Original Article

Lipid Profile and Ankle Brachial Index in Obese Male Subjects with Obstructive Sleep Apnea: Cross Sectional Analytical Study

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Abstract

Background: Obstructive sleep apnea (OSA) and dyslipidemia are common medical disorders that independently increase vascular morbidity and mortality. Currently, there is no conclusive data indicating that Obstructive Sleep Apnea serves as a risk factor for disrupted lipid profiles and subclinical atherosclerosis, as assessed by ankle-brachial index (ABI).

Objective: The objective of this cross-sectional study was to assess lipid profiles, blood sugar levels, and ankle brachial index in obese male participants with OSA and to compare them with obese individuals lacking OSA.

Methods: In the present study, 64 obese males with BMI > 25kg/m2 were included between ages 20 - 45 years. Subjects having acute or chronic inflammatory conditions were excluded. Obstructive sleep apnea (OSA) diagnosis involved two subjective assessment tools, the Berlin and STOP BANG questionnaires, followed by overnight portable pulse oximetry. The study participants were partitioned into two distinct groups, 32 with OSA and 32 without OSA. Following an overnight fast lasting between 10 to 12 hours, blood samples were collected. Fasting blood glucose and lipid profiles were then analyzed using a spectrophotometer. ABI was measured by using a Doppler ultrasound device. The data was collected and then entered SPSS version 22 and analyzed. The study utilized both Independent Samples t-test as well as Mann-Whitney U test to analyze and compare the quantitative variables across the two groups.

Results: Comparison of ABI between the study groups showed a non-significant difference p-value= 0.435. Fasting blood sugar levels showed insignificant difference (p-value=0.778) among the study groups. Comparison between the groups showed a nonsignificant difference in triglyceride levels (p=0.413) cholesterol (p-value=0.523), HDL (p-value=0.190), and LDL (p-value=0.888).

Conclusion: Normal lipid profile and normal ABI indicate the absence of detectable atherosclerosis in young apparently healthy OSA subjects without known comorbidities.

Keywords: Obstructive sleep apnea, Ankle-brachial index, Dyslipidemia

Introduction

Obstructive sleep apnea (OSA) manifests as the partial or complete collapse of the upper airway during sleep, leading to decreased intrathoracic pressure, intermittent hypoxia, and disrupted sleep patterns.[1] This condition is notably prevalent among obese males.[2] Moreover, despite being frequently underdiagnosed, OSA is notably linked to elevated rates of cardiovascular morbidity and mortality.[3] The connection between OSA and cardiovascular risk stems from several key mechanisms: repeated intermittent hypoxia, stimulation of the

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central nervous system, and fluctuations in intrathoracic pressure. These processes trigger oxidative stress, inflammation, disruptions in vasomotor function, and heightened sympathetic activity. Ultimately, they contribute to the development of atherosclerosis in the blood vessels.[4] Dyslipidemia stands out as a significant risk factor for cardiovascular diseases and is notably prevalent in OSA.[5] Moreover there is an increased risk for atherosclerosis in male patients with severe OSA.[6] The Ankle Brachial Index (ABI) reflects the ratio between ankle and brachial systolic blood pressure, serving as a valuable marker for subclinical atherosclerosis. ABI values below 0.9 indicate the presence of peripheral arterial disease (PAD) and serve as a robust predictor of cardiovascular events.[7] ABI serves as a valuable tool for evaluating both the risk of atherosclerosis and the extent of coronary involvement in suspected patients.[8] While obstructive sleep apnea is linked to cardiovascular diseases, the precise underlying mechanism remains incompletely understood. OSA is considered a potential atherogenic factor that contributes to arterial wall damage. Middle-aged individuals with OSA often exhibit early indicators of atherosclerosis.[9] Considering elements of the metabolic syndrome, certain studies have observed elevated triglyceride levels[10,11] and diminished high-density lipoproteins (HDL) levels in individuals having obstructive sleep apnea.[12] Conversely, other investigations have failed to establish a significant correlation between obstructive sleep apnea and dyslipidemia.[13,14] It is worth noting that most of these researches were not explicitly tailored to evaluate lipid profile. Hence, further evidence is required to draw definitive conclusions in this regard. Enhanced comprehension of the distinct associations between obstructive sleep apnea, metabolic syndrome, and insulin resistance is crucial for the development of tailored therapeutic interventions aimed at mitigating the elevated cardiometabolic risks observed in OSA patients. The objective of the current, cross-sectional study was to measure the lipid profile, blood sugar and ankle brachial index in obese male subjects having obstructive sleep apnea and compare them with obese subjects without OSA.

Methods

This cross-sectional study was conducted at Postgraduate Medical College (PGMI), Lahore, after obtaining ethical approval from the Institutional Review Board (IRB) during the years 2014-2015. The study enrolled employees and students of PGMI who met the inclusion and exclusion criteria. Sixty-four obese apparently healthy male subjects within the age of 20-45 years, with a value of BMI more than 25 kg/m2, were recruited after providing written informed consent.

The screening for obstructive sleep apnea (OSA) utilized two questionnaire proformas, namely the Berlin questionnaire and STOP-BANG questionnaire. Overnight pulse oximetry was done with portable pulse oximetry on all subjects, regardless of their risk level based on the questionnaires. Subjects were classified into the group of individuals with obstructive sleep apnea if they exhibited ≥4 percent oxygen desaturation index (ODI) with 5 to 15 events in an hour.[15] A portable pulse oximeter (Spirodoc pulsox) was utilized for the assessment. Prior to bedtime, the device was connected to the patients. The pulse oximeter sensor was placed on a fingertip, and the device was fastened to the chest. The next day, the researcher collected the device. The data, saved in the device's memory, was then transferred to a computer through a specialized interface. Afterwards, the data underwent analysis using specific software (Winspiro PRO 5.6.0; Medical International Research). The pulse oximeter captured parameters including heart rate, minimum and baseline oxygen saturation (SpO2), and Oxygen Desaturation Index (ODI). A diagnostic criterion of Oxygen Desaturation Index ≥4% (Chung et al., 2012), with 5-15 events per hour (ODI≥4%), was employed. Oxygen Desaturation Index (ODI) refers to the cumulative count of oxyhemoglobin desaturations of ≥4% from the initial baseline, measured per hour of recording. SpO2 is the arterial oxygen saturation level, with minimum SpO2 is the minimum SpO2 level during period of analysis while baseline SpO2 is the initially mean SpO2 level in the first 3 minutes of the recording. Delta index is the index of SpO2 fluctuation calculated in intervals of 12 seconds and pulse rate variation index is the variation of pulse frequency by hour of analysis. Using sterilized technique, blood sample was drawn from vein following a 10-12 hour fasting period. The sample was dispensed into a yellow top serum vial. The blood was centrifuged at a speed of 3000 revolutions per minute (rpm) for 10 minutes. Following centrifugation, the serum was extracted and preserved at -40°C until needed for future use.

Blood glucose levels were measured using the

enzymatic colorimetric method with a kit manufactured by Fortress Diagnostic, United Kingdom. Total cholesterol in the serum was measured using the enzymatic colorimetric method with a kit also manufactured by Fortress Diagnostic, United Kingdom. Triglyceride levels in the serum were determined using the GPO-POD enzymatic colorimetric method, with a kit manufactured by Analyticon Biotechnologies AG, Germany. HDL cholesterol levels in the serum were determined using the precipitation method, with a kit manufactured by Analyticon Biotechnologies AG, Germany. LDL cholesterol levels in the serum were measured using a kit from Analyticon Biotechnologies AG, Germany.

To measure the Ankle Brachial Index, an ordinary sphygmomanometer and a Doppler ultrasound device equipped with an 8-MHz probe (Hi dop, Bistos) were employed. Blood pressure readings of the upper and lower limbs were taken after a 30-minute resting period. The subject's blood pressure was measured in the supine position. Blood pressure cuffs were placed over each brachial artery for brachial blood pressure and above each malleolus for ankle blood pressure. The cuffs were inflated to 20 mmHg above the systolic pressure and then deflated at a rate of 2 mm/sec. Systolic blood pressure measurements were taken in the right and left brachial arteries, dorsalis pedis, and posterior tibial arteries.[16]

The data was recorded and analyzed using IBM-SPSS (Statistical Package for the Social Sciences), version 22. Distribution of the data was assessed using the Kolmogorov-Smirnov test. For normally distributed variables, mean ± standard deviation was presented, while median with interquartile range was utilized for variables with non-normal distribution. Qualitative variables were presented as frequencies and percentages.

Mann-Whitney U test was employed to compare quantitative variables with non-normal distribution between the two groups and an independent samples t-test was utilized for normally distributed quantitative variables. Statistical significance was defined as a p-value less than 0.05.

Results

In this study, 64 subjects were classified into two groups. In group I, there were 32 obese males diagnosed with obstructive sleep apnea, while in group II 32 obese males without obstructive sleep apnea were included. Median IQR of age for Group I showed a value of 31.00 (28.25-35.00) years for age (Median IQR) and for group II it was 30.50(24.25-32.00) with no statistically significant difference. Median IQR of ABI of study population was 1.08 (1.00 – 1.16). In group I median IQR of ABI was 1.08 (1.00 – 1.16) and in group II was 1.09 (1.01 – 1.16) and the comparison of the study groups show a insignificant difference p= 0.435 (Table II). In group I median IQR of fasting blood glucose(mg/dl) was 89.75 (71.48 – 109.25) and in group II it was 86.15 (72.66 – 109.68). Fasting blood sugar level showed no significant difference (p= 0.778) between the study groups as shown in Table II. In group I the median IQR of triglycerides(mg/dl) was 183.50 (133.25 – 272.25) and in group II was 168.00 (126.75 – 268.00) as shown in Table I. Comparison between the groups showed a non-significant difference of p= 0.413. In group I mean ± SD of cholesterol (mg/dl) was 179.72±33.36 and in group II was 173.47±43.81. Comparison of cholesterol showed no significant difference p=0.523 (Table I).

Table I: *Comparison of lipid profile across the two groups*

Variables	Group-I (Obese subjects with OSA) n=32	Group-II (Obese subjects without OSA) n=32	*p value*
HDL (mg/dl) [b]	39.2±6.7[d]	41.5±7.2[d]	0.190
Cholesterol (mg/dl) [b]	179.7±33.3[d]	173.4±43.8d	0.523
Triglycerides (mg/dl)[a]	183.5 (133.2 – 272.2) [c]	168.0 (126.7 – 268.0) [c]	0.413
LDL (mg/dl) [a]	85.0 (67.7 – 135.9) [c]	88.2 (67.4 – 108.7) [c]	0.888

OSA: Obstructive sleep apnea, HDL: High density Lipoprotein, LDL: Low density lipoprotein,
Values presented as median (IQR)c and mean ± SD d
a Compared using Mann- Whitney U test
b Compared using Independent Sample "t-test"
p < 0.05 considered significant
HDL indicates High Density Lipoproteins and LDL for Low Density Lipoproteins

In group I mean ± SD of HDL (mg/dl) was 39.22±6.76 and in group II was 41.53 ±7.20 as shown in Table I. Comparison of HDL (mg/dl) between the study groups showed p =0.190. In group I the median IQR of LDL (mg/dl) was 85.00 (67.75 – 135.95) and in group II was 88.20 (67.45 – 108.75). No significant difference was found in the comparison between the two groups p value

Table II: *Comparative analysis of fasting blood sugar and ankle brachial index across the two groups*

Variables	Group I (Obese subjects with OSA) n=32	Group II (Obese subjects without OSA) n=32	*p-value*
Blood Sugar Fasting (mg/dl) [a]	89.7 (71.4 – 109.2) [c]	86.1 (72.6 – 109.6) [c]	0.778
ABI [a]	1.08 (1.00 – 1.16) [c]	1.09 (1.01 – 1.16) [c]	0.435

Values are given as median (IQR)c
a Comparison by Mann-Whitney U test
p < 0.05 considered significant
ABI: Ankle Brachial Index

0.888 (Table I).

Discussion

Increasing evidence suggests that OSA is associated with dyslipidemia due to intermittent hypoxia, which triggers lipid peroxidation and disrupts the sympathetic system.[17] The present study has not shown any significant difference of triglycerides (p= 0.413), HDL (p= 0.190), LDL (p =0.888), cholesterol (p= 0.523), and fasting blood glucose (p= 0.778) between the two groups i.e., obese subjects diagnosed with OSA and obese subjects not having OSA. Our findings align with the study by Karkinski et al. (2017), which similarly reported no significant differences in lipid blood levels among obese subjects with and without OSA.[18] Previously prevalence rate of metabolic syndrome in patients who were not obese has been reported up to 22.5% in studies investigating the relationship between metabolic syndrome and individuals of normal weight, overweight, and obesity.[19] Likewise, Sharma et al., 2007 conducted a comparison among three patient groups: 40 patients with obesity and OSA, 40 obese subjects who were OSA-negative, and 40 subjects with normal-weight and no OSA. They discovered no variance in metabolic status among the subjects with obesity and OSA and obese subjects with no OSA. The findings of multivariate analysis in their study revealed obesity as the primary factor influencing metabolic abnormalities in this cohort and these results support the current study.[20]

The present study has reported a nonsignificant difference (p= 0.435) of Ankle Brachial Index (ABI). A research study conducted on C57BL/6J mice examined the effects of intermittent air exposure and Chronic Intermittent Hypoxia (CIH) on mice fed either a regular diet or a high cholesterol diet. The findings revealed that mice exposed to both CIH and a high cholesterol diet displayed elevated levels of total cholesterol, very low-density lipoprotein (VLDL), and low-density lipoprotein (LDL) compared to mice fed only a high cholesterol diet. This suggests that chronic intermittent hypoxia, when combined with a high cholesterol diet, contributes to dyslipidemia and potentially accelerates the development of atherosclerosis.[21] Furthermore, it's important to note that Ankle Brachial Index, a screening test for detecting subclinical atherosclerosis, may not be sufficiently sensitive in identifying early-stage atherosclerosis in asymptomatic middle-aged individuals.[22] Given that our study focused on young (aged 20-45 years) and healthy subjects, ABI may not be the most effective screening tool for detecting vascular changes in this population. Additionally, Steiropoulos et al. investigated the presence of early atherosclerotic lesions in newly diagnosed obstructive sleep apnea (OSA) patients without known comorbidities using Transcranial Doppler ultrasound, Common Carotid Artery Intima Media Thickness (CCA-IMT), and Ankle Brachial Index measurements. Their study concluded that OSA patients without recognized comorbidities exhibited only a minimal increase in CCA-IMT, and there was no other evidence of significant vascular disease present.[23] The lack of differences in metabolic parameters among obese individuals with OSA and individuals without OSA, challenges the conventional perception of the relationship and link among OSA and metabolic health. One possible explanation for our findings could be the heterogeneity of OSA severity and its effects on metabolic outcomes. It is plausible that the metabolic impact of OSA may vary depending on factors such as the degree of nocturnal hypoxia, sleep fragmentation, and individual metabolic susceptibility.

Furthermore, our study underscores the complexity of the interplay between OSA and metabolic health. While OSA is commonly associated with metabolic disturbances, it is essential to recognize that obesity itself is a significant risk factor for dyslipidemia, insulin resistance, and cardiovascular disease. Thus, the metabolic abnormalities observed in obese individuals may be predominantly driven by obesity-related factors rather than OSA alone.

Conclusion

Normal lipid profile and normal ABI indicate absence of detectable atherosclerosis in young apparently healthy OSA subjects without known comorbidities.

Conflict of Interest: None

Funding Disclosure: None

Ethical Consideration: The study was approved by the ethical review board. Informed written consent was obtained from the participants, and the confidentiality of their data was clearly explained.

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Authors Contribution

All the authors contributed equally in accordance with ICMJE guidelines and are accountable for the integrity of the study.

SK: Conception of idea & design, acquisition, analysis & interpretation of data, drafting the article, critical review, final approval of the manuscript

HH: Acquisition of data, drafting the article, critical review, final approval of the manuscript

RI: Analysis & interpretation of data, drafting the article, critical review, final approval of the manuscript

MS: Conception of idea & design, analysis & interpretation of data, final approval of the manuscript

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