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Association of demographics and hematological biomarkers with obstructive sleep apnea severity in pulmonary patients undergoing STOP-Bang screening

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ABSTRACT

Obstructive sleep apnea (OSA) is a common sleep disorder characterized by repeated partial or complete obstruction of the upper airways during sleep. In this study, we aimed to investigate the association of demographics and hematological biomarkers with obstructive sleep apnea severity in patients with pulmonary disease who were candidates for the STOP-Bang test. This cross-sectional study was conducted in 2022 on 122 pulmonary disease patients, who were candidates for the STOP-Bang test, at the outpatient clinic of Razi Hospital, Rasht, northern Iran. Patients scoring <3 on the STOP-Bang test were excluded from the study. Conversely, patients with a score of ≥3, categorized as high-risk, were candidates for home sleep apnea testing (HSAT). Furthermore, patients identified as candidates for OSA were also tested for C-reactive protein (CRP) to quantitatively assess the relationship between CRP levels and the severity of OSA. Out of 122 patients, 51.6% were male. The mean age and body mass index (BMI) were 57.53 ± 13.99 years and 32.05 ± 4.41 kg/cm2, respectively. It has been demonstrated that height CRP, thyroid-stimulating hormone (TSH), and systolic blood pressure (SBP) are significantly associated with hypopnea-apnea index (HAI) in patients (P<0.05). Body mass index (BMI), age, neck circumference, and history of diabetes illustrated no statistically significant association with the severity of OSA (P<0.05). The severity of OSA was related to the male gender and the presence of OSA (P<0.05). According to the results, male gender and coexistence of OSA results in more severe conditions in these patients.

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1. Introduction

Obstructive sleep apnea (OSA) is a common sleep disorder characterized by repeated partial or complete obstruction of the upper airways during sleep [1]. This process causes periods of apnea and intermittent awakening from sleep, eventually leading to sleepiness during the day [2]. The primary risk factors for OSA include obesity, male gender, advancing age, hypertension, hyperlipidemia, and diabetes mellitus [3–5]. Additionally, there is a higher prevalence of OSA in patients with certain medical conditions, and is associated with an increased risk of neurologic conditions and cardiovascular diseases, including hypertension, coronary artery disease, heart failure, and stroke. It can also lead to metabolic disturbances, such as insulin resistance, glucose intolerance, and dyslipidemia [6–8]. Multiple factors contribute to the development of OSA, with upper airway anatomy and physiological changes during sleep playing a central role [9]. Obesity, particularly excessive fat deposition around the neck and upper airway, is a significant risk factor for OSA. Structural abnormalities, such as a narrowed or collapsible upper airway, can impede airflow during sleep [10,11].

Clinical evaluation, including comprehensive medical history, physical examination, and assessment of symptoms, is also essential for diagnosing OSA. Effective therapy for OSA aims to alleviate symptoms, improve sleep quality, and reduce associated health risks [12]. Weight loss, positional therapy, and lifestyle modifications can contribute to the better management of OSA [13]. The high frequency of OSA leads to better quality of life, reduced health risks for affected individuals, and targeted therapies to improve patient outcomes [14]. This study aimed to investigate the association of demographics and hematological biomarkers with obstructive sleep apnea severity in patients with pulmonary disease who were candidates for the STOP-Bang test.

2. Materials and Methods

2.1 Study design

This cross-sectional study was conducted in 2022 on 122 pulmonary disease patients, who were candidates for the STOP-Bang test, at the outpatient clinic of Razi Hospital, Rasht, northern Iran. The patients' data including age, gender, weight, height, and body mass index (BMI): underweight (BMI <18.5 kg/m2), average weight (BMI = 18.5–24.99 kg/m2), overweight (BMI = 25–29.9 kg/m2) and obese (BMI ≥30 kg/m2), neck circumstance, underlying disease (diabetes, hypertension, hypothyroidism, hyperlipidemia, cardiovascular disease, diabetes, neurological disease, asthma, and allergy), systolic blood pressure (SBP), diastolic blood pressure (DBP), C reactive protein (CRP) with normal range of <6 ml/dL, thyroid stimulating hormone (TSH) with normal range of 0.3-5 mU/L, fasting blood sugar (FBS) with normal range of 70-110 mg/dL, snoring, OSA, and severity of OSA was recorded. Patients with chronic lung diseases such as chronic obstructive pulmonary disease (COPD) and interstitial lung disease (ILD) were excluded from the study.

2.2 STOP-Bang questionnaire and home sleep apnea testing (HSAT)

STOP-Bang questionnaire was used to screen OSA. The questionnaire consisted of two components: STOP, which evaluated signs and symptoms of potential OSA, and Bang, which assessed characteristics associated with an increased risk of OSA. STOP items included snoring, daytime sleepiness, observed episodes of sleep apnea, and high blood pressure. A positive response to two or more items suggests a high risk of OSA [15]. Due to the scores of the STOP-Bang questionnaire, patients with a score less than 3 were excluded from the study, and patients with a score greater than 3, were candidates for HSAT. Based on other sub-objectives of the research, the patients who were candidates for obstructive sleep apnea were tested for CRP.

HSA test was evaluated by hypopnea-apnea index (HAI), that is the combined average number of apneas and hypopneas that occur per hour of sleep and categorized as mild (5-15 events/hour), moderate (15-30 events/hour), and severe (> 30 events/hour) [16]. HAS was performed as follows; the device was connected to the patient's body during the night, and parameters such as breathing pattern, breathing pauses, and air flow were monitored by a breathing sensor (breathing sensor). The chest and abdomen movements were recorded, and a pulse oximeter recorded blood oxygen levels. Finally, according to the information collection, OSA based on the AHI was classified as mild, moderate, and severe.

2.3 Statistical analysis

Mean ± standard deviation (D), frequency, and percentage were used to report the data. Pearson's correlation coefficient and independent T-test were used to investigate the relationship between variables. All analyzes were performed by SPSS 26.0 statistical software (IBM Corp., Armonk, NY). A P-value less than 0.05 was considered statistically significant.

3. Results

Of 122 patients, 63 (51.6%) were males, and 59 (48.4%) were female. The mean of age, weight, height, BMI, and neck circumstance were 57.53±13.99 (5-89 years) year, 84.81±15.77 kg (11-130 kg), 163.44±9.11 cm (130-188 cm), 32.05±4.41 kg/cm^2 (23.89-50.78 kg/cm^2), and 42.12±2.7 cm (34-51 cm), respectively. The average of CRP, TSH, FBS, SBP, and DBP were 12.38±3.65 ml/dL, 12.38±3.65 mU/L, 131.35±43.3

mg/dL, 120.74±11.72 mmHg, and 76.64±9.06 mmHg, respectively. Among patients, 114 (93.4%) and 93 (76.2%) had snoring and OSA, respectively. The mean severity score of OSA was 16.63 ± 18.22 (0.2-74.9). As illustrated in Table 1, the frequency of hypertension was higher than other underlying diseases (39.3%), and asthma/allergies were less frequent.

Table 1. Frequency of underlying disease among patients

Underlying disease	Frequency n(%)
Hypertension	48 (39.3)
Hyperlipidemia	37 (30.3)
Hpothyroiditis	8 (6.6)
Cardiovascular disease	15 (12.3)
Diabetes	20 (16.4)
Neurological disease	6 (4.9)
Asthma/Allergy	1 (0.8)

It has been demonstrated that height, CRP, TSH, and SBP had a significant association with HAI among patients (P<0.05), while other variables showed no statistically significant association with HAI (P>0.05). For an increase of one unit in height, CRP, TSH, and SBP, the HAI was significantly increased (P<0.05), Table 2. Moreover, the severity of OSA was significantly higher in male gender and patients with OSA (P<0.05) (Table 3).

Table 2. Association between apnea-hypopnea index with demographical and clinical data of patients

Variables	AHI Pearson correlation	*P* value
Age	0.105	0.251
Neck circumstance	0.136	0.136
Weight	0.017	0.851
Height	0.200	0.027
BMI	-0.026	0.780
CRP	0.472	0.004
TSH	0.486	<0.001
FBS	-0.038	0.678
SBP	0.204	0.025
DBP	-0.002	0.983

Table 3. Association between the mean of gender and symptoms of obstructive sleep apnea with the severity of obstructive sleep apnea in patients

Variables		The severity of OSA Mean±SD	*P* value
Gender	Male	20.58±20.79	0.024
	Female	12.34±13.90	
OSA	Yes	19.55±19.68	0.001
	No	7.37±6.87	
Snoring	Yes	17.12±18.50	0.127
	No	8.71±10.84	

4. Discussion

OSA is a common disease that causes significant morbidity if left untreated. The current study investigated the frequency and related factors to the severity of OSA in pulmonary patients who are candidates for the STOP-bang test 2022. The majority of the study population was middle-aged and males. While females are more likely to represent non-specific symptoms of OSA, such as mood disturbance, morning headache, insomnia, etc. [17,18]. It reported that the female gender predicts a better response to mandibular advancement device treatment and less severe OSA [19,20]. A study by Bauters et al. on assessing the STOP-bang questionnaire between gender reported a lower score of females than males [21].

Aging was reported to be associated with sleep dysregulation and increased rates of sleep complaints in the older population [22]. Moreover, consuming multiple medications is common among the elderly, which may contribute to more sleep disturbance [23]. In the current study, most patients were middle-aged, and no significant association was observed between age and HAI score among patients. Senaratna et al. reported that the risk of OSA increases with age and BMI [24]. Individuals with obesity have shorter sleep duration and more sleep problems than non-obese people, which is associated with poor sleep quantity and quality [25]. A meta-analysis study reported the association between OSA and metabolic syndrome [26]. Kong et al. demonstrated a strong relationship between OSA and obesity in adults [27]. Most patients in the current study were overweight or obese, representing higher OSA frequency. Also, the mean of CRP and FBS was higher than the normal range among the study population. A higher level of FBS and CRP in these patients could be due to their obesity. Obesity is associated with metabolic diseases such as diabetes and increased inflammatory markers such as CRP [28].

Also, in individuals with obesity, narrowing of the upper respiratory muscles occurs due to the accumulation of fatty tissues [29]. Obstruction in breathing due to the narrowing of the upper airway causes a noticeable increase in intrathoracic pressure and causes OSA and hypoxia [30]. There is increased activation of the sympathetic system due to episodes of apnea/hypoxia in patients with OSA. Periods of hypoxemia/apnea can decrease oxyhemoglobin saturation depending on the duration of the apnea period [31]. Due to the hypoxia associated with OSA, oxidative stress produces excessive reactive oxygen species, which can cause endothelial dysfunction and atherosclerosis [32]. Studies showed that the inflammatory markers CRP, tumor necrosis factor α (TNF-α), and interleukin-6 (IL-6) were increased in patients with OSA [30,33–35].

Additionally, Foroughi et al. reported that OSA was associated with upper age and a history of cardiovascular disease [36]. Silva et al. study showed increased hypertension frequency among older adults with OSA [37]. Also, it was demonstrated that the apneic episodes in OSA increase in blood preasure, which exposes the patient to cerebrovascular and cardiovascular risks [38].

Hypertension was the most prevalent underlying disease among our study population, and we observed that by one unit increase in SBP, the AHI significantly increased, which susceptible patients to severe OSA. Similarly, Cai et al. reported that OSA is a major

modifiable risk factor for hypertension, and patients with these complications are at increased risk for cardiovascular diseases [39].

The mean of TSH in the current study was higher than the normal range, and hypothyroidism had a frequency of 6.6% among patients. Tharavaputta et al. demonstrated that even after adjustment for potential confounding variables, hypothyroidism showed a significant association with sleep apnea [40]. Different studies reported contradictory results on the association between hypothyroidism and sleep apnea; some reported a strong association, while others reported no significant association [40–42].

In our study, patients with clinical suspicion were included due to the lack of sufficient funds for HSA testing. It is suggested that in future studies, the control group be considered to obtain a more accurate association between risk factors and severity of OSA.

The findings highlighted the role of gender and hypothyroidism in the severity of OSA in patients with obstructive disease. Also, obesity, diabetes, and hypertension were more prevalent in these patients, requiring better clinical management to improve the patient's outcome.

Authors' contributions

Supervision, Conceptualization and Methodology: AJ, AA, AT, RS; Data collection, Analysis and Interpretation: MK, AJ, RS; Writing draft and Editing: MK, AJ, AA, AT. All authors have read and approved the final manuscript.

Conflict of interest

No potential conflict of interest was reported by the authors.

Ethical declarations

The study desgin was confirmed by the ethical committee of the Guilan University of Medical Sciences, Rasht, Iran [IR.GUMS.REC.1401.593]. Informed consent was obtained from all individual participants included in the study. Written informed consent was obtained prior to participation.

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References

1. Senaratna CV, Perret JL, Lodge CJ, Lowe AJ, Campbell BE, Matheson MC, Hamilton GS, Dharmage SC. Prevalence of obstructive sleep apnea in the general population: A systematic review. Sleep Med Rev. 2017;34:70-81. DOI: 10.1016/j.smrv.2016.07.002 PMID: 27568340
2. Pinto JA, Ribeiro DK, Cavallini AF, Duarte C, Freitas GS. Comorbidities Associated with Obstructive Sleep Apnea: a Retrospective Study. Int Arch Otorhinolaryngol. 2016;20(2):145-50. DOI: 10.1055/s-0036-1579546 PMID: 27096019
3. Mitra AK, Bhuiyan AR, Jones EA. Association and Risk Factors for Obstructive Sleep Apnea and Cardiovascular Diseases: A Systematic Review. Diseases. 2021;9(4):88. DOI: 10.3390/diseases9040088 PMID: 34940026
4. Santilli M, Manciocchi E, D'Addazio G, Di Maria E, D'Attilio M, Femminella B, Sinjari B. Prevalence of Obstructive Sleep Apnea Syndrome: A Single-Center Retrospective Study. Int J Environ Res Public Health. 2021;18(19):10277. DOI: 10.3390/ijerph181910277 PMID: 34639577
5. 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):1311-22. DOI: 10.3978/j.issn.2072-1439.2015.06.11 PMID: 26380759
6. Yeghiazarians Y, Jneid H, Tietjens JR, Redline S, Brown DL, El-Sherif N, et al. Obstructive Sleep Apnea and Cardiovascular Disease: A Scientific Statement From the American Heart Association. Circulation. 2021;144(3):e56–67. DOI: 10.1161/CIR.0000000000000988
7. Kareem O, Tanvir M, Bader GN. Obstructive Sleep Apnea and Metabolic Syndrome. Sleep Vigil. 2022;6(1):85–99. DOI: 10.1007/s41782-022-00204-5
8. Ferini-Strambi L, Lombardi GE, Marelli S, Galbiati A. Neurological Deficits in Obstructive Sleep Apnea. Curr Treat Options Neurol. 2017;19(4):16. DOI: 10.1007/s11940-017-0451-8 PMID: 28374233
9. Dempsey JA, Veasey SC, Morgan BJ, O'Donnell CP. Pathophysiology of sleep apnea. Physiol Rev. 2010;90(1):47-112. DOI: 10.1152/physrev.00043.2008 PMID: 20086074
10. Eckert DJ, Malhotra A. Pathophysiology of adult obstructive sleep apnea. Proc Am Thorac Soc. 2008;5(2):144-53. DOI: 10.1513/pats.200707-114MG PMID: 18250206
11. Tan SN, Yang HC, Lim SC. Anatomy and pathophysiology of upper airway obstructive sleep apnoea: review of the current literature. Sleep Medicine Research. 2021;12(1):1-8. DOI: 10.17241/smr.2020.00829
12. Abbasi A, Gupta SS, Sabharwal N, Meghrajani V, Sharma S, Kamholz S, Kupfer Y. A comprehensive review of obstructive sleep apnea. Sleep Sci. 2021;14(2):142-154. DOI: 10.5935/1984-0063.20200056 PMID: 34381578
13. Gottlieb DJ, Punjabi NM. Diagnosis and Management of Obstructive Sleep Apnea: A Review. JAMA. 2020;323(14):1389-1400. DOI: 10.1001/jama.2020.3514 PMID: 32286648
14. Xia F, Sawan M. Clinical and Research Solutions to Manage Obstructive Sleep Apnea: A Review. Sensors (Basel). 2021;21(5):1784. DOI: 10.3390/s21051784 PMID: 33806496
15. Abumuamar AM, Dorian P, Newman D, Shapiro CM. The STOP-BANG questionnaire shows an insufficient specificity for detecting obstructive sleep apnea in patients with atrial fibrillation. J Sleep Res. 2018;27(6):e12702. DOI: 10.1111/jsr.12702 PMID: 29682848
16. Medicine AA of S. Obstructive sleep Apnea. Am Acad Sleep Med. 2008. URL: https://aasm.org/resources/factsheets/sleepapnea.pdf
17. Levartovsky A, Dafna E, Zigel Y, Tarasiuk A. Breathing and Snoring Sound Characteristics during Sleep in Adults. J Clin Sleep Med. 2016;12(3):375-84. DOI: 10.5664/jcsm.5588 PMID: 26518701
18. Nigro CA, Dibur E, Borsini E, Malnis S, Ernst G, Bledel I, González S, Arce A, Nogueira F. The influence of gender on symptoms associated with obstructive sleep apnea. Sleep Breath. 2018;22(3):683-693. DOI: 10.1007/s11325-017-1612-4 PMID: 29392572
19. Chen H, Eckert DJ, van der Stelt PF, Guo J, Ge S, Emami E, Almeida FR, Huynh NT. Phenotypes of responders to mandibular advancement device therapy in obstructive sleep apnea patients: A systematic review and meta-analysis. Sleep Med Rev. 2020;49:101229. DOI: 10.1016/j.smrv.2019.101229 PMID: 31785583

20. Won CHJ, Reid M, Sofer T, Azarbarzin A, Purcell S, White D, Wellman A, Sands S, Redline S. Sex differences in obstructive sleep apnea phenotypes, the multi-ethnic study of atherosclerosis. Sleep. 2020;43(5):zsz274. DOI: 10.1093/sleep/zsz274 PMID: 31687772
21. Bauters FA, Loof S, Hertegonne KB, Chirinos JA, De Buyzere ML, Rietzschel ER. Sex-specific sleep apnea screening questionnaires: closing the performance gap in women. Sleep Med. 2020;67:91-98. DOI: 10.1016/j.sleep.2019.10.023 PMID: 31918123
22. Moraes W, Piovezan R, Poyares D, Bittencourt LR, Santos-Silva R, Tufik S. Effects of aging on sleep structure throughout adulthood: a population-based study. Sleep Med. 2014;15(4):401-9. DOI: 10.1016/j.sleep.2013.11.791 PMID: 24657204
23. Christensen LD, Reilev M, Juul-Larsen HG, Jørgensen LM, Kaae S, Andersen O, Pottegård A, Petersen J. Use of prescription drugs in the older adult population-a nationwide pharmacoepidemiological study. Eur J Clin Pharmacol. 2019;75(8):1125-1133. DOI: 10.1007/s00228-019-02669-2 PMID: 30949726
24. Senaratna CV, English DR, Currier D, Perret JL, Lowe A, Lodge C, Russell M, Sahabandu S, Matheson MC, Hamilton GS, Dharmage SC. Sleep apnoea in Australian men: disease burden, co-morbidities, and correlates from the Australian longitudinal study on male health. BMC Public Health. 2016;16(Suppl 3):1029. DOI: 10.1186/s12889-016-3703-8 PMID: 28185594
25. Gohil A, Hannon TS. Poor sleep and obesity: concurrent epidemics in adolescent youth. Frontiers in endocrinology. 2018;9:364. DOI: 10.3389/fendo.2018.00364
26. Kong DL, Qin Z, Wang W, Pan Y, Kang J, Pang J. Association between obstructive sleep apnea and metabolic syndrome: a meta-analysis. Clin Invest Med. 2016;39(5):E161-E172. DOI: 10.25011/cim.v39i5.27148 PMID: 27805899
27. Foster GD, Sanders MH, Millman R, Zammit G, Borradaile KE, Newman AB, et al. Obstructive sleep apnea among obese patients with type 2 diabetes. Diabetes Care. 2009;32(6):1017–9. DOI: 10.2337/dc08-1776 PMID: 19279303
28. Khanna D, Khanna S, Khanna P, Kahar P, Patel BM. Obesity: A Chronic Low-Grade Inflammation and Its Markers. Cureus. 2022;14(2):e22711. DOI: 10.7759/cureus.22711 PMID: 35386146
29. Elliot JG, Donovan GM, Wang KCW, Green FHY, James AL, Noble PB. Fatty airways: implications for obstructive disease. Eur Respir J. 2019;54(6):1900857. DOI: 10.1183/13993003.00857-2019 PMID: 31624112
30. Destors M, Tamisier R, Galerneau LM, Lévy P, Pepin JL. Pathophysiology of obstructive sleep apnea syndrome and its cardiometabolic consequences. Presse Medicale (Paris, France: 1983). 2017;46(4):395-403. DOI: 10.1016/j.lpm.2016.09.008 PMID: 28126503
31. Dewan NA, Nieto FJ, Somers VK. Intermittent hypoxemia and OSA: implications for comorbidities. Chest. 2015;147(1):266-274. DOI: 10.1378/chest.14-0500 PMID: 25560865
32. Eisele HJ, Markart P, Schulz R. Obstructive Sleep Apnea, Oxidative Stress, and Cardiovascular Disease: Evidence from Human Studies. Oxid Med Cell Longev. 2015;2015:608438. DOI: 10.1155/2015/608438 PMID: 26167241
33. Phosat C, Panprathip P, Chumpathat N, Prangthip P, Chantratita N, Soonthornworasiri N, et al. Elevated C-reactive protein, interleukin 6, tumor necrosis factor alpha and glycemic load associated with type 2 diabetes mellitus in rural Thais: a cross-sectional study. BMC Endocr Disord.. 2017;17(1):44. DOI: 10.1186/s12902-017-0189-z
34. Nadeem R, Molnar J, Madbouly EM, Nida M, Aggarwal S, Sajid H, Naseem J, Loomba R. Serum inflammatory markers in obstructive sleep apnea: a meta-analysis. J Clin Sleep Med. 2013;9(10):1003-12. DOI: 10.5664/jcsm.3070 PMID: 24127144
35. Kheirandish-Gozal L, Gozal D. Obstructive Sleep Apnea and Inflammation: Proof of Concept Based on Two Illustrative Cytokines. Int J Mol Sci. 2019;20(3):459. DOI: 10.3390/ijms20030459 PMID: 30678164
36. Foroughi M, Malekmohammad M, Sharafkhaneh A, Emami H, Adimi P, Khoundabi B. Prevalence of Obstructive Sleep Apnea in a High-Risk Population Using the Stop-Bang Questionnaire in Tehran, Iran. Tanaffos. 2017;16(3):217-224. PMID: 29849675
37. Silva MDS, Poyares D, Silva LO, Souza KM, Andersen ML, Ohayon MM, Tufik S, Piovezan RD. Associations of the Severity of Obstructive Sleep Apnea With Age-Related Comorbidities: A Population-Based Study. Front Neurol. 2022;13:802554. DOI: 10.3389/fneur.2022.802554 PMID: 35620781
38. Bangash A, Wajid F, Poolacherla R, Mim FK, Rutkofsky IH. Obstructive Sleep Apnea and Hypertension: A Review of the Relationship and Pathogenic Association. Cureus. 2020;12(5):e8241. DOI: 10.7759/cureus.8241 PMID: 32582500
39. Cai A, Wang L, Zhou Y. Hypertension and obstructive sleep apnea. Hypertens Res. 2016;39(6):391-5. DOI: 10.1038/hr.2016.11 PMID: 26888120
40. Thavaraputta S, Dennis JA, Laoveeravat P, Nugent K, Rivas AM. Hypothyroidism and Its Association With Sleep Apnea Among Adults in the United States: NHANES 2007-2008. J Clin Endocrinol Metab. 2019;104(11):4990-4997. DOI: 10.1210/jc.2019-01132 PMID: 31305928
41. Zhang M, Zhang W, Tan J, Zhao M, Zhang Q, Lei P. Role of hypothyroidism in obstructive sleep apnea: a meta-analysis. Curr Med Res Opin. 2016;32(6):1059-64. DOI: 10.1185/03007995.2016.1157461 PMID: 26907534
42. Bielicki P, Przybyłowski T, Kumor M, Barnaś M, Wiercioch M, Chazan R. Thyroid Hormone Levels and TSH Activity in Patients with Obstructive Sleep Apnea Syndrome. Adv Exp Med Biol. 2016;878:67-71. DOI: 10.1007/5584_2015_180 PMID: 26542600