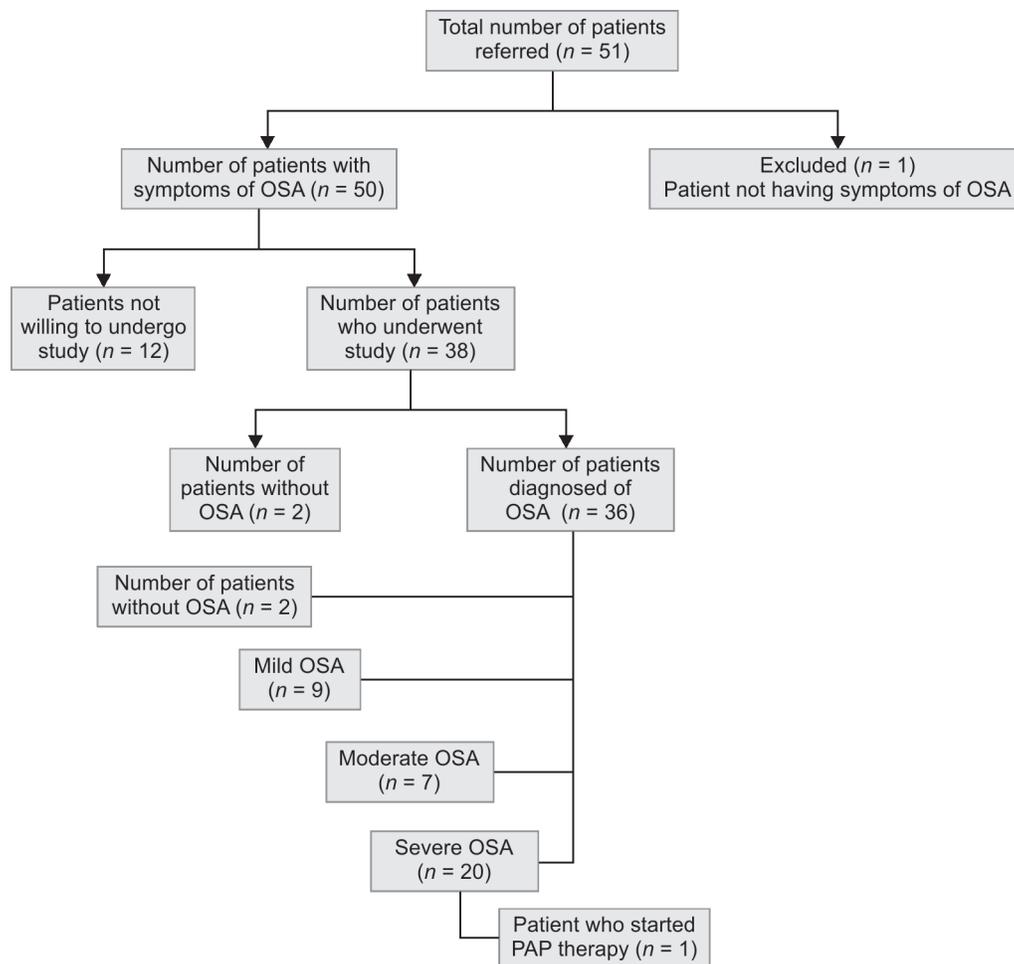
The association of OSA with metabolic and vascular disorders has been extensively studied and well accepted.³ Vascular involvement of the eye, such as diabetic retinopathy, retinal vein, and arterial disorders have been clearly associated with OSA⁷ and few other ophthalmologic disorders, such as glaucoma have also been noted to have a significant association. In this study, we explore the association between FES and OSA and further the feasibility of simple screening by Ophthalmologists to refer patients appropriately for further evaluation in a sleep clinic.

Though various studies have explored the association between the two diseases, the definitive underlying pathophysiology linking the two is yet to be explained. One of the probable explanations is that rubbing of the eyelids against the pillows causes mechanical trauma and is common in patients with OSA as they tend to sleep on their sides.^{7,10,11} Another theory suggested is that hypoxia (during sleep) and sudden reperfusion (on awakening) may damage the tarsal plate and initiate a papillary reaction.⁷ Alternate explanations include poor eyelid-to-globe apposition, inflammation of the Meibomian glands or Demodex eyelid infestation. A possibility of genetically transmitted disease has also been considered.^{7,10,11}

Previous studies^{12–14} have observed a male predominance with regards to concurrence of FES and OSA, which has been reestablished in our study. As observed in previous studies,^{12–14} hypertension, weight gain, and diabetes mellitus were common comorbidities among the patients which may worsen the prognosis of FES in such patients.¹³

In our study, significant proportion of the patients were not ready to undergo the sleep study or commence treatment despite being diagnosed and explained the consequences of untreated OSA. A qualitative analysis by Shaw et al.¹⁵ aimed at assessing the knowledge, beliefs, and attitudes toward OSA evaluation and

Flowchart 1: Patients with FES who underwent sleep study for the diagnosis of OSA



treatment observed that misconception with regards to OSA and its evaluation might prevent people from early diagnosis and treatment. Patients may relate their symptoms like snoring and daytime sleepiness to their lifestyle and working conditions and may not perceive them as symptoms of a disease condition. This may also signify that although they are aware that the sedentary nature of their lifestyle and unhealthy habits contribute to chronic conditions, such as obesity and cardiovascular disease, they seem to underestimate or fail to see the correlation to OSA.¹⁶

It is noteworthy that out of 36 patients diagnosed with OSA, 20 had severe OSA, but only one of these patients accepted treatment with PAP. Studies have evaluated the barriers of acceptance and adherence to PAP therapy. Various factors including cost of CPAP, limited insurance coverage, inability to tolerate the device, inconvenience of nightly use, lack of knowledge on the use, fear of social judgment, and lack of awareness regarding OSA have been recorded in these studies.^{17,18} A study by Yang et al.¹⁹ observed that CPAP acceptance reduces with age. Another study by Lee et al.²⁰ stated that CPAP counseling prior to ordering a sleep study might be prudent to better manage patient expectations.

Several studies conducted across many countries have concurred the poor knowledge and awareness regarding OSA and its associations even among medical professionals.^{21–24} A

comforting prospect in this study was that ophthalmologists were able to effectively screen patients for OSA with simple screening questions about snoring and daytime hypersomnolence. Knowledge about OSA and its association with disorders specific to their domain helped the physicians treat patients more holistically and consequently improve the overall prognosis.

A previous Indian study had looked into the prevalence of systemic disorders like OSA in FES.⁸ In our study, we had taken a step further and tried to assess how many patients were willing to undergo relevant assessment and further management. But our study is not devoid of limitations. One of the limitations is the small sample size, which could be due to the fact that FES is not a very common diagnosis and also a frequently overlooked entity, and no further statistical analysis was possible due to the small sample size. Presence of male participants alone could denote a possible selection bias when it comes to screening for OSA. Possibility of effects of confounding factors like gender, comorbidities, hypertension, obesity, etc. was not ruled out. Poor follow up was one of the major limitations of the study. This could be a reflection of lack of awareness with regards to OSA and its consequences. Future studies with bigger sample size of prospective designs are warranted to better understand the impact of the confounding factors, causes for poor follow up, and influence of treatment of OSA on the patients with FES.

CONCLUSION

Ophthalmologists should consider systemic disorders, such as OSA while evaluating patients with FES. Simple screening questions seem to have a high yield in appropriately identifying patients with OSA which was confirmed by portable sleep studies in most of these patients. The proportion of patients with FES having OSA is significant and most of them had moderate or severe OSA. Educating the patients and making them understand the association remains a challenge and can only be improved with increasing awareness among the Ophthalmologists and general public on the importance of treating coexisting OSA.

REFERENCES

- Spicuzza L, Caruso D, Maria G. Obstructive sleep apnoea syndrome and its management. *Ther Adv Chronic Dis* 2015;6(5):273–285. DOI: 10.1177/2040622315590318.
- Franklin KA, Lindberg E. Obstructive sleep apnea is a common disorder in the population—a review on the epidemiology of sleep apnea. *J Thorac Dis* 2015;7(8):1311–1322. DOI: 10.3978/j.issn.2072-1439.2015.06.11.
- Bonsignore MR, Baiamonte P, Mazza E, et al. Obstructive sleep apnea and comorbidities: a dangerous liaison. *Multidiscip Respir Med* 2019;14:8. DOI: 10.1186/s40248-019-0172-9.
- Pinto JA, Ribeiro DK, Da Silva Cavallini AF, et al. Comorbidities associated with obstructive sleep apnea: a retrospective study. *Int Arch Otorhinolaryngol* 2016 Apr 1;20(2):145–150. DOI: 10.1055/s-0036-1579546.
- Goyal A, Aswin P, Pakhare AP. Poor knowledge and attitude regarding obstructive sleep apnea (OSA) among medical students in India: a call for MBBS curriculum change. *Sleep Vigil* 2018 Jun 11;2(1):45–50. DOI: 10.1007/s41782-017-0028-3.
- Abdal H, Pizziment J, Purvis C. The eye in sleep apnea syndrome. *Sleep Med* 2006 Mar 3;7(2):107–115. DOI: 10.1016/j.sleep.2005.08.010.
- Skorin L, Knutson R. Ophthalmic diseases in patients with obstructive sleep apnea. *J Am Osteopath Assoc* 2016 Aug 1;116(8):522–529. DOI: 10.7556/jaoa.2016.105.
- Tyagi R, Kulkarni V, Anjana. A study of floppy eyelid syndrome and its ophthalmic and systemic associations. *Int J Adv Res* 2018;6(2):1589–1594. DOI: 10.21474/IJAR01/6596.
- Hudgel DW. Sleep apnea severity classification—revisited. *Sleep* 2016 May;39(5):1165–1166. DOI: 10.5665/sleep.5776.
- Idowu OO, Ashraf DC, Vagefi MR, et al. Floppy eyelid syndrome: ocular and systemic associations. *Curr Opin Ophthalmol* 2019 Nov 1;30(6):513–524. DOI: 10.1097/ICU.0000000000000617.
- Muniesa M, Huerva V, Sánchez-de-la-Torre M, et al. The relationship between floppy eyelid syndrome and obstructive sleep apnoea. *Br J Ophthalmol* 2013 Nov 12;97(11):1387–1390. DOI: 10.1136/bjophthalmol-2012-303051.
- Chambe J, Laib S, Hubbard J, et al. Floppy eyelid syndrome is associated with obstructive sleep apnoea: a prospective study on 127 patients. *J Sleep Res* 2012 Jun;21(3):308–315. DOI: 10.1111/j.1365-2869.2011.00968.x.
- Leibovitch I, Selva D. Floppy eyelid syndrome: clinical features and the association with obstructive sleep apnea. *Sleep Med* 2006;7(2):117–122. DOI: 10.1016/j.sleep.2005.07.001.
- Ezra DG, Beaconsfield M, Sira M, et al. The associations of floppy eyelid syndrome: a case control study. *Ophthalmology* 2010 Apr;117(4):831–838. DOI: 10.1016/j.ophtha.2009.09.029.
- Shaw R, McKenzie S, Taylor T, et al. Beliefs and attitudes toward obstructive sleep apnea evaluation and treatment among blacks. *J Natl Med Assoc* 2012;104(11–12):510–519. DOI: 10.1016/s0027-9684(15)30217-0.
- Vlachantoni I-T, Gerakopoulou P, Amfilochiou A, et al. Facilitating factors and barriers in the screening and diagnosis process of obstructive sleep apnea in taxi drivers. *Pneumon. Pneumon* 2015; 28(1):40–47.
- Rezaie L, Phillips D, Khazaie H. Barriers to acceptance and adherence to continuous positive airway pressure therapy in patients with obstructive sleep apnea: a report from Kermanshah province, western Iran. *Patient Prefer Adherence* 2018;12:1299–1304. DOI: 10.2147/PPA.S165905.
- Ranganathan L, Nagarajan R, Sundaram AK, et al. CPAP therapy in OSA—a gap analysis between recommendation and usage. *Indian J Sleep Med* 2012;7(4):150–156. DOI: 10.5958/J.0974-0155.7.4.022.
- Yang MC, Lin CY, Lan CC, et al. Factors affecting CPAP acceptance in elderly patients with obstructive sleep apnea in Taiwan. *Respir Care* 2013 Sep 1;58(9):1504–1513. DOI: 10.4187/respcare.02176.
- Lee CHK, Leow LC, Song PR, et al. Acceptance and adherence to continuous positive airway pressure therapy in patients with obstructive sleep apnea (OSA) in a Southeast Asian privately funded healthcare system. *Sleep Sci* 2017;10(2):57–63. DOI: 10.5935/1984-0063.20170010.
- Sharma S, Sriji P. Sleeping over a sleep disorder - Awareness of obstructive sleep apnoea as a modifiable risk factor for hypertension and stroke: A survey among health care professionals and medical students. *Ann Indian Acad Neurol* 2013 Apr;16(2):151–153. DOI: 10.4103/0972-2327.112446.
- Reuveni H, Tarasiuk A, Wainstock T, et al. Awareness Level of obstructive sleep apnea syndrome during routine unstructured interviews of a standardized patient by primary care physicians. *Sleep* 2004 Dec;27(8):1518–1524. DOI: 10.1093/sleep/27.8.1518.
- Mahendran R, Subramaniam M, Chan YH. Medical students' behaviour, attitudes and knowledge of sleep medicine. *Singapore Med J* 2004 Dec;45(12):587–589.
- Kovačić Z, Marenić M, Šoljić M, et al. Knowledge and attitude regarding sleep medicine of medical students and physicians in Split, Croatia. *Croat Med J* 2002;43(1):71–74.