Original Article

A Study of Myocardial Performance Index (MPI) and Apnoea Hypopnoea Index (AHI) in Obese Patients

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ABSTRACT

Introduction : Obesity is chronic and rising global epidemic that is causally related to serious medical illnesses, such as hypertension, diabetes mellitus, coronary heart disease, respiratory problems etc. Obesity in particular central obesity is associated with obstructive sleep apnea which may further be associated with cardiovascular disturbances such as MI, heart failure, etc. OSA is associated with global dysfunction of heart (both systolic and diastolic). In view of limited Indian data with OSA we conducted this study with the aim to assess LVM, LVMI and MPI in OSA patients and to study its relationship.

Design and setting : Ananalytical cross sectional study conducted between September 2016 and November 2018 in tertiary hospital in Nagpur, India.

Patients and Methods : Sixty eight obese subjects with BMI = 30 and ESS score = 10 without any cardiac and pulmonary diseases who consulted physician were evaluated for OSA by overnight sleep study. All subjects underwent echocardiographic examination. According to apnea hypopnea index (AHI), subjects were classified into controls with no OSA (AHI < 5, n1 = 12), mild OSA subjects (AHI = 5 - < 15, n2 = 19), moderate OSA subjects (AHI = 15 - < 30, n3 = 13) and severe OSA subjects (AHI = 30, n4 = 24). LVM and LVMI to BSA were calculated using appropriate formula. The left ventricular MPI was calculated by Doppler echocardiography.

Results : No statistically significant differences were observed in ESS score and body mass index among the groups, but both systolic and diastolic blood pressure were statistically different among different groups. No statistical association was found between LA, LVEDD, and LVEF with AHI whereas there was statistically significant association between LVESD, IVST, PWT, LVM, and LVMI with AHI and thus severity of OSA. MPI was found to be 0.45 ± 0.057 in controls, 0.54 ± 0.089 in mild OSA, 0.62 ± 0.06 in moderate OSA, 0.72 ± 0.064 in severe OSA subjects. Thus MPI was correlating with AHI with correlation coefficient of 0.8003 and p value <0.001.

Conclusions : Demonstrable cardiac changes are noted in patients with OSA that increase with severity. MPI may be used as a reproducible, simple and noninvasive method for left ventricular global function in patients with OSA.

Key-words : Obesity, OSA, AHI, LVM, LVMI, MPI

Introduction :

The prevalence of obesity is rising in the world and in India with 16.2 % rise in prevalence of obesity in India from 1990 to 2013[1]. Obesity is a risk factor for many noncommunicable disease including metabolic syndrome, coronary artery disease[2], etc. It is associated with associated with pulmonary diseases such as obesity hypoventilation syndrome and obstructive sleep apnea[3,4]. Obese patients display an altered breathing pattern due to pharyngeal muscles collapse that occur during sleep in part due to neck fat accumulation[5,6]. It had been estimated that obesity increases risk of having OSA by greater than 102.

Obstructive sleep apnea can further accelerates the cardiovascular morbidity[7] as it is associated with increased risk of having cardiovascular diseases such as systemic hypertension, coronary artery disease, pulmonary hypertension, various conduction abnormalities, heart failure and stoke. As OSA is strongly associated with hypertension, left ventricular hypertrophy and left ventricular diastolic dysfunction are common abnormalities found in echocardiography. Each arousal associated

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with OSA resulting from either apnea or hypopnea causes a transientrise in systemic blood pressure, the magnitude of which may vary from a small increase to a doubling of both systolic and diastolic pressures[8]. Even when there are no visually discernible features of arousal on the EEG these blood pressure changes occur. Such repeated rise in blood pressure hundreds of times per night over years presumably may lead to increase morbidity and mortality from cardiovascular and cerebrovascular disease in patients with OSA. Also repeated episodes of hypoxia, hypercapnea, arousal and intrathoracic pressure fluctuations lead to sympathetic hyperactivity, oxidative stress, systemic inflammation which if persistent for some time triggers chronic changes in vascular bed that ultimately leads to various cardiovascular morbidities[8].

OSA patients have both systolic and diastolic dysfunction of heart, of which diastolic precedes systolic impairment[9] and accounts for approximately 30% - 40% of patients with left ventricular failure[10]. Most of the times, systolic and diastolic functions cooexist and hence it is better to apply combined measure of left ventricular performance rather than systolic and diastolic measures alone[11]. Tei and his co-workers in 1995 used Myocardial Performance Index (MPI / Tei Index)[12], which includes both systolic and diastolic time intervals to assess the global cardiac dysfunction. Tei Index uses the measurement possible on flow wave Doppler and is as sensitive as the tissue Doppler measurements. It is quick, non invasive, simple and reproducible technique to evaluate global heart dysfunction[12].

This study was designed, based on above findings and in view of limited Indian data regarding this, to estimate the left ventricular mass (LVM), left ventricular mass index (LVMI) and left ventricular MPI in obese patients with OSA and to assess whether there is any correlation between the severity of OSA with respect to MPI and LVM.

Materials and Methods :

This hospital-based analytical cross sectional study was performed in the tertiary care center, Nagpur between November 2016 and October 2018. Subjects with obesity with body mass index (BMI) = 30 and with complaints of excessive daytime sleepiness and nocturnal snoring were screened for inclusion in the study. Subjects with Epworth Sleepiness Scale (ESS) score[13] above or equal to 10 / 24 were included in the study. All the subjects were interviewed, examined, and investigated as per the predesigned proforma. General physical examination was carried out in all subjects to determine blood pressure (both systolic and diastolic), heart rate, and respiratory rate in sitting position. All subjects were subjected to routine investigations such as complete blood count, blood urea, serum creatinine, ECG, serum sodium and potassium, liver function test, to determine the exclusion. Serum lipid profile (includes total cholesterol, LDL-C, HDL-C, and serum triglycerides) was determined for each subjects. Patients who had known cardiac illness, lung diseases, renal diseases, diabetes mellitus, chronic renal diseases and serum electrolyte abnormalities were excluded from the study. All subjects underwent sleep study and electrocardiography. Study subjects were categorized into 4 groups according to the apneahypopnea index (AHI)[15] :

1. Control subjects with snoring without OSAHS (AHI < 5 events/h);
2. Patients with mild OSAHS (5 events/h = AHI < 15 events/h);
3. Patients with moderate OSAHS (15 events/h = AHI < 30 events/h); and
4. Patients with severe OSAHS (AHI = 30 events/h).

Approval for the study was taken by the institutional ethics committee. Informed written consent was obtained from all the subjects before conducting the study.2.1. SLEEP STUDY

The device use in this study was ApneaLink Air of ResMed which is a US FDA approved home sleep testing device which had been validated in multiple studies[16] for diagnosis of Obstructive Sleep Apnea (OSA). The device monitors the patient's nasal flow, snoring (derived from flow), respiratory effort, oxygen saturation and pulse throughout the night.

Breathing effort is monitored with a chest and abdominal piezoelectric belts with 0.053 Hz filtration, and airflow is monitored by a nasal cannula. A finger-pulse oximeter is used for oxygen saturation and pulse monitoring. Based on this, it derives various parameters like the Apnea-Hypopnea Index (AHI), the respiratory disturbance index (RDI), the Oxygen Desaturation Index (ODI), flow limitations and snoring.

Airflow cessation of at least 10-s duration is considered as apnea, and a decrease in 3% or more capillary oxygen saturation is accepted as desaturation. An episode of reduced airflow by at least 50% during sleep lasting 10 s or longer with an arousal or desaturation is accepted as a hypopnea. A partially obstructed breath that does not meet the criteria for hypopnea but provides evidence of increasing inspiratory effort (usually through pleural pressure monitoring) punctuated by an arousal is defined as RERA (Respiratory effortrelated arousal).The number of episodes' obstructive apnea or hypopnea per hour of sleep is termed as AHI. The number of scored desaturations divided by the estimated sleep duration (time in bed waking times) results in the ODI. Number of apneas plus hypopneas plus RERAs per hour of sleep is denoted as Respiratory disturbance index (RDI)[17]. The diagnosis of OSAHS will be made when the AHI is more than 5 per hour according to the American Academy of Sleep Medicine[18].

2.2. ECHOCARDIOGRAPHY

Echocardiographic indices of study subjects were evaluated using PHILLIPS HD11XE echocardiography machine with frequency of 3.5 MHz. Left ventricular mass was calculated using a simple and anatomically validated formula:

$$\mathbf{LVM = 0.8 \times 1.04\,[(IVS + LVEDD + LVPW)^3 - LVEDD^3] + 0.6}$$

LVM is corrected for body surface area and LVM index was calculated.

The left ventricular ejection fraction was calculated using the modified quinines equation as:

$$\mathbf{\%\Delta D2 = \frac{LVEDD2 - LVESD2}{LVEDD2}}$$

$$\mathbf{LVEF = (\%\Delta D2) + [(1 - \%\Delta D2)(\%\Delta L)]}$$

Transmitral flow Doppler measurement: The sample volume of the pulsed Doppler was placed between the tips of the mitral leaflets in the apical four-chamber view for recordings of the mitral inflow velocity pattern. From thetransmitral recordings, the following measurements were carried out: peak E velocity in meters per second (peak early transmitral filling velocity during early diastole), peak A velocity in meters per second (peak transmitral atrial filling velocity during late diastole), and E/A ratio was calculated.

MPI measurement : As described by Tei and co-workers[12], doppler time intervals were measured from mitral inflow and left ventricular outflow Doppler tracings. The interval 'a' from cessation to onset of mitral inflow is equal to the sum of isovolumic contraction time (IVCT), ejection time (ET), and isovolumic relaxation time (IVRT). ET 'b' is derived from the duration of the left ventricular outflow Doppler velocity profile. The sum of ICT and IRT was obtained by subtracting b from a. The MPI was calculated as shown in ***(Figure 1)*** :

MPI = a - b/b = IVRT + IVCT / ET

The normal adult MPI of 0.39 ± 0.05 increases with worsening left ventricular dysfunction. Global left ventricular dysfunction was defined as an MPI =0.5012. ***Figure 1*** shows schema for analysis of Doppler time intervals.

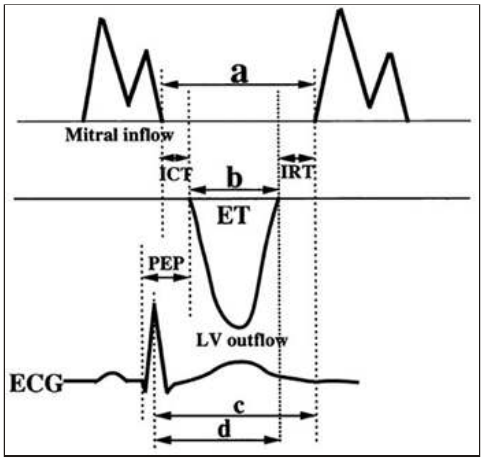


Figure 1 : **Schema for analysis of Doppler time intervals[12]**

Continuous variables were presented as mean and SD (standard deviation). Categorical variables were expressed in frequency and percentages. Biochemical and echocardiographic parameters were compared among different categories of subjects classified according to severity of OSAHS (controls, mild, moderate, severe) by performing one way ANOVA test. Multiple comparisons were carried out to test the difference and their level of significance between any two categories of OSAHS by performing Bonferroni t-test. Pearson's correlation coefficient (r) was used to assess the magnitude and nature of correlation of various echocardiography parameters namely LVM, LVMI, and MPI with AHI, of ESS score with AHI, and of SBP and DBP with AHI. P-value < 0.05 was considered as statistically significant. Statistical software STATA version 14.0 was used for data analysis.

Results :

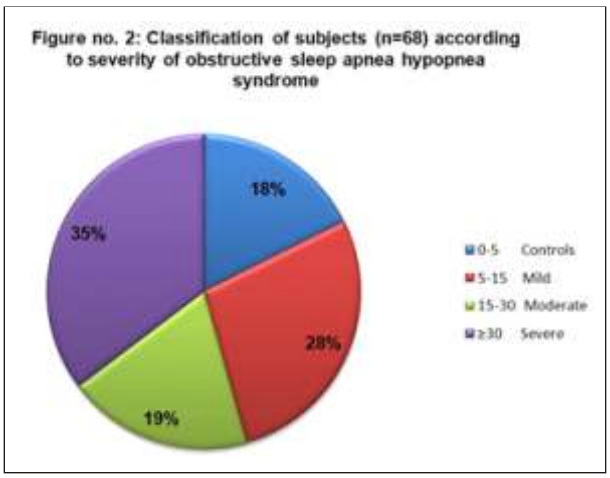
During study period out of the total 68 patients studied 37 (54%) were males and rest 31 (46%) were females with maximum patients in the age group of 51-60 with mean of 55.35 ± 9.97. Subjects were classified into 4 groups as shown in ***Figure 2***

- Controls with no OSA (n1=12),
- mild OSA subjects (n2=19),
- moderate OSA subject (n3=13), and
- Severe OSA subject (n4=24).

Basic characteristics of the patients are shown in ***Table 1.*** No significant difference was observed between ESS score ***(Figure 3)*** and BMI ***(Figure 4)*** of the subjects (p>0.5). However systolic ***(Figure 5)*** and diastolic blood pressures ***(Figure 6)*** were having significant positive association with severity of OSA. Of the total subjects 22 (32%) were hypertensive of which 18 (82%) belongs to severe OSA group. RDI and ODI were highest in severe OSA group which increases with severity of OSA (p>0.0001). In contrast minimum and average SpO2 were negatively associated with severity of OSA (p<0.0001).

Echocardiographic measurements of left ventricle of the subjects as shown in table 2 reveals that LA dimension, LVEDD, and LVEF was not associated with AHI (OSA severity) with p value of 0.8350, 0.2814 and 0.1352 respectively whereas LVESD, IVST, PWT, LVM, LVMI, E/A ratio was found to have statistically significant association with AHI (severity of OSA) with p value of 0.0074, <0.0001, 0.0275, <0.0001, 0.0135, and 0.0039 respectively. The left ventricular MPI was significantly associated with severity of OSA (AHI) with p value >0.0007. Also it was found that while comparing any 2 of the 4 groups, MPI was significantly different in them which were not seen with LVM, and LVMI as shown in ***Table 3.***

A positive correlation was found between AHI reflecting severity of OSA and LVM, LVMI or MPI with r-value 0.5567, 0.4079, 0.8003 respectively and p-value <0.0001, 0.0006, <0.0001 respectively as shown in ***figure 7, 8 & 9*** respectively. Also our study found that AHI better correlates with MPI than LVM and LVMI.



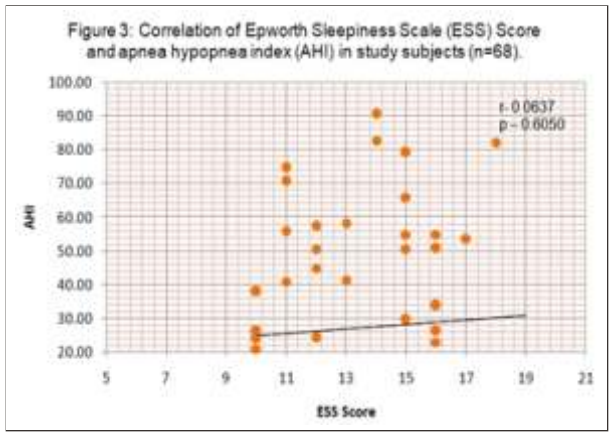
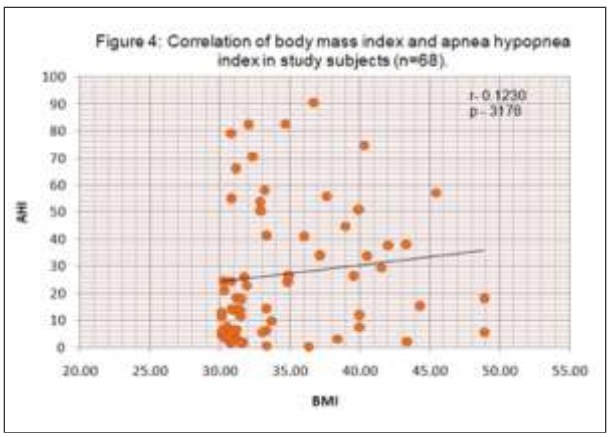


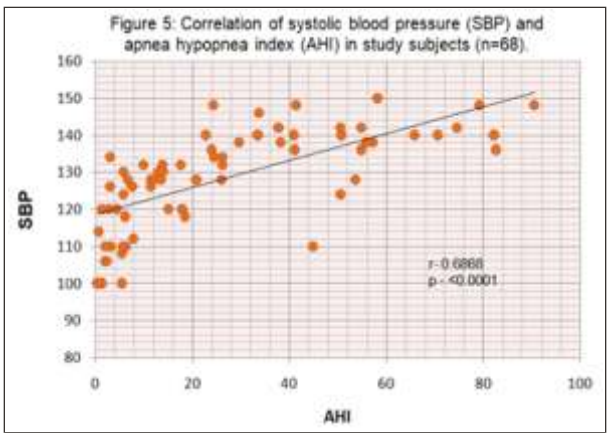
Table 1 : **Basic characteristics of study subjects (n=68)**

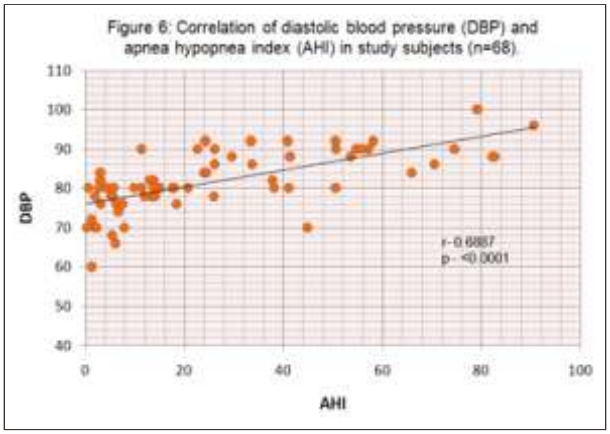
Basic characteristics of Subjects	Controls no OSA N1=12	Mild OSA n2=19	Moderate OSA n3=13	Severe OSA n4=24	p-value
Mean ESS score	13.0 ± 2.13	14.10 ± 2.68	12.30 ± 2.28	13.58 ± 2.32	0.6056
Mean BMI	33.26 ± 4.07	33.23 ± 4.79	35.52± 6.10	35.80 ± 4.33	0.3178
Mean SBP	113.83±10.46	122.74±9.85	131.38±8.62	138.83±8.52	<0.0001, HS
Mean DBP	75.17±6.90	77.58±5.40	83.69±5.15	87.67±6.15	<0.0001, HS
No. of Hypertensive Subjects (%)	0 (0)	1 (5)	3 (23)	18 (75)	<0.0001, HS
Apnea Hypopnea Index (AHI) per hour	2.24± 1.16	9.26± 3.41	22.58± 4.26	55.99± 16.59	<0.0001, HS
Respiratory Disturbance Index (RDI)	3.21± 1.16	18.72 ±3.64	24.72± 4.17	58.26 ±.15	<0.0001,HS
Oxygen Desaturation Index (ODI) per hour	4.43 ±2.44	10.37 ±4.37	25.69± 6.18	53.17± 12.27	<0.0001,HS
Minimum Nocturnal Oxygen Saturation	82.16± 9.43	71.21 ±14.30	72.76± 12.87	58.41± 9.76	<0.0001,HS
Average SpO2	93.25 ±2.70	93.89± 2.25	92.38± 5.07	88.20± 5.75	0.0003,HS

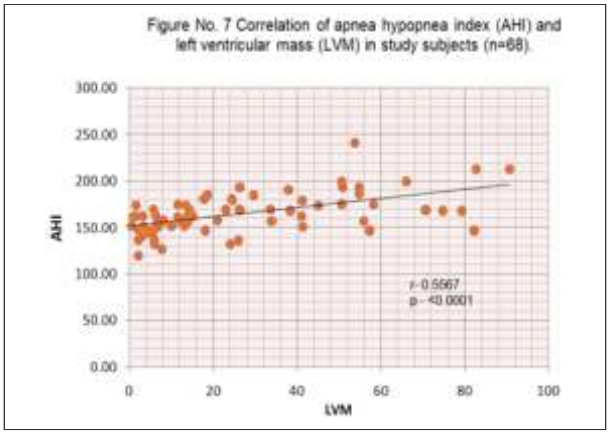
Table 2 : **Echocardiographic measurements of the left ventricle in subjects (n=68)**

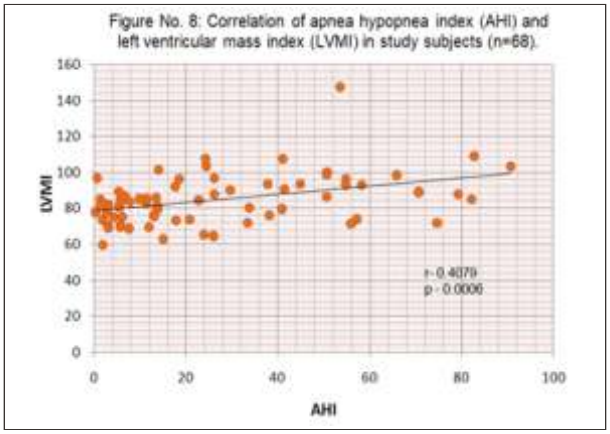
Variable	Controls	Mild OSA	Mod OSA	Severe OSA	p-value
LA	32.33 ± 2.90	32.21 ± 2.48	32.15 ± 2.70	31.62 ± 2.49	0.8350,NS
LVEDD	49.58 ±2.23	48.49± 2.44	50.30± 3.03	50.37± 2.76	0.2814,NS
LVESD	26.5± 1.38	27.05 ±1.77	27.38 ±1.66	28.41 ±1.69	0.0074,HS
IVST	8.58± 0.66	8.94± 0.62	9.15± 0.55	10.04± 1.23	<0.0001,HS
PWT	8.91± 0.28	9.31± 0.67	9.53 ±0.66	9.58± 0.71	0.0275,S
LVEF	75.64± 2.22	73.83 ±3.35	74.46± 4.61	72.73 ±3.61	0.1352,NS
LVM	150 ± 14.31	154.85 ± 13.87	167.84± 19.51	179.35± 23.11	<0.0001,HS
LVMI	77.81 ± 9.27	81.27 ±8.14	84.65 ±15.06	91.73± 16.24	0.0135,S
E/A	1.06 ± 0.10	1.03 ± 0.065	1.01 ± 0.074	0.96± 0.094	<0.0001,HS
a	0.34 ± 0.022	0.38 ± 0.03	0.41 ± 0.026	0.46 ± 0.047	<0.0001,HS
b(ET)	0.24 ± 0.018	0.24 ± 0.015	0.25± 0.016	0.26 ± 0.026	0.0007,HS
MPI	0.45 ± 0.057	0.54 ± 0.089	0.62 ± 0.06	0.72± 0.064	0.0007,HS

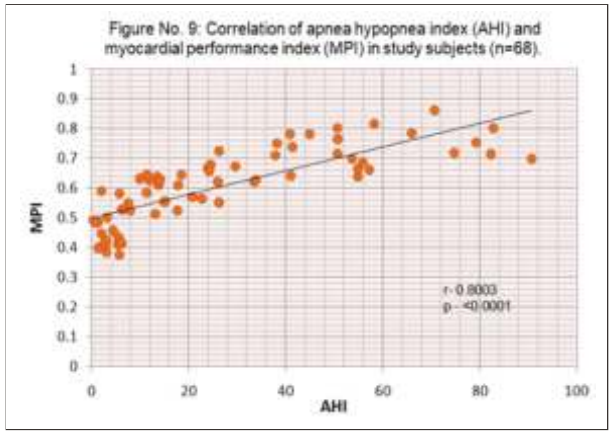












Discussion :

OSA leads to increase in cardiovascular morbidity such as left / right ventricular dysfunction, arrhythmias, hypertension etc. Since these leads to early cardiovascular mortality we need to have a reprodicble, simple and noninvasive tool for estimation of left ventricular global dysfunction in OSA patients. Hence we studied LVM, LVMI and left ventricular global function using MPI in OSA patients including relationship between AHI and MPI. These data might allow us to explore the utility of MPI in determining early cardiac dysfunction in OSA patients.

Correlation between OSA and myocardial structure and function is a controversial issue. While studies conducted by Maro JA *et al*[20], Niroumand M *et al*[21], and Otto ME *et al*[22] found a positive relation between LVH, AHI and duration of saturation periods, another study conducted by Chami HA *et al*[23] on obese patients with or without OSA found no differences in their LVM. The results of The Sleep Heart Health Study[24] however showed that increase in LVM and in LVH prevalence were related to OSA severity independent of sex, age, BMI, DM and previous myocardial infarction. The mechanism responsible for this cardiac dysfunction seen in patients of OSA is not properly understood. It is abelief that OSA may increase cardiac risk due to imbalance between myocardial oxygen demand and supply as a result of hypoxia, hypercapnea, arousal and increased symapathetic activity occurring during apnea[25]. However disease associated with OSA such as DM, hypertension and coronary artery disease often leads to LVH. The study conducted by us included subjects with BMI = 30 as obesity is confounding factor associated with both left ventricular dysfunction and OSA and thus selecting only obese subjects will eliminate bias by matching. In our study we excluded subjects with DM and CAD but 22 out of 68 (32%) subjects were hypertensive, the majority of them 18 (82%)were in

the severe OSA group. We were of the belief that it would have been inappropriate if we exclude hypertensive subjects from the analysis as there is a compelling evidence of a causal link between OSA and hypertension and that causal pathway leading to left ventricular diastolic dysfunction from OSA may well involve hypertension. Lavie *et al*[26] in their study conducted in 2677 people found that OSA significantly contributed to hypertension independent of all known confounding variables.

1% to the risk of having hypertension would be added by each apneic event per hour8. In our study subjects with severe OSA had lowest average SpO2 and lowest minimum SpO2 during sleep duration. This hypoxia duration during sleep may lead to arousal and increased sympathetic activity which in turn leads to temporary blood pressure elevation and ultimately sustained hypertension. Hence we were of the opinion that if we were to select subjects without hypertension, we may be choosing subjects who are somewhat resistant to OSA consequences as described by Atlintas et al8and that may lead to selection errors in our study results.

In our study we found left ventricular function measured by MPI was severely impaired with severe OSA and had statistical significant association with severity of OSA although LVEF was normal in all subjects in our study. In contrast, Laaban *et al*[27] in their study found that OSA was the cause of daytime LVEF dysfunction. However several cross sectional studies concordant with our findings found that LVEF was normal in patients of OSA with no significant difference with severity of OSA. The discordance of Laaban's study may be due to the fact that we had included subjects with LVEF = 60 for analysis.

The cause of diastolic dysfunction in OSA patients is not clear however, nocturnal elevations of blood pressure and sympathetic overactivity in OSA subjects[28] create ventricular pressure overload and this pressure overload leads to activation of multiple cellular signals that leads to myocardial tissue hypertrophy and interstitial fibrosis and ultimately to increasing passive stiffness[29]. These changes leads to impaired coronary flow reserve worsening ventricular active relaxation leading to rise in ventricular diastolic pressure.

In our study we also found that MPI was correlating with severity of OSA more than LVM and LVMI, finding which needs several longitudinal studies for confirmation.

Study conducted by us has various strengths including its novelty, but we acknowledge few limitations of it. We had a relatively small size of sample and thus we were underpowered for some of our assessments particularly during subgroup analysis. We also acknowledge the fact that the instrument used in our study for determining sleep parameters is a HSAT (Home Sleep Apnea Testing) device which is recommended[30] for testing in only highly suspicious patients as it is inferior to polysomnography for diagnostic accuracy having significant false positive rate. But this device is cheap, convenient, accessible, and can be done at home. We also realize that as numbers of covariates are present it is difficult to determine the effect of OSA from hypoxia. However, we believe that our data is an important addition to already published study because of our novelty and the hypothesis that severity of OSA (AHI) is positively correlated with LVM, LVMI and MPI.

Conclusion :

We found that OSA leads to left ventricular dysfunction whose severity increase as the severity of OSA.The MPI is an easy, simple, noninvasive and reproducible measure of finding global left ventricular function in obese patients. Since important prognostic information is provided with the help of left ventricular global function the results of this study should be confirmed by several other longitudinal studies.

Conflict of interest : None.

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