ORIGINAL ARTICLE

EFFECTS OF OBSTRUCTIVE SLEEP APNOEA ON LIPID METABOLISM: A CROSS SECTIONAL STUDY FROM A TERTIARY CARE HOSPITAL OF PAKISTAN

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Background: A peak in sudden death during night, disturbed metabolic profile and cardiovascular diseases are the main source of health deterioration and deaths in Obstructive sleep apnoea (OSA) patients. Interest has been focused in recent years to understand the interactions between OSA and cardio-vascular diseases (CVDs). Studies advocate the possible causal role of OSA in development of abnormal lipid profile which may place a person at a high risk of CVDs progression. Objective of the present study was to examine the effects of OSA on lipid metabolism in our local population in Karachi. **Methods:** This cross-sectional analytical study was carried out on 100 individuals, including 50 OSA patients and 50 age and BMI matched controls in Sleep Lab, Dow University of Health Sciences, Ojha Campus, Karachi. After verbal and written informed consent, history and complete physical examination was carried out. Individuals having sign and symptoms of OSA and positive Epworth Sleep Scale (ESS) score went through over night polysomnography to diagnose their OSA and its severity. All the elements of lipid profile including high density lipoproteins, low density lipoproteins, total cholesterol and triglycerides were examined and compared with a group of persons without sleep disturbance to determine their correlations with OSA by using SPSS-20. **Results:** Frequency of dyslipidemia was higher in OSA group. Mean total cholesterol (TC), triglycerides and low-density lipoprotein (LDL) were higher in OSA patients but difference didn't reach to statistically significant level, while mean high-density lipoproteins (HDL) was significantly higher in OSA group. Frequency of subjects with high serum total cholesterol was significantly higher in OSA group. Disturbance in all lipid profile components showed more subjects with abnormal levels in moderate and severe apnoea groups as compare to mild apnoea group, however; high triglycerides showed strong association with the severity of apnoea. **Conclusion:** OSA is associated with disturbed lipid metabolism in our local population.

Keywords: Obstructive sleep apnoea, lipid profile, cardiovascular diseases

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INTRODUCTION

Sleep is a distinct behavioural state that is characterized by disconnection of the central nervous system from the external environmental stimuli.[1] Generally it is supposed that appropriate quantity and quality of sleep is essential for keeping us fully awake, attentive and active throughout the day**.** Sleep is complexly associated to various body systems like hormonal and metabolic systems.[2] Studies have described that inadequate or poor-quality sleep is possibly a reason to encourage lipid and glucose metabolic abnormalities, neuro-cognitive impairments, chronic health conditions, end-organ dysfunction and increased mortality.[3,4]

Obstructive sleep apnoea (OSA) is a sleep related breathing disorder represented by repetitive collapse or partial collapse of the upper respiratory passage during sleep that lasts for more than 10 seconds, resulting in decreased respiratory flow (hypopnoea) or complete termination of airflow (apnoea). Total number of apnoeas and hypopnoea per hour of sleep, can be described as Apnoea-Hypopnoea Index (AHI) which indicates severity of OSA.[5] American Academy of Sleep Medicine (AASM) states criteria for the identification of OSA. A diagnosis of OSA syndrome can only be made when more than five obstructive breathing events per hour of sleep are present in conjunction with excessive daytime sleepiness. Apnoea is classified according to the Chicago criteria as recommended by the AASM into mild, moderate and severe categories for AHI 5–15, AHI 15–30, and AHI >30 respectively.[6]

A peak in sudden death during the night, disturbed metabolic profile and their cardiovascular outcomes are the main source of health deterioration and deaths in OSA patients. The pathogenesis of cardiovascular complications of OSA is not fully understood, so it has become a focus of interest to understand this association. Metabolic Syndrome (MS) presents as a collection of risk factors that places a person at a high risk of CVD progression. Components of MS are hypertension, obesity, high FBS and disturbed lipid profile (high triglycerides and low HDL).[7] Overall prevalence of metabolic syndrome was

also found to be significantly higher in Pakistani OSA population according to our previous research.[8]

Disturbed lipid profile is an important component of MS. Multiple observational and experimental evidences advocate the possible causal role of OSA in abnormal lipid metabolism, which can place a person at a high risk of CVD progression such as systemic and pulmonary hypertension, cerebrovascular accidents, myocardial infarctions, congestive heart failure and arrhythmias.[9,10] Previously, this relationship was not that much clear due to presence of some confounders like obesity, however some recent large-scale studies have concluded that OSA is associated with these CVDs risk factors and disturb lipid profile, with sufficient statistical control for identified confounding factors like obesity.[5,10]

Despite multiple studies, relationship between OSA and different components of lipid profile has been reported with conflicting results which indicates the requirement of more investigations. The aim of this study was to examine the effects of OSA on lipid metabolism in our local population.

MATERIAL AND METHODS

Total 100 subjects, aged between 30 to 65 years were recruited for this cross-sectional analytical study. Fifty were cases with OSA, diagnosed at Sleep Lab, Dow University Hospital and 50 were age and BMI matched controls, without any sleep disturbance. Participants were included through non-probability convenience sampling after getting written informed consent. The approval of this research study was taken by the ethical review board of the university.

Data were collected through a structured proforma including questions relative to demographic profile, anthropometric measurement, blood pressure, socio-economical status, physical activity, medical and surgical history and medication etc. Epworth Sleep Scale (ESS) score of all participants was recorded by using ESS questionnaire to confirm their reported sleep status and day time sleepiness.[11] ESS score of 9 was considered as cut off point.

Subjects with sleep disturbance, day time sleepiness and ESS score more than 9, underwent full night polysomnography (PSG). A PSG is a comprehensive multi-channel recording of the bio-physiological changes that occur during sleep. Polysomnography was performed under continuous supervision and monitoring by a sleep lab technician. Data from overnight PSG parameters confirmed their OSA. After overnight PSG and confirmation of OSA, blood sample was obtained in fasting state to examine lipid profile. The controls, having ESS score less than 9 without any sign and symptoms of sleep disturbance, were selected from the employees of Dow University of Health Sciences. Fasting blood samples were collected in morning to examine their lipid profile.

Components of lipid profiles were determined by using spectrophotometric method. To analyze lipid disturbance, we considered cut-off values for serum triglycerides ≥150 mg/dl, HDL cholesterol ≤40 mg/dl for males and ≤50 mg/dl for females, LDL-cholesterol ≥100 mg/dl and serum cholesterol ≥200 mg/dl. Statistical analysis was carried out on SPSS-20 and $p \leq 0.05$ was considered as significant. Continuous variables were summarized as mean and standard deviation whereas categorical variables as proportions. Independent samples *t*-test was used for comparison between groups. Categorical variables were examined by Chi-square test to scrutinize different components of lipid profile in OSA group and in controls.

RESULTS

The mean age along with anthropometric parameters for cases and controls are tabulated as Table-1, showing no significant difference between both groups. Male to female ratio was 3:2 in both groups. Mean AHI was 32.795±22.70 for cases. The number of OSA subjects were 12 (24%), 17 (34%) and 21 (42%) (12) in mild, moderate and severe apnoea groups.

Mean HDL-cholesterol, which are considered as good cholesterol was significantly lower in OSA group as compared to controls (p=0.018). Mean serum triglycerides, mean LDL and total cholesterol values were also higher in OSA group as compared to the controls.

Comparison of percentage of subjects with abnormal lipid components level in OSA and control group showed that a higher percentage of population in OSA group was with unhealthy HDL levels and with higher triglycerides. Surprisingly frequency of subjects with high LDL level was equal in both groups. Percentage of population with high total cholesterol was significantly higher in OSA group (p=0.026) (Table-2).

Disturbance in all lipid profile components and their association with severity of apnoea was discussed and showed more subjects with abnormal levels in moderate and severe apnoea groups as compared to mild apnoea group; however, high triglycerides level showed good association with the severity of apnoea and showed 33.3%, 64.7% and 66.7% population of mild, moderate and severe apnoea population with higher triglycerides in their respective population. Analysis of percentage of subjects with low HDL level, high LDL level and high serum cholesterol in mild, moderate, and severe apnoea group is mentioned in Table-3.

Table-1: Comparison of mean baseline characteristics with 95% confidence intervals among subjects with and without OSA

Baseline characteristics	Controls	Cases	*p*
Age (years)	47.04	49.42	0.133
Height (m)	1.65	1.67	0.405
Weight (Kg)	83.12	89.22	0.079
BMI	29.89	31.98	0.087
Neck circumference (m)	0.38	0.39	0.101
Waist circumference (m)	1.04	1.10	0.086
Hip circumference (m)	1.11	1.17	0.093
Waist to Hip ratio	0.92	0.94	0.343
Systolic BP (mmHg)	129.4	138.6	0.002*
Diastolic BP (mmHg)	80.90	85.84	0.081
Total Cholesterol (mg/dL)	180.76	199.44	0.093
Triglycerides (mg/dL)	173.06	185.18	0.476
LDL (mg/dL)	112.26	128.30	0.070
HDL (mg/dL)	41.68	37.38	0.018*

*Statistically significant, *p*-values generated by *t*-test

Table-2: Comparison of OSA and Control group subjects with normal and abnormal lipid profile

Components of Lipid Profile		Controls n (%)	Cases n (%)	*p*
Serum HDL	Normal	21 (42)	18 (36)	0.539
	Low	29 (58)	32 (64)	
Serum LDL	Normal	14 (28)	14 (28)	0.588
	High	36 (72)	36 (72)	
Triglycerides	Normal	25 ((50)	21 (42)	0.422
	High	25 (50)	29 (58)	
Total Cholesterol	Normal	39 (78)	29 (58)	0.026*
	High	11 (22)	21 (42)	

*Statistically significant, *p*-values generated by *t*-test

Table-3: Number and percentage of subjects in mild, moderate and severe OSA groups with normal and abnormal lipid profile components

Lipid Profile		OSA CASES		
		Mild Apnoea (AHI=5–15) n (%)	Moderate Apnoea (AHI=15–30) n (%)	Severe Apnoea (AHI>30) n (%)
Serum HDL	Normal	7 (58.3)	4 (23.5)	7 (33.3)
	Low	5 (41.7)	13 (76.5)	14 (66.7)
Serum LDL	Normal	4 (33.3)	3 (17.6)	7 (33.3)
	High	8 (66.7)	14 (82.4)	14 (66.7)
Triglycerides	Normal	8 (66.7)	6 (35.3)	7 (33.3)
	High	4 (33.3)	11 (64.7)	14 (66.7)
Total Cholesterol	Normal	7 (58.3)	8 (47.1)	14 (66.7)
	High	5 (41.7)	9 (52.9)	7 (33.3)

DISCUSSION

We concluded that OSA is associated with disturbed lipid metabolism. Mean HDL-cholesterol, which are considered as good cholesterol and should be high in good lipid metabolism was significantly lower in OSA group. Mean triglyceride, total cholesterol and LDL were also higher in OSA subjects but difference was not statically significant in this research. Frequency of subjects with high serum total cholesterol was significantly higher in OSA group, while frequency of population with high triglycerides was associated with the severity of apnoea. Our results advocate that OSA has negative influence on lipid metabolism.

It is not a single pathway, but rather a combination of mechanisms which could lead to disturbance in lipid metabolism of OSA patients. According to studies some intermediate mechanisms like hyperlipidemia, lipid peroxidation, systemic inflammation and increased oxidative stress, enhances lipid uptake into macrophages, increased cell adhesion molecules and causes HDL dysfunction.[13] Some studies explained that chronic intermittent hypoxia (CIH) causes elevated blood cholesterol and phospholipids, up-regulate triglycerides and phospholipids biosynthesis, and inhibit cholesterol uptake in the liver.[14] Studies also suggested a direct link between the adrenergic system and lipid levels and this chronically elevated sympathetic activity in OSA patients causes decrease in HDL level and increase in serum TG levels.[5]

Drager *et al*[15] examined the deregulation of lipid metabolism and suggested that CIH which is an important characteristic of OSA inhibits clearance of triglyceride-rich lipoproteins and an increase in fasting very-LDL. They showed a remarkable 80% decline in LPL activity in adipose tissue.[15] In a cross-sectional analysis Kono *et al* reported that OSA is associated with dyslipidaemia in non-obese patients, independent of visceral fat obesity.[16] A recent research carried out in Eastern Europe showed a significantly elevated level of triglycerides, total cholesterol and decreased level of HDL in their OSA patients as compare to controls. They also found higher LDL level in OSA patients but difference was non-significant for LDL levels in both groups.[17] In their study BMI in OSA subjects was higher in OSA subjects as compare to controls, but our present study where BMI was matched in control selection, possibility of biasness due to this confounder is eliminated. In conclusion; the data on the relationship of individual component of lipid profile in OSA is not precisely reflected; it may be due to differences in ethnicities, source and selection of the study population and environmental factors including life style habits.

Presence of disturbed lipid profile in OSA subjects represent considerable risk factors for the development of CVDs. Better understanding is essential to develop appropriate therapeutic strategies to lower the cardiovascular diseases in OSA subjects and to improve lives of our people. Screening for lipid profile along with the work up of OSA will allow early detection of complications to reduce mortality. In our community, OSA is still an underestimated, under diagnosed and under treated disorder with all its co-morbidities.

CONCLUSION

OSA is associated with disturbed lipid metabolism in our local population. As OSA is being increasingly recognized as a cause of morbidity and mortality all over the world, there is need to examine our OSA population for different aspects of this disorder.

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