

Quality of life impairment in patients of obstructive sleep apnea and its relation with the severity of disease

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ABSTRACT

Background: Several studies have demonstrated considerable impairment of quality of life (QOL) in obstructive sleep apnea (OSA) patients, but its relation with severity of OSA is yet unclear. **Study Objectives:** To investigate the effects of OSA on the QOL and its association with the disease severity. **Design and Setting:** Observational, prospective case-control study. **Materials and Methods:** QOL of 69 OSA patients and 41 healthy controls were assessed using the Calgary sleep apnea quality of life index (SAQLI) on the morning following the polysomnography (PSG) study. **Statistics:** All statistical analyses were performed using the SPSS 17.0 (SPSS Inc., Chicago). Differences between sleep-related symptoms and SAQLI subscales scores were assessed with the Chi-square test and the Student *t*-test. Due to non-normal distribution, differences between SAQLI scores of controls and OSA patients were evaluated using a non-parametric Mann-Whitney test. Spearman correlation and backward multiple regression analysis were used to analyze the association between SAQLI scores and sleep indices and anthropometric variables and PSG variables. **Results:** Study included 69 cases (57 male and 12 females) with a mean age, weight, height, neck circumference, and body mass index 48.45 ± 10.12 years, 83.03 ± 16.48 kg, 159.75 ± 28.29 cm, 44.01 ± 3.23 cm and 30.77 ± 6.71 kg/m². Mean apnea-hypopnea index was 26.39 ± 16.62 . The median score of four SAQLI domains daily function, social interaction, emotional, symptoms and total mean SAQLI score were 3.64 (3.46-3.90), 3.77 (3.51-3.88), 3.64 (3.53-3.83), 4.80 (4.68-5.11), 4.09 (3.88-4.09), and 1.36 (1.29-1.71), 1.38 (1.24-1.62), 1.45 (1.23-1.62), 2.00 (1.78-2.26), 1.55 (1.46-1.73) for patients and controls respectively. All the individual domain scores and the mean SAQLI scores of patients were significantly higher than the controls. **Conclusion:** OSA causes significant impairment of QOL, but the severity of impairment is not directly proportional to the severity of OSA.

KEY WORDS: Apnea, obstructive sleep, quality of life, sleep apnea quality of life index

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INTRODUCTION

Obstructive sleep apnea (OSA) is characterized by the occurrence of daytime sleepiness, loud snoring, witnessed breathing interruptions, or awakenings due to gasping or choking in the presence of at least five obstructive

respiratory events (apneas, hypopneas or respiratory effort related arousals) per hour of sleep. The presence of 15 or more obstructive respiratory events per hour of sleep in the absence of sleep related symptoms is also sufficient for the diagnosis of OSA due to the greater association of this severity of obstruction with important consequences such as increased cardiovascular disease risk. The combination of sleep-disordered breathing with daytime sleepiness is referred to as the *OSA syndrome*.^[1] Prevalence surveys have estimated that about 4% of the middle-aged men and 2% of the middle-aged women are afflicted by OSA in developed countries.^[2] Indian prevalence studies estimated disease prevalence rates of 3.5-13.7% (4.4-19.5% in males and 2.5-7.4% in females). Prevalence of OSAS in India is 1.7-3.6% (2.4-7.5% in males and 1-2.1% in females).^[3-6]

Access this article online	
Quick Response Code: 	Website: www.lungindia.com
	DOI: 10.4103/0970-2113.120603

The daytime sleepiness is the most common manifestation of OSA. However, other common daytime effects include irritability, decreased concentration, memory impairment, decreased energy and depressive symptoms.^[7] Nocturnal symptoms include, restlessness, diaphoresis, awakenings with a sensation of choking or dyspnea, esophageal reflux, heartburn, laryngospasm, frequent nocturia, dry mouth etc. The most catastrophic result of excessive daytime sleepiness (EDS) is falling asleep behind the wheel and causing fatal automobile accidents.^[8] Many studies have indicated an association between sleep apnea and cardiovascular/cerebrovascular related morbidity and mortality. It has been associated with the hypertension, coronary artery disease, congestive heart failure, arrhythmias and stroke.^[9-13] It has also been associated with an increased mortality.^[14]

Recently, the studies have confirmed that the impact of OSA on patient's quality of life (QOL) is rather more widespread than EDS, increased risk of cerebrovascular/cardiovascular events and other common features mentioned above. Certainly, there are many other domains of life, which remain unexplored in the sleep laboratory. In such cases, Flemons and Reimer and Lacasse *et al.* have outlined 4 such key domains of health related quality of life (HRQoL) viz. somatic sensation, physical function, emotional state, and social interaction.^[15] As the measurements of physiological parameters alone cannot be taken surrogate markers of HRQoL, this emphasizes the need to measure QOL directly.^[16]

Diverse self-reported instruments have been used to assess resulting impairment like medical outcomes study survey, Short-form 36 health survey Questionnaire (SF-36), Satisfaction with Life Scale, Nottingham Health Profile, General health questionnaire-28.^[17-21] These HRQoL instruments have multiple subclasses, each signifying different domains of life.

Question mark on the ability of generic questionnaire to detect subtle effects of disease on QOL and effects on QOL brought about by various treatment modalities led to the development of disease specific questionnaire for OSA like Calgary sleep apnea quality of life index (SAQLI), functional outcome of sleepiness questionnaire (FOSQ), and OSA Patient-Oriented Severity Index.^[22-24] These disease specific questionnaires have been compared with generic questionnaire. In a study, SAQLI was more responsive to changes in QOL in patients receiving OSA specific treatment than SF-36 and has strong content and constructive validity, but has to be administered by an interviewer.^[16] These OSA specific questionnaires are being used increasingly in the newer studies and gradually replacing the generic scales.^[25] A comparative study between these disease specific questionnaires have found SAQLI more sensitive than FOSQ.^[26]

We undertook this study to investigate the overall effect of OSA on human life and where does it affect so that a

complete therapy can be planned addressing the specific needs of the patient. Any treatment modality chosen on the basis of derangements in the physiological parameters only is unlikely to be complete as these parameters may not be the true representative of the extent of sufferings of the OSA patients. Thus, there is a need for a complete holistic treatment considering physiological, emotional, and social impairment of the individual patient.

The HRQoL has cross-cultural and regional differences even in same clinical condition.^[27] Thus, the conclusions drawn from researches done outside India cannot be used to gauge QOL impairment in Indian OSA patients. This study was the need of the hour as there has not been any such study in India.

MATERIALS AND METHODS

The present study was conducted over a period of 18 months between March 2006 and August 2007, in an urban population in a North Indian City. The study was conducted after due approval from Ethics Committee of the Institute.

During the 1.5 year period consecutive adult patients of either sex who had been referred for snoring, EDS, multiple sleep awakenings were screened with Berlin Questionnaire. Those scored as high-risk cases were subjected to overnight Polysomnography (PSG) following clinical and lab evaluation. Patients with an apnea/hypopnea index ≥ 15 or ≥ 5 with symptoms of OSA were labeled as OSA cases. Those diagnosed as a case of OSA had their QOL assessed by SAQLI questionnaire. The original English version of the questionnaire developed by Flemons and Reimer was translated to the vernacular language of the patients.^[22] The translated questionnaire was administered to each patient by the investigator, and the QOL was assessed by the ultimate score obtained by the patient.

Subjects who had experienced chronic psychiatric disorders, alcoholism, drug abuse, psychotropic drug abuse, unstable medical disorder, other sleep disorder were excluded. Similarly, severe respiratory disease ($FEV_1 < 50\%$ predicted), respiratory failure, hypothyroidism, or any illness, which could potentially bias perception of QOL, e.g., chronic obstructive lung diseases, bronchial asthma, heart failure, renal failure, depression etc., were excluded. The patients who were having stable medical conditions (e.g., Hypertension, Diabetes Mellitus) for more than 6 months were included in the study.

Controls

Age and gender matched controls were also assessed using the PSG and further subjected to SAQLI. Their SAQLI scores were compared with those of OSA patients. These control subjects were healthy volunteers, mostly attendants of patients admitted in our pulmonary

medicine ward. Those with stable medical conditions were also included.

PSG

Each high-risk patient fulfilling inclusion criteria underwent whole night PSG using 44 channel Compumedics E-series-44 polysomnographic system. Parameters recorded were- EEG (Electroencephalogram), EOG (Electrooculogram), Chin and Leg EMG (Electromyogram), ECG (Electrocardiogram), Body positioning, thoracic and abdominal inductive respiratory Plethysmography, Pulse oximetry, airflow monitoring using the oronasal thermistors and snoring recording with the microphone. Sleep was scored in 30 s epochs while analysis and interpretation was performed according to standard criteria (R & K).^[28]

Calculated sleep variables included total time on bed, total sleep time (TST), sleep latency, number of apneas, number of hypopneas, number of arousals (Arousals), number of arousals associated with the respiratory events (Respiratory Arousals) and RDI (Respiratory Disturbance Index). Apnea was defined as complete cessation of airflow for more than 10 s, hypopnea was defined as decrease in airflow of more than 50% with a desaturation of more than 4% for 10 s. Apnea-hypopnea index (AHI) was calculated as number of apneas and hypopneas per hour.

Calgary SAQLI

The SAQLI is a 35 item OSA specific QOL questionnaire having four main domains: daily functioning, social interactions, emotional functioning, and symptoms. In the first three domains, questions are framed to measure “how often” and “how much” symptoms interfere with daily activities, social interactions, and emotional state or are stated in degrees of frequency or difficulty and probe “how much of a problem” particular tasks are to perform. In the symptom domains, patients select the top five symptoms they experience related to OSA (from a list of 21). The questionnaire is administered by the interviewer.

A note about scoring

For each item of the SAQLI, patients were asked to give a graded subjective response. The degree of impairment/difficulty was rated on a 7-point Likert scale (1 to 7) ranging from not at all (1) to very large (7). One needs to reverse the response value for each of these items before summing for the total. That is, if the respondent gave a 1, you make it a 7; if they gave a 2 you make it a 6; 3 = 5; 4 = 4; 5 = 3; 6 = 2; and 7 = 1. These scores were then averaged for each domain by dividing by the number of questions in the domain. A total score was calculated by summing the four domains score and dividing by four, as has been described for the SAQLI.

Statistical analysis

All statistical analyses were performed using the SPSS 17.0 statistical program (SPSS Inc., Chicago, Ill., USA). Total as well as individual domains SAQLI scores of OSA patients and controls were tested for normal distribution of the data.

Shapiro-Wilk test was applied for this analysis and values for total SAQLI scores were normally distributed among cases and controls (Sig. value 0.077 and 0.090 for cases and controls—value should be more than 0.05 for normal distribution). However, the individual SAQLI domains scores were mostly distributed non-normally. Thus, for the sake of uniformity values were considered to be distributed non-normally and SAQLI Scores were expressed as medians with 95% confidence intervals while polysomnographic and anthropometric values were expressed as means \pm SD. Differences between sleep-related symptoms and subscales of the SAQLI scores were assessed using the Chi-square test and the Student *t*-test. Differences between controls and OSA patients were evaluated using a non-parametric test (Mann-Whitney *U* test). Association between the SAQLI scores and sleep indices were explored with the spearman correlation analysis. The correlation between the total score on the SAQLI, the anthropometric variables and PSG variables were determined by backward multiple regression analysis. $P < 0.05$ was considered significant.

RESULTS

Patient characteristics

A total of 93 subjects were suspected of having OSA on the basis of a positive result of Berlin questionnaire. All suspected cases were subjected to overnight PSG study. PSG revealed 74 patients having confirmed OSA syndrome. Amongst 74 OSA patients, 2 were excluded as they were diagnosed to be suffering from Narcolepsy too. Two patients were found having hypothyroidism, hence excluded from the study. Another patient was having a history of significant depressive illness was also excluded from further evaluation. Finally, 69 OSA patients were included in our analysis out of which 22 patients had mild, 21 moderate, and 26 suffered severe OSA. Out of these 69 patients, 12 (17.4%) were females and rest 57 (82.6%) were males. 43 (62.3%) patients were graduate/postgraduate, two patients (2.9%) were uneducated and rest 24 (34.7%) were school pass-outs. 47 (68.1%) patients gave a history of snoring while history of EDS, Multiple sleep awakenings and sleepiness while driving was present in 42 (60.8%), 29 (42%) and 17 (24.6%) patients respectively. 39 patients (56.5%) patients were hypertensive, 23 (33.3%) were diabetics and family history of OSA was present in 14 (20.3%) cases. Forty-one normal healthy controls were also included in the study. Table 1 shows mean \pm SD values for anthropometric, clinical and polysomnographic parameters among the analyzed patients and controls. The two groups were significantly different in age, height, weight, body mass index and neck circumference. As far as polysomnographical parameters are concerned, Table 1 reveals statistically significant differences between the groups. The OSA group had higher Recording time, AHI, rapid eye movement (REM) latency, non-rapid eye movement (NREM)-2 and 3% and lower REM sleep percentage and NREM-4%.

Table 1: Clinical characteristics and polysomnography results of the OSA patients and controls

Variable	Controls (n=41)	Cases (n=69)	P value
Sex-Male/Female	31/10	57/12	
Age (years)	41.54 (13.99)	48.45 (10.12)	0.003
Height (cm)	167.76 (6.03)	159.75 (28.29)	<0.001
Weight (kg)	66.22 (7.24)	83.03 (16.48)	<0.001
Neck circumference (cm)	35.41 (2.36)	44.01 (3.23)	<0.001
BMI (kg/m ²)	23.52 (2.24)	30.77 (6.71)	<0.001
Record time (min)	396.28 (63.18)	446.52 (94.57)	0.001
Sleep time (min)	295.93 (74.25)	304.43 (107.88)	NS
Sleep efficiency (%)	74.75 (15.40)	68.28 (19.99)	NS
AHI	0.45 (0.14)	26.39 (16.62)	<0.001
REM %	19.93 (6.23)	8.64 (6.02)	<0.001
REM latency (min)	55.46 (27.92)	101.28 (97.50)	0.015
NREM-1	12.90 (7.72)	11.70 (8.94)	NS
NREM-2	31.67 (12.73)	43.72 (12.93)	<0.001
NREM-3	17.87 (8.38)	22.07 (12.78)	0.020
NREM-4	17.38 (9.44)	13.24 (12.22)	0.010

Data are presented as means (SD), Values for sleep stages are expressed as percentages of sleep period time. NS: Not significant, BMI: Body mass index, AHI: Apnea-hypopnea index, REM: Rapid eye movement, NREM: Non-rapid eye movement, OSA: Obstructive sleep apnea

SAQLI score

SAQLI scores of patients and controls are given in Table 2. All the individual domain scores and the mean SAQLI scores of patients were significantly higher than the controls suggesting poorer QOL.

Correlation of QOL and severity of OSA

The association between the AHI and the SAQLI scores was explored with spearman correlation analysis as the data were non-parametric. Among the cases of OSA, mean SAQLI score ($r = -0.035$, $P = 0.774$) and symptoms domain score ($r = -0.162$, $P = 0.185$) showed non-significant negative correlation with AHI. Daily function ($r = 0.064$, $P = 0.603$), social Interaction ($r = 0.123$, $P = 0.315$) and emotional ($r = 0.001$, $P = 0.992$) domains scores had non-significant positive correlation with AHI. Thus there was no significant correlation of severity of OSA with severity of QOL impairment.

QOL and polysomnographic variables

Table 3 shows the correlation of SAQLI Score and polysomnographic variables. The emotional domain of SAQLI statistically significant negative correlation with percentage of REM sleep ($r = -0.287$, $P < 0.05$) while symptoms domain score showed significant positive correlation with NREM-1 sleep ($r = 0.315$, $P < 0.01$) and negative correlation with NREM-3 ($r = -0.294$, $P < 0.05$).

DISCUSSION

We studied the QOL in patients of OSA and observed that QOL was impaired in patients of OSA in our study. All the 4 domains of SAQLI scale viz.; daily activities, emotional functioning, social interactions, and symptoms were significantly impaired in OSA cases when compared to that of controls. Daily functioning, social interaction and emotional functioning had almost equal impairment, but the symptoms domain was worst affected which is on expected lines as these 5 most affected symptoms were

Table 2: Comparison of the SAQLI score of the patients and controls

SAQLI domain	Controls	Cases	P value
Daily function	1.36 (1.29-1.71)	3.64 (3.46-3.90)	0.001
Social interaction	1.38 (1.24-1.62)	3.77 (3.51-3.88)	0.001
Emotional	1.45 (1.23-1.62)	3.64 (3.53-3.83)	0.001
Symptoms	2.00 (1.78-2.26)	4.80 (4.68-5.11)	0.001
Mean SAQLI score	1.55 (1.46-1.73)	4.09 (3.88-4.09)	0.001

Data presented as median (95% confidence interval) because of non-normal distribution of the data. SAQLI: Sleep apnea quality of life index

chosen by patients themselves. It was observed that all aspects of life covered under SAQLI scale were affected in the disease state. Somewhat similar results have been observed by many researchers across different parts of the globe.

Although study by Lacasse *et al.* revealed much lower scores of all four domains viz., “daily life activities”; 1.0, “social interactions”; 1.0, “emotions”; 0.7, and “symptoms”; 2.5, but here too symptoms domain was the one which was most affected.^[16] D'Ambrosio *et al.* used SF-36 for measuring QOL and observed that all dimensions of the QOL were significantly impaired in patients of OSA as compared to the normal population.^[29] Akashiba *et al.* observed that 6 of the eight domains score of the SF-36 scale and the overall total SF-36 scale score was significantly lower than that in the control subjects. The two domains viz. physical functioning and body pain were not found affected. This could be explained on the basis that SF-36 questionnaire is not specific for OSA and such generic questionnaires are likely to have domains which are not affected by a specific disease.^[18] Fornas *et al.* administered Nottingham Health Profile questionnaire to measure QOL and observed that OSA patients showed deterioration of general health status parameters in comparison to healthy subjects^[21] Gall *et al.* using SF-36 observed that patients with OSA have significant impaired social functioning^[30] Finn *et al.* studied self-reported general health status in sleep-disordered breathing cases in Wisconsin Sleep

Table 3: Spearman's correlation coefficient between SAQLI scores, and polysomnography variables of OSA cases

PSG variable	Daily functions	Social interaction	Emotional	Symptoms	Mean SAQLI score
AHI	0.064	0.123	0.001	-0.162	-0.035
Recording time	-0.010	-0.076	0.011	0.117	0.046
TST	-0.028	-0.016	0.041	0.185	0.088
Sleep efficiency	-0.044	0.019	-0.046	0.096	0.003
REM %	-0.072	-0.069	-0.287*	0.107	-0.161
NREM-1	-0.125	0.077	-0.024	0.315**	0.048
NREM-2	-0.048	-0.133	-0.022	0.116	-0.093
NREM-3	0.027	0.079	0.026	-0.294*	-0.020
NREM-4	0.135	0.005	0.087	-0.199	0.037
REM latency	-0.161	-0.027	0.056	0.030	-0.005

**Correlation is significant at the 0.01 level (2-tailed), *Correlation is significant at the 0.05 level (2-tailed), NREM: Non rapid eye movement, REM: Rapid eye movement, AHI: Apnea-hypopnea index, TST: Total sleep time, SAQLI: Sleep apnea quality of life index

Cohort Study. Even mild sleep-disordered breathing of apnea-hypopnea index of 5, was associated with decrement in SF-36.^[31] These results are especially notable because they come from a population-based sample. However, it is worth emphasizing here that in this study, the SF-36 was self-administered by sending to all participants through the postal service and was completed about 3 years after the diagnosis by PSG. Hence, the bias due to such a long gap cannot be ruled out. Manocchia *et al.* observed a direct association between sleep problems and decrement in HRQoL in OSAS cases as measured by SF-36 scale^[17] but their patients also had other co-morbid conditions, which could have caused sleepiness/other effects and hence these results may not be truly due to OSAS alone. The study by Moore *et al.* suggested that RDI and number of arousals were significantly associated with mobility, cognitive functioning, social functioning, energy, fatigue, and health distress. There was also significant correlation between pain severity and RDI, number of arousals or arousals with respiratory events. Interestingly patients had been well screened and were not suffering from severe or even moderate levels of pain.^[32] Pain complaints of any kind are not generally thought to be part of the clinical picture in OSA. Author explained that though not directly a feature of OSA, pain is an important part of the symptom complex in other disorders that may include disturbed sleep such as fibromyalgia. Therefore, this may be taken as another evidence of redundancy and inadequacy of generic questionnaires. Sforza *et al.* discovered that all HRQoL dimensions were decreased in sleep related breathing disorder patients, with a greater impact on SF-36 sub scores for "vitality," "physical role," "social functioning," "mental health," and "role emotional dimensions."^[33] Several other studies also found QOL impaired in one or more domains.^[34]

Some other studies observed there is no impairment of QOL in patients of OSA. Głębicka *et al.*, didn't find any significant psychological disturbances in patients of OSA as compared to normal healthy adults.^[20] Author

attributed rather unexpected lack of psychological differences to the rapid mood improvement in OSA patients on anticipation of being diagnosed and taken care of in the hospital setting.

In our study, we observed that the QOL impairment was not in direct proportion with severity of OSA disease. Some patients with mild OSA were having QOL impairment equivalent or even more than what was observed in patients with severe OSA. Conversely, some patients with severe OSA were found having only minimal impairment of QOL. Many other studies have observed similar results.^[34,30]

Our study is having some limitations, which might have affected the results. (1) The cases may not be the true representative of the population as females were under represented as compared to population prevalence (2) Original SAQLI questionnaire is written in English; it may not be equally suitable in other language and cultures. However, studies have shown that SAQLI has been used in other cultures and languages quite successfully.^[35] (3) Our sampling was directly not from community as suspected patients coming to hospital were enrolled in the study, although, patients were selected randomly. (4) The patients in the community might be having disease stages different than to those who reported to hospital. (5) We used a translated version of the SAQLI questionnaire which was not validated. The true morbidity of OSA might be more than this because of little awareness of OSA in India. Population based studies are required to gauge the sufferings of OSA patients in the community.

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How to cite this article: Dutt N, Janmeja AK, Mohapatra PR, Singh AK. Quality of life impairment in patients of obstructive sleep apnea and its relation with the severity of disease. *Lung India* 2013;30:289-94.

Source of Support: Nil, **Conflict of Interest:** None declared.