

# Correlation between Degree of Desaturation and Severity of Obstructive Sleep Apnoea: A Cross-sectional Study

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## ABSTRACT

**Introduction:** Obstructive Sleep Apnoea (OSA) is major Non Communicable Disease (NCD) which is becoming very common worldwide. The OSA results in day time hypersomnolence, nocturnal hypoxia and snoring. Repeated desaturation events during sleep results in aerobic metabolism at tissue level changing to anaerobic metabolism, which results in cellular inflammation and insulin resistance further complicating metabolic syndrome.

**Aim:** To study correlation between degree of desaturation and severity of obstructive sleep apnoea.

**Materials and Methods:** This cross-sectional study was conducted in Department of Pulmonary medicine at KS Hegde Medical Academy (tertiary care hospital), Mangaluru, Karnataka, India, from March 2018 to February 2021. Total 54 patients who underwent overnight polysomnography and diagnosed to have OSA were included in the study. The minimum recorded oxygen saturation (SpO<sub>2</sub>) defined as maximum desaturation was noted. Relative desaturation was defined as drop in saturation by 3% or more from the pre-event baseline. Correlation between total number of relative desaturation and Apnoea Hypopnea Index (AHI) was analysed. The correlation between two variables were analysed by Pearson's correlation and the coefficient was calculated. The p-value was calculated by regression analysis and Analysis of Variance (ANOVA).

**Results:** Total of 54 patients was included in the study. Out of which, 22 were mild, 14 moderate and 18 severe OSA, respectively. Number of relative desaturations recorded was from 0-636. The correlation between AHI and mean  $SpO_2$  in sleep was r-value=-0.4542 (p-value=0.001) and the correlation between AHI and minimum  $SpO_2$  was r-value=-0.45577 (p-value=0.001), respectively. Correlation between mean  $SpO_2$  and minimum  $SpO_2$  was r-value=-0.4566 (p-value <0.001) and the correlation between AHI and relative desaturation was r-value=-0.876698 (p-value=0.001).

**Conclusion:** As the severity of the obstructive sleep apnoea worsened, there was greater degree of desaturation in sleep and the lowest  $SpO_2$  was also observed during severe obstructive sleep apnoea.

#### Keywords: Anaerobic metabolism, Hypoxia, Relative desaturation

# INTRODUCTION

Obstructive Sleep Apnoea (OSA) is the most common type of sleep related breathing disorder characterised by repetitive episodes of upper airway obstruction leading to desaturations, arousals, variations in heart rate, daytime sleepiness and impaired quality of life during daytime. OSA is diagnosed typically after overnight polysomnographic test showing events of apnoea (complete or more than 90% cessation of oronasal airflow for more than or equal to 10 seconds) and hypopnoea (more than 30% reduction in oronasal airflow lasting for more than or equal to 10 seconds with >3% fall in SpO, from the pre-event baseline and/or arousal) of more than per hour of sleep with symptoms suggestive of OSA [1]. There are various systems used to classify the severity of OSA. The worldwide accepted system being American Academy of Sleep Medicine (AASM) Apnoea Hypopnea Index (AHI), where AHI of 5-15 events per hour is mild, 15-30 events/hour is moderate and more than 30 events per hour is severe OSA [2].

The disruptions to breathing have lead to repeated blood gas disturbances (hypercapnia and hypoxaemia) and sympathetic nervous system activation [3]. Repeated desaturation events might result in aerobic metabolism at tissue level changing to anaerobic metabolism, which results in cellular inflammation and insulin resistance further complicating metabolic syndrome [4]. Previous study has been conducted on SpO<sub>2</sub> less than 90% and respiratory arousal indices [5]. However severity of OSA and its relation to degree of desaturation were not compared previously. Hence, to address this lacuna it was hypothesised that more severe the OSA, more severe the desaturation and this research was conducted to

study degree of desaturation and severity of OSA to understand the metabolic implications of hypoxia.

#### MATERIALS AND METHODS

A cross-sectional study was conducted in Department of Pulmonary Medicine at KS Hegde Medical Academy (tertiary care hospita), Mangaluru, Karnataka, India from March 2018 to February 2021. The ethical clearance was obtained from the Institutional Ethical Committee (NU/CEC/2018/0201).

Sample size calculation: The sample size was calculated using Cochran formula:

$$N = \frac{Z^2 pq}{e^2} = 53.16$$

Where, n=sample size,

Z=standard normal deviate {1.96 (taking a confidence interval of 95%)} p=proportion in the target population having OSA {0.036 (taking 3.6% of population having OSA)} [6]

q=proportion in the target population not having OSA {1-p=0.964} e=degree of accuracy required (0.05)

Inclusion and Exclusion criteria: All consenting 54 patients who underwent overnight polysomnography and diagnosed to have OSA by the pulmonologists were included in the study. Subjects diagnosed to have central sleep apnoea and not consenting for the study were excluded from the study.

#### **Study Procedure**

 Demographic details like age, sex, height, weight and BMI were taken. Rashmi Soori et al., Correlation between Obstuctive Sleep Apnoea and Desaturation

- Sleep study data included
- -Apnoea Hypopnoea Index (AHI),
- -Number of relative desaturations,
- -Mean SpO<sub>2</sub> recorded in sleep,
- -Minimum SpO<sub>2</sub> recorded in sleep

These parameters are part of the routine sleep study which were recorded in polysomnography laboratory {Alice-5 (Philips Respironics)} and retrieved from the software system. AHI is the current method for severity grading of OSA, which includes number of apnoea and hypopnea per hour of sleep. AHI severity grading OSA is divided [7]:

- Mild OSA: AHI of 5-15
- Moderate OSA: AHI >15 upto 30
- Severe OSA: AHI>30

The AHI below 5 per hour was considered as normal and not included in the study. The minimum recorded  $\text{SpO}_2$  defined as maximum desaturation was noted. Relative desaturation was defined as drop in saturation by 3% or more from the pre-event baseline [1].

# STATISTICAL ANALYSIS

Statistical analysis was done using the software Statistical Package for Social Sciences (SPSS) version 2.0. Correlation between total number of relative desaturation and AHI was analysed. Nominal data were analysed as frequency and percentages. The correlation between two variables were analysed by Pearson's correlation and the coefficient was calculated. The p-value was calculated by regression analysis and Analysis of Variance (ANOVA).

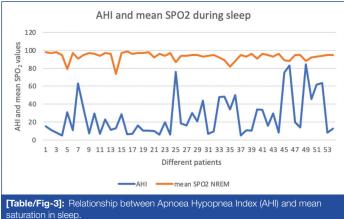
# RESULTS

Out of total 54 patients, 70.37% were males. Majority of them were between the age group 45-57 years followed by 18-31 years. Total 18 patients had a BMI between 26-31.4 kg/m<sup>2</sup> followed by 15 patients between 20.5-25.9 kg/m<sup>2</sup>. One patient was paraplegic and hence BMI could not be assessed. Out of the total, 22 had mild, 14 moderate and 18 severe OSA, respectively [Table/Fig-1]. Number of relative desaturations recorded was from 0-640 [Table/Fig-2]. Among desaturation details of all the patients, the minimum saturation (SpO<sub>2</sub>) recorded during sleep ranged from 27-97% [Table/Fig-3] and mean SpO2 ranged between 74-99% [Table/Fig-4].

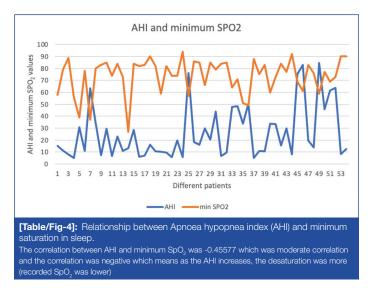
Demographic details	Frequency	Percentage
Age (years)		
18-31	17	31.48%
32-44	12	22.22%
45-57	19	35.18%
58-70	6	11.11%
Gender		
Males	38	70.37%
Females	16	29.62%
Body mass index (kg/m²)*		
14.9-20.4	9	16.66%
20.5-25.9	15	27.77%
26-31.4	18	33.33%
31.5-36.9	10	18.51%
37-42.4	1	1.85%
Obstuctive sleep apnoea severity as per Apnoea Hypopnea Index (AHI)		
Mild (5-15)	22	40.74%
Moderate (15.1-30)	14	25.92%
Severe (>30)	18	33.33%
[Table/Fig-1]: Demographic details.		

\*One patient was paraplegic so; BMI could not be calcula

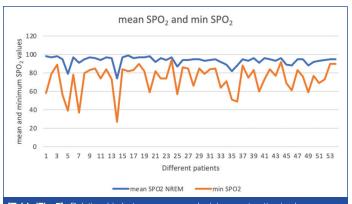
Parameters	Number of patients	Percentage	
Mean SpO <sub>2</sub>			
74-78.4	1	1.85%	
78.5-82.8	2	3.7%	
82.9-87.2	1	1.85%	
87.3-91.6	7	12.96%	
91.7-96	31	57.4%	
96.1-100	12	22.22%	
Minimum SpO <sub>2</sub>			
27-41	3	5.55%	
41.1-55	2	3.7%	
55.1-69	11	20.37%	
69.1-83	22	40.74%	
83.1-97	16	29.62%	
Relative desaturation			
0-160	34	62.96%	
161-320	10	18.51%	
321-480	6	11.11%	
481-640	4	7.4%	
[Table/Fig-2]: Details of desaturations in sleep of the patients included for the study.			



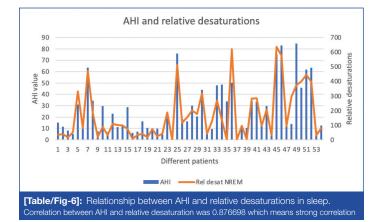
The correlation coefficient between AHI and mean SpO<sub>2</sub> in sleep was-0.4542 which was moderate correlation and the correlation is negative which means as the AHI increases, the desaturation was more (recorded SpO, was lower)



The correlation between AHI and mean SpO<sub>2</sub> in sleep was r-value=-0.4542, p-value=0.001 and the correlation between AHI and minimum SpO<sub>2</sub> was r-value=-0.45577, p-value=0.001, respectively. Correlation between mean SpO<sub>2</sub> and minimum SpO<sub>2</sub> was r-value=0.747266, p-value <0.001 and the correlation between AHI and relative desaturation was r-value=0.876698, p-value=0.001 [Table/Fig-3-6].



[Table/Fig-5]: Relationship between mean and minimun saturation in sleep. Correlation between mean SpO, and minimum SpO, was 0.747266 which means strong correlation



#### DISCUSSION

This study showed that OSA is more prevalent in males than females and a male to female ratio was 2.3:1 which is similar to previous studies showing a ratio of 3:1 to 5:1 in the general population [8-10]. OSA is commonly seen in the age group between 44-57 years and is consistent with previous study which was common in 45-53 years [8]. Minimum SpO<sub>2</sub> ranged from 27-94% in various subjects with OSA in our study. Minimum SpO, and severity of OSA (as determined by AHI) had only moderate correlation (r of -0.45), mean SpO<sub>2</sub> and AHI also had moderate correlation (r of -0.45), relative desaturation and AHI had a strong correlation (r-value=0.87) which is consistent with previous study, in which Wali SO et al., found that parameters such as Desaturation Index (DI), the sum of all desaturations, desaturation below 90%, the average duration of respiratory events, and indices of total arousals and respiratory arousals correlated directly with severity OSA (p-value <0.001). The correlation between mean SpO and minimum SpO<sub>2</sub> in sleep was 0.75. This means that nocturnal hypoxia and the nadir saturation in sleep are linked [5].

The type of metabolism at cellular level is determined by the oxygen concentration in the mitochondria [11-14]. This is because the final step for aerobic metabolism takes place in the mitochondria. Cellular metabolic demands, the cell type and its adaptability to hypoxia are the factors which determine the response to various levels of hypoxia from substantial adaptation to cell death [14-16]. If tissue hypoxia occurs, global compensatory respiratory and cardiac mechanisms like regional pulmonary vasoconstriction to improve ventilation perfusion (V<sup>-</sup>/Q<sup>-</sup>) matching, hyperventilation to improve alveolar oxygen tension, acidosis-related right shift of the oxyhaemoglobin dissociation curve and increase in cardiac output occur to improve oxygen delivery are activated [13-16].

Hypoxia Inducible Factors (HIFs) are a group of heterodimeric proteins that interact with hundreds of genes in response to hypoxia [13-19]. It plays a central role in adaptive tissue responses like up-regulation of erythropoietin, angiogenic factors, and vasoactive mediators; activation of glycolytic enzymes to produce anaerobic

metabolism (with resulting lactate production); and even a mitochondrial hibernation-like phenomenon resulting in decreased oxygen demands [8,18-28].

Mean SpO<sub>2</sub><92% and minimum SpO<sub>2</sub><80% in sleep were associated with carotid plaque formation regardless of their normotensive or hypertensive status [29,30]. Ventricular ectopic in OSA patients is more likely if SpO<sub>2</sub> drops below 60% and unlikely if SpO<sub>2</sub> stays above 60% [30]. It was also observed symptoms of OSA were closely related to oxygen desaturations than AHI [31]. Similarly resistance to ischaemic conduction failure is a sensitive but non specific marker of nocturnal hypoxemia in OSA patients [32]. Repeated hypoxia and normoxia induces endothelial dysfunction [33]. Oxygen desaturation plays a key role in the connection between obstructive sleep apnea and hypercoagulability state [34]. Nocturnal hypoxia due to OSA is an independent predictor of atrial fibrillation in patients with subacute ischaemic stroke [35]. In this study it has been observed as severity of the OSA worsens there is steeper fall of saturation which leads pronounced physiological impact of apnoea.

#### Limitation(s)

Study involved sample size of 54 which was smaller to conclude physiological impacts of apnoea and hypopnea. Study should have also incorporated heart rate variations as other physiological variant to assess severity of OSA.

### CONCLUSION(S)

Degree of desaturation worsened with increasing severity of OSA. Greater degree of desaturation and lowest recorded saturation was seen during severe obstructive sleep apnoea. Further studies are required to confirm that desaturation is a surrogate indicator of severity of obstructive sleep apnoea.

#### REFERENCES

- [1] Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, et al. Rules for scoring respiratory events in sleep: Update of the 2007 AASM manual for the scoring of sleep and associated events: Deliberations of the sleep apnea definitions task force of the American Academy of Sleep Medicine. J Clin Sleep Med. 2012;8(5):597-19.
- [2] Budhiraja R, Javaheri S, Parthasarathy S, Berry RB, Quan SF. The association between obstructive sleep apnea characterised by a minimum 3 percent oxygen desaturation or arousal hypopnea definition and hypertension. J Clin Sleep Med. 2019;15(9):1261-70.
- [3] Eckert DJ, Malhotra A. Pathophysiology of adult obstructive sleep apnea. Proc Am Thorac Soc. 2008;5(2):144-53.
- [4] Epstein LJ, Kristo D, Strollo Jr PJ, Friedman N, Malhotra A, Patil SP, et al. Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med. 2009;5(3):263-76.
- [5] Wali SO, Abaalkhail B, AlQassas I, Alhejaili F, Spence DW, Pandi-Perumal SR. The correlation between oxygen saturation indices and the standard obstructive sleep apnea severity. Ann Thorac Med. 2020;15(2):70.
- [6] Arnardottir ES, Bjornsdottir E, Olafsdottir KA, Benediktsdottir B, Gislason T. Obstructive sleep apnoea in the general population: Highly prevalent but minimal symptoms. Eur Respir J. 2016;47(1):194-02.
- [7] Kapur VK, Auckley DH, Chowdhuri S, Kuhlmann DC, Mehra R, Ramar K, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: An American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2017;13(3):479-04.
- [8] Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med. 1993;328(17):1230-35.
- [9] Quintana-Gallego E, Carmona-Bernal C, Capote F, Sánchez-Armengol Á, Botebol-Benhamou G, Polo-Padillo J, et al. Gender differences in obstructive sleep apnea syndrome: A clinical study of 1166 patients. Respir med. 2004;98(10):984-89.
- [10] Lin CM, Davidson TM, Ancoli-Israel S. Gender differences in obstructive sleep apnea and treatment implications. Sleep Med Rev. 2008;12(6):481-96.
- [11] Mason RJ, Broaddus VC, Martin TR, King TE, Schraufnagel D, Murray JF, Nadel JA. Murray and Nadel's Textbook of Respiratory Medicine E-Book: 2-Volume Set. Elsevier Health Sciences; 2010.
- [12] West JB. Pulmonary Physiology and Pathophysiology: An Integrated, Case-Based Approach. Philadelphia: Lippincott Williams & Wilkins, 2001; Japanese translation, 2002; Greek translation, 2002. ISBN 978-0-7817-6701-9.
- [13] Finch CA. Oxygen transport in man. Chest. 1972;61(2):12S-3S.
- [14] MacIntyre NR. Tissue hypoxia: Implications for the respiratory clinician. Respir care. 2014;59(10):1590-96.

- [15] Leach RM, Treacher DF. Oxygen transport 2. Tissue hypoxia. BMJ. 1998;317(7169):1370-73.
- [16] Martin DS, Khosravi M, Grocott MP, Mythen MG. Concepts in hypoxia reborn. Crit Care. 2010;14(4):01-07.
- [17] Deng X, Gu W, Li Y, Liu M, Li Y, Gao X. Age-group-specific associations between the severity of obstructive sleep apnea and relevant risk factors in male and female patients. PLoS One. 2014;9(9):e107380.
- [18] Schumacker PT. Hypoxia-inducible factor-1 (HIF-1). Crit Care Med. 2005;33(12 Suppl):S423-25.
- [19] Semenza GL. Hypoxia-inducible factors in physiology and medicine. Cell. 2012;148(3):399-08.
- [20] Chandel NS, Maltepe E, Goldwasser E, Mathieu CE, Simon MC, Schumacker P. Mitochondrial reactive oxygen species trigger hypoxia-induced transcription. Proc Natl Acad Sci USA. 1998;95(20):11715-20.
- [21] Formenti F, Constantin-Teodosiu D, Emmanuel Y, Cheeseman J, Dorrington KL, Edwards LM, et al. Regulation of human metabolism by hypoxia-inducible factor. Proc Natl Acad Sci USA. 2010;107(28):12722-27.
- [22] Kaelin Jr WG, Ratcliffe PJ. Oxygen sensing by metazoans: The central role of the HIF hydroxylase pathway. Mol cell. 2008;30(4):393-02.
- [23] Majmundar AJ, Wong WJ, Simon MC. Hypoxia-inducible factors and the response to hypoxic stress. Mol cell. 2010;40(2):294-09.
- [24] Yoon D, Ponka P, Prchal JT. Hypoxia. 5. Hypoxia and hematopoiesis. Am J Physiol Cell Physiol. 2011;300(6):C1215-22.
- [25] Dehne N, Fuhrmann D, Brune B. Hypoxia-inducible factor (HIF) in hormone signaling during health and disease. Cardiovascular & Hematological Agents in Medicinal Chemistry. 2013;11(2):125-35.
- [26] Fukuda R, Zhang H, Kim JW, Shimoda L, Dang CV, Semenza GL. HIF-1 regulates cytochrome oxidase subunits to optimize efficiency of respiration in hypoxic cells. Cell. 2007;129(1):111-22.

- [27] Papandreou I, Cairns RA, Fontana L, Lim AL, Denko NC. HIF-1 mediates adaptation to hypoxia by actively downregulating mitochondrial oxygen consumption. Cell Metab. 2006;3(3):187-97.
- [28] Resar JR, Roguin A, Voner J, Nasir K, Hennebry TA, Miller JM, et al. Hypoxiainducible factor 1α polymorphism and coronary collaterals in patients with ischemic heart disease. Chest. 2005;128(2):787-91.
- [29] Baguet JP, Hammer L, Leívy P, Pierre H, Launois S, Mallion JM, et al. The severity of oxygen desaturation is predictive of carotid wall thickening and plaque occurrence. Chest. 2005;128(5):3407-12.
- [30] Shepard Jr JW, Garrison MW, Grither DA, Dolan GF. Relationship of ventricular ectopy to oxyhemoglobin desaturation in patients with obstructive sleep apnea. Chest. 1985;88(3):335-40.
- [31] Temirbekov D, Güneş S, Yazıcı ZM, Sayın İ. The ignored parameter in the diagnosis of obstructive sleep apnea syndrome: The oxygen desaturation index. Turk Arch Otorhinolaryngol. 2018;56(1):01.
- [32] Mayer P, Dematteis M, Pepin JL, Wuyam B, Veale DA, Vila A, et al. Peripheral neuropathy in sleep apnea: A tissue marker of the severity of nocturnal desaturation. Am J Respir Crit Care Med. 1999;159(1):213-19.
- [33] Nácher M, Farré R, Montserrat JM, Torres M, Navajas D, Bulbena O, et al. Biological consequences of oxygen desaturation and respiratory effort in an acute animal model of obstructive sleep apnea (OSA). Sleep Med. 2009;10(8):892-97.
- [34] Shitrit D, Peled N, Shitrit AB, Meidan S, Bendayan D, Sahar G, et al. An association between oxygen desaturation and D-dimer in patients with obstructive sleep apnea syndrome. Thromb Haemost. 2005;94(09):544-47.
- [35] Chen CY, Ho CH, Chen CL, Yu CC. Nocturnal desaturation is associated with atrial fibrillation in patients with ischemic stroke and obstructive sleep apnea. J Clin Sleep Med. 2017;13(5):729-35.

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#### AUTHOR DECLARATION:

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- For any images presented appropriate consent has been obtained from the subjects. NA

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