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RESEARCH ARTICLE
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CORRELATION OF INSULIN RESISTANCE WITH SEVERITY OF OBSTRUCTIVE SLEEP APNOEA

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ABSTRACT

Background: OSA, or obstructive sleep apnea, is a common but underdiagnosed sleep disorder in which the upper airway gets blocked during sleep, causing periods of low oxygen, sleep fragmentation, and being too sleepy during the day. It has been strongly associated with metabolic disorders, including IR (Insulin Resistance), a key factor in the pathogenesis of type 2 diabetes mellitus and metabolic syndrome. While various studies have postulated a correlation between OSA severity and insulin resistance, conflicting findings necessitate further investigation. This study aims to evaluate the relationship between the severity of OSA and insulin resistance using polysomnographic data and metabolic parameters.

Methods: A hospital-based cross-sectional study was conducted on 60 patients diagnosed with OSA through overnight PSG (Polysomnography). The severity of OSA was classified based on the AHI (Apnea-Hypopnea Index) into mild, moderate, and severe categories. Fasting blood glucose and insulin levels were measured to calculate the HOMA-IR (Homeostasis Model Assessment of Insulin Resistance). Statistical analysis was performed to assess the correlation between OSA severity and insulin resistance, with a p-value <0.05 considered significant.

Results: A significant correlation was observed between increasing OSA severity and higher HOMA-IR values, suggesting a positive association between OSA and insulin resistance. Severe OSA cases demonstrated significantly higher fasting insulin levels and HOMA-IR indices compared to mild and moderate OSA groups. However, no significant association was found between BMI (Body Mass Index) and insulin resistance, indicating that OSA may contribute to metabolic dysfunction independently of obesity.

Conclusion: The study highlights a significant association between OSA severity and insulin resistance, supporting the hypothesis that OSA is an independent risk factor for metabolic dysfunction. These findings emphasize the need for early screening and management of insulin resistance in patients with moderate to severe OSA to mitigate the risk of metabolic syndrome and

cardiovascular complications. Further large-scale longitudinal studies are recommended to explore causality and potential therapeutic interventions.

Keywords: Obstructive Sleep Apnea, Insulin Resistance, HOMA-IR, Polysomnography, Metabolic Syndrome, Apnea-Hypopnea Index.

INTRODUCTION

Obstructive sleep apnea is a highly prevalent sleep-related breathing disorder, affecting approximately 4% of men and 2% of women in the general population.[1] It has been strongly linked to the global obesity epidemic, which is a major public health concern. OSA is characterized by recurrent episodes of upper airway obstruction, leading to significant reductions in ventilation. These episodes result in recurrent arousals during sleep and episodic oxyhemoglobin desaturations.[2] OSA occurs due to the repetitive, partial, or complete obstruction of the upper airway during sleep, despite continued respiratory effort. The disorder is classified into three major types: obstructive, central, and mixed sleep apnea. Obstructive sleep apnea specifically refers to the cessation or reduction of airflow in the presence of ongoing respiratory effort, primarily due to the collapse of the upper airway, typically at the oropharyngeal level. In contrast, central sleep apnea occurs when the neural drive to respiratory muscles is transiently abolished, often secondary to neurological conditions such as brainstem tumors, encephalitis, or high cervical spinal cord compression.

OSA is associated with a broad spectrum of clinical consequences, including excessive daytime sleepiness, neurocognitive dysfunction, cardiovascular diseases (such as hypertension, stroke, myocardial infarction, and heart failure), metabolic dysfunction, respiratory failure, and cor pulmonale. The major risk factors for OSA include obesity, male gender, post-menopausal status in women, and increasing age.[3] With the rising prevalence of obesity in countries like the United States, OSA is expected to become an escalating public health issue.[4]

Sleep plays a crucial role in metabolic regulation, and sleep deprivation is believed to have adverse effects on biochemical processes, particularly carbohydrate metabolism. Van Helder et al. demonstrated that insulin response to an oral glucose tolerance test was significantly higher following acute sleep deprivation (about 60 hours of continuous wakefulness) compared to normal sleep conditions, suggesting that an insulin-resistant state may be induced by sleep deprivation.[5] Individuals experiencing prolonged sleep deprivation exhibit irritability, fatigue, disorientation, and difficulty concentrating, which contributes to physiological stress.[6] The secretion rates of ACTH (Adrenocorticotropic Hormone) and cortisol follow a 24-hour cyclic pattern, with elevated levels during early morning hours and lower levels in the late evening, regulated by hypothalamic signaling mechanisms.

Previous studies have indicated that glucose tolerance is significantly better in the morning compared to the evening.[7] Spiegel et al. further postulated that sleep deprivation impairs glucose tolerance.[8] Acute sleep deprivation, whether partial or total, has been linked to altered HPA (Hypothalamo-Pituitary-Adrenal) axis function, as evidenced by increased evening cortisol levels on the following day.[9] Studies conducted both locally and internationally suggest a strong correlation between OSA and metabolic syndrome, with insulin resistance playing a key role in this association.

Currently, there is no universally recognized 'gold standard' for diagnosing OSA. However, PSG (Polysomnography) serves as the reference standard for diagnosis, assessing various sleep variables such as the AHI (Apnea-Hypopnea Index) or RDI (Respiratory Disturbance Index). According to the American Sleep Association, sleep apnea is categorized as follows: mild (5–14 apneas per hour), moderate (15–29 apneas per hour), and severe (≥30 apneas per hour).

This study aims to investigate the association between OSA and insulin resistance while also analyzing whether an increase in insulin resistance values corresponds with the severity of OSA.

AIMS AND OBJECTIVES

This study aims to investigate the correlation between insulin resistance and the severity of OSA (Obstructive Sleep Apnoea) to enhance the understanding of their interrelationship. The objectives include assessing insulin resistance levels in individuals with varying degrees of OSA, determining the strength and direction of their correlation, and evaluating potential risk factors that contribute to both conditions. Additionally, the study seeks to explore whether worsening OSA severity is associated with increasing insulin resistance, thereby providing insights into potential metabolic implications. The findings may help in identifying high-risk individuals and guiding targeted interventions for improved management of both conditions.

MATERIALS AND METHODS

Study Design

This time-bound, hospital-based, cross-sectional study was conducted at K.S. Hegde Hospital, which is affiliated with K.S. Hegde Medical Academy, a unit of Nitte University, Deralakatte, Mangalore. The study was carried out in two phases, from January 2016 to June 2018.

Inclusion and Exclusion Criteria

The study included patients diagnosed with OSA based on the Berlin questionnaire and polysomnography, as determined by AHI values, with only consenting individuals being eligible. Patients were excluded if they had been previously diagnosed with other sleep disorders such as narcolepsy, were on specific medications including immunosuppressants, narcotics, antidepressants, or sedatives, or had consumed alcohol prior to the study. Additionally, all non-consenting individuals were excluded from participation.

Sample Size Calculation

60 patients (based on anticipated prevalence of 20 percent, precision of 10 percent, level of significance of 5 percent, and sample size of 60) have been arrived at. The formula that has been used to calculate the sample size is $n=4pq/d^2$.

Data Collection Method

The data collection for this study was conducted using a comprehensive approach to evaluate OSA through multiple assessment methods. A detailed history of symptoms related to OSA was documented, incorporating standardized sleep study questionnaires such as the Berlin Questionnaire to assess risk factors and severity. A thorough clinical examination was performed to identify relevant physical findings associated with OSA. Objective sleep assessment was carried out using overnight polysomnography (Alice 5 Sleepware Polysomnography) to analyze sleep architecture, respiratory events, and oxygen saturation levels. Additionally, blood investigations were conducted to assess biochemical markers, including triglyceride levels and fasting blood sugars.

Statistical Analysis

The Chi-square test was employed to determine associations between categorical variables. The prevalence and frequency of OSA was analyzed in relation to triglyceride levels and fasting glucose levels to explore potential correlations.

RESULTS

Table 1 shows the gender distribution of the study population, indicating that the majority of participants were male (73.07%), while females constituted 26.92% of the total subjects.

Sex	**Frequency**	**Percentage (%)**
Male	57	73.07
Female	21	26.92
Total	**78**	**100**

Table 1: Gender Distribution of Patients

Age Group (Years)	Frequency	Percentage (%)
≤30	12	15.4
31 – 40	23	29.5
41 – 50	20	25.6
51 – 60	15	19.2
>60	8	10.3
Total	**78**	**100**

Table 2: Age Distribution of Study Population

In Table 2 participants were categorized into five age groups. The highest proportion of subjects fell within the 31-40 age group (29.5%), while the smallest representation was from those above 60 years (10.3%).

BMI (kg/m²)	Frequency	Percentage (%)
<25	23	29.5
25 - 30	39	50.0
>30	16	20.5
Total	**78**	**100**

Table 3: Distribution of BMI (Body Mass Index)

Table 3 shows the majority of participants (50%) had a BMI between 25-30, indicating that half of the study population fell in the overweight category. About 20.5% of subjects had a BMI above 30, indicating obesity.

Insulin Resistance	Frequency	Percentage (%)
Present	44	56.4
Absent	34	43.6
Total	**78**	**100**

Table 4: Insulin Resistance in the Study Population

Table 4 shows the distribution of insulin resistance (IR) among the participants. More than half (56.4%) of the subjects had insulin resistance, whereas 43.6% did not.

OSA Severity	Frequency	Percentage (%)
Mild	30	38.5
Moderate	12	15.4
Severe	36	46.2
Total	**78**	**100**

Table 5: Distribution of OSA Severity

In Table 5, OSA severity was classified into mild, moderate, and severe categories. The largest proportion of participants (46.2%) had severe OSA, while the smallest group (15.4%) had moderate OSA.

BMI (kg/m²)	IR Present (n)	IR Present (%)	IR Absent (n)	IR Absent (%)	Total (n)	Total (%)
<25	11	47.8	12	52.2	23	100
25 - 30	20	51.3	19	48.7	39	100
>30	13	81.3	3	18.8	16	100
Total	**44**	**56.4**	**34**	**43.6**	**78**	**100**

Table 6: BMI and Insulin Resistance Association

Table 6 examines the association between BMI and insulin resistance. The presence of insulin resistance increased with BMI, with 81.3% of obese individuals (>30 BMI) showing insulin resistance.

AHI Severity	IR Present (n)	IR Present (%)	IR Absent (n)	IR Absent (%)	Total (n)	Total (%)
Mild	11	36.7	19	63.3	30	38.5
Moderate	7	58.3	5	41.7	12	15.4
Severe	26	72.2	10	27.8	36	46.2
Total	**44**	**56.4**	**34**	**43.6**	**78**	**100**

Table 7: AHI and Insulin Resistance Association

Table 7 shows how insulin resistance correlates with OSA severity. Insulin resistance was significantly higher in severe OSA cases (72.2%) compared to mild cases (36.7%).

DISCUSSION

The present study aimed to investigate the association between the severity of OSA and insulin resistance, measured using the TG/HDL (Triglyceride-To-High-Density Lipoprotein) ratio. OSA is known to contribute to the development of IR through multiple physiological mechanisms, including autonomic activation, neuroendocrine dysfunction, direct effects of hypoxemia on glucose metabolism, and the release of proinflammatory cytokines such as interleukin-6 and tumor necrosis factor-alpha.[2]

A total of 78 participants were included in the study, with a predominance of males (73.07%). Age distribution indicated that 29.5% of subjects were between 31-40 years, and 25.6% were in the 41-50 years group. BMI classification revealed that 50% of the study population were overweight (BMI 25-30 kg/m²), and 20.5% were obese (BMI >30 kg/m²). Among the total sample, insulin resistance was present in 56.4% of the subjects. Notably, insulin resistance was more prevalent in individuals with severe OSA, with 72.2% of severe cases exhibiting IR. In comparison, 58.3% of moderate OSA cases and 36.7% of mild OSA cases were found to have IR. The Chi-square test demonstrated a statistically significant association between AHI and IR, with a p-value of 0.015. Further analysis revealed that when moderate and severe OSA were grouped together and compared against mild OSA, the association with IR became even stronger ($p = 0.005$). Additionally, a TG/HDL ratio cut-off value of ≥ 3.25 was identified as a marker of increased OSA severity and associated insulin resistance.

Several studies corroborate these findings. Baburao et al.,[10] assessed insulin resistance in non-diabetic individuals with moderate-to-severe OSA and found that CPAP therapy significantly improved insulin sensitivity over one month, even without notable changes in BMI. Similarly, Iftikhar et al.,[11] conducted a meta-analysis supporting OSA as an independent risk factor for IR. They proposed that intermittent hypoxia, a hallmark of OSA, plays a pivotal role in the development of IR by inducing oxidative stress and inflammatory pathways. Makino et al.[12] investigated the role of sleep-disordered breathing and plasma adiponectin levels in relation to IR. Their study concluded that AHI, BMI, and plasma adiponectin levels were independent predictors of IR, aligning with the present study's conclusion that increasing OSA severity is significantly linked to worsening insulin resistance.

Contrasting results were reported by some studies. Ip MS et al.,[13] found that while OSA was associated with insulin resistance, obesity remained the primary determinant of IR. Stepwise regression analysis revealed that AHI and minimum oxygen saturation were independent predictors of fasting insulin and HOMA-IR, reinforcing the complex interplay between OSA and metabolic dysregulation. Shamsuzzaman et al.,[14] found no significant difference in insulin resistance between OSA and non-OSA groups when stratified by BMI, but they observed that ODI (Oxygen Desaturation Index) was significantly associated with increased fasting glucose and insulin resistance. Similarly, Bhushan et al.,[15] analyzed metabolic changes in obese children and found that glucose homeostasis alterations were related to OSA severity, highlighting that OSA-related metabolic dysfunction is not exclusive to adults.

Gruber et al.,[16] analyzed metabolic syndrome prevalence in OSA patients and found that while OSA subjects exhibited higher rates of metabolic syndrome, their insulin resistance status was not significantly different from non-OSA subjects. These findings contrast with those of the present study, which identified a strong correlation between increasing OSA severity and IR. Finally, Punjabi et al.,[2] demonstrated that OSA severity, as indicated by AHI, was significantly associated with worsening insulin resistance and impaired glucose tolerance, even after adjusting for obesity. They

noted that a 4% decline in oxygen saturation significantly increased the odds of glucose intolerance, suggesting that intermittent hypoxia contributes to metabolic dysfunction independent of BMI.

CONCLUSION

The present study found that age and body mass index had no significant association with insulin resistance. However, the AHI demonstrated a significant correlation with insulin resistance, with a p-value of 0.015. Furthermore, severe-to-moderate forms of OSA exhibited a highly significant association with insulin resistance ($p = 0.005$) when compared to mild OSA, with an odds ratio of 3.8 for the risk estimation between severe OSA and insulin resistance. The study also facilitated the development of a receiver operating characteristic curve analysis, which identified a cut-off insulin resistance value of ≥ 3.25 as being associated with increased OSA severity. This threshold corresponded to a sensitivity of 72.2% and a specificity of 61.9%, further emphasizing the strong relationship between severe OSA and metabolic dysfunction.

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