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RESEARCH ARTICLE

A STUDY OF PREVALANCE OF OSA IN APPARENTLY HEALTHY ADULT POPULATION AND INDIVIDUALS WITH METABOLIC SYNDROME- CROSS SECTIONAL STUDY

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Abstract

Aim: To compare prevalence of obstructive sleep apnea (OSA) in metabolic syndrome (MetS) patients and age, sex-matched controls without MetS.

Materials & Methods: A total of 50 MetS patients (as per IDF criteria) and a total of 100 age and sex-matched individuals without MetS were enrolled in the study as cases and controls. Screening for OSA was done using Berlin Questionnaire. OSA prevalence was ascertained by polysomnography. Apnea-Hypopnea index (AHI) 5-15, 16-30 and >30 was considered as mild, moderate and severe OSA. Data was analyzed using Chi-square and Independent sample t-tests.

Results: Mean age of cases was 50.80±10.16 years. Majority of cases were males (80%). Mean BMI, waist circumference, SBP, DBP, FBS and TG of cases were significantly higher while mean HDL was significantly lower as compared to that of controls ($p<0.001$). Number of MetS factors 3, 4 and 5 were seen in 28%, 34% and 38% respectively in cases and 0, 1, 2 and 3 in 22%, 47%, 30% and 1% controls respectively ($p<0.001$). Prevalence of OSA was 58% in cases as compared to 20% in controls ($p<0.001$). Mild, moderate and severe OSA was seen in 10%, 22% and 26% of cases and 12%, 6% and 2% of controls ($p<0.001$). On overall evaluation and in case groups, there was a significant increase in prevalence and severity of OSA ($p<0.05$).

Conclusion: MetS patients were at a high risk for moderate to severe OSA.

Clinical Significance: Prevention and control of OSA must be targeted as the treatment goal in MetS.

Introduction:-

Metabolic syndrome is a cluster of some clinical factors that together reflect metabolic disorders of different types. As per International Diabetic Federation (IDF) criteria[1], it is defined as presence of central obesity (male waist circumference ≥90 cm/female waist circumference ≥80 cm), with any of the following four conditions, *viz.*, hypertension (SBP/DBP>130/85 mmHg), raised fasting glucose (>100 mg/dl), raised triglyceride (>150 mg/dl) and low HDL (males <40 mg/dl, females <50 mg/dl). Metabolic syndrome depicts a high cardiovascular risk[2]. Metabolic

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syndrome is also found to be associated with cognitive impairment[3], psychiatric illnesses[4], rheumatological disorders[5] and respiratory illnesses[6]. The component factors of metabolic syndrome are recognized as lifestyle disorders which eventually have an impact on different dimensions of human health. Recent studies have shown a relationship between metabolic syndrome and sleep disorders too[7,8].

Obstructive sleep apnea (OSA)is "a sleep-related breathing condition that is characterized by episodes of complete (apnea) or partial (hypopnea) upper airway obstruction during sleep, leading to repetitive oxygen desaturation and sleep fragmentation"[9]. The known risk factors for OSA include obesity[10], male sex[11] and metabolic disorders[12]. A number of recent studies have shown metabolic syndrome to be associated with an increased risk of OSA[13-15]. Hence, the present study was carried out to assess the prevalence of OSA in metabolic syndrome patients and to compare it with age-, sex-matched population without metabolic syndrome.

Material And Method:-

The present study was carried out at Department of Pulmonary Medicine in collaboration with Department of Medicine, Era's Lucknow Medical College, Lucknow after obtaining approval from the Institutional Ethics Committee (vide letter no. ELMC&H/RCell,EC/2020/118 dated 28/04/2020) and obtaining informed consent from the participants.

This was a case-control study that included 50 Metabolic syndrome (MetS) patients (as per IDF criteria)[1]as cases and a total of 100 age-, sex-matched individuals without MetS as controls. Sample size estimation was based on a study by Soin*et al.*[13] who reported the prevalence of OSA in MetS cases to be 66% as compared to 12% in controls. Sample size estimation was done at 95% confidence and 80% power after allowing for 10% absolute error.

The inclusion criteria for cases was age between 30 and 70 years, Metabolic syndrome as per 2005 IDF criteria[1]*viz.*

1. Central obesity (waist circumference >90cm in male and >80cm in females) And any of the following two:
2. Serum triglycerides >150mg/dL or specific treatment for lipid abnormality.
3. Serum HDL cholesterol <40mg/dL in males and <50mg/dL in females or specific treatment for this lipid abnormality
4. Blood Pressure – systolic BP >130 or Diastolic >85mm Hg or treatment of previously diagnosed hypertension.
5. Fasting blood sugar >100mg/dL or previously diagnosed type 2 diabetes.

Pregnant women, those with chronic respiratory problems, congestive heart failure history, cognitive impairment, history of cerebrovascular accident, having current history of sedative, antipsychotic or anti-obesity drug use were excluded from the study.

The controls were age and sex-matched individuals fulfilling all the inclusion as well as exclusion criteria except for presence of MetS as per IDF criteria.

All the participants (cases and controls) were clinically examined and demographic details were recorded on a structured proforma, anthropometric parameters (height, weight, waist circumference) were measured and calculated (BMI). Blood pressure measurements were taken. Blood specimen was taken and assessed for fasting glucose, triglyceride and high-density lipoprotein (HDL).

All the subjects were administered modified Berlin Questionnaire[16] to screen for risk of Obstructive Sleep Apnea. It is an eleven-item questionnaire that addresses three problem areas – snoring and breathing (category I), sleep deprivation (Category II) and blood pressure (Category III). A patient having high scores on two or more categories is considered to be in high-risk category. High risk subjects (in both the groups – Cases and Controls) were subjected to Polysomnography). Obstructive sleep apnea was categorized on the basis of Apnea-Hypopnea Index (AHI) which were divided into mild (5-15), moderate (>15 to 30) and Severe OSA (>30).

Data Analysis:

Data was analyzed using IBM Statistical Package for Social Sciences (SPSS) version 21.0. Chi-square and Independent samples 't'-tests were used to compare the data. An association was considered significant when 'p' value was less than 0.05.

Results:-

Age of cases as well as controls ranged from 30 to 70 years. Mean age of cases and controls was 50.80±10.16 and 50.24±11.20 years respectively. Majority of cases as well as controls were males (80%). Statistically, there was no significant difference between two groups with respect to age and sex ($p>0.05$). Mean BMI and waist circumference of cases was 34.53±5.84 kg/m^2 and 117.18±13.57 cm respectively as compared to 30.48±4.59 kg/m^2 and 96.64±14.05 cm respectively for controls. Both BMI as well as waist circumference of the cases were significantly higher as compared to that of controls ($p<0.001$). Mean systolic and diastolic blood pressure values were 132.92±13.37 and 87.58±9.60 mmHg respectively in cases as compared to 125.34±9.23 and 79.96±7.74 mmHg respectively in controls. For both the parameters, mean values were significantly higher in cases as compared to that of controls ($p<0.001$). Mean fasting blood sugar, triglyceride and HDL levels were 118.68±18.65, 187.20±56.79 and 38.34±10.22 mg/dl respectively in cases as compared to 92.16±9.67, 136.35±8.95 and 45.63±7.71 mg/dl respectively in controls. A statistically significant difference between two groups was observed for all the parameters. Mean fasting blood sugar and triglyceride levels were significantly higher in cases as compared to that in controls ($p<0.001$). Number of MetS factors 3, 4 and 5 were seen in 28%, 34% and 38% respectively in cases and 0, 1, 2 and 3 in 22%, 47%, 30% and 1% controls respectively ($p<0.001$) (Table 1).

A total of 58% cases and 20% controls were screened positive for OSA using Berlin Questionnaire ($p<0.001$). Mild, moderate and severe OSA was seen in 10%, 22% and 26% of cases and 12%, 6% and 2% of controls ($p<0.001$) (Table 2).

With increasing number of metabolic syndrome factors, there was a significant increase in prevalence as well as severity of OSA on overall evaluation as well as in case group ($p<0.001$). Though in control group too, an increasing trend of OSA prevalence was seen with increasing number of metabolic syndrome factors yet this association was not significant statistically ($p=0.188$) (Table 3).

Discussion:-

In the present study, majority of MetS patients (58%) had OSA as compared to one-fifth (20%) of controls (Relative Risk; RR=2.9). The prevalence of OSA was significantly higher in cases as compared to that in controls. Moreover, prevalence of moderate to severe OSA was also much higher in cases (48%) as compared to that in controls (8%) (RR=6). Prevalence of OSA in metabolic syndrome patients has been reported to be very high. As these patients do not only have obesity, which is a traditional risk factor of OSA[10] but also has other metabolic conditions that have their own independent association with OSA. Darger*et al.*[17] in their study reported the prevalence of OSA to be 60.5% in their MetS population. However, Moideen*et al.*[18] found this prevalence to be only 34%. The prevalence of OSA in MetS patients has been reported to be as high as 96% in the study of Dubey *et al.*[19]. In other studies too, prevalence of OSA in MetS patients has been reported to vary from 59% to 95%[13,14,20-22].

The relationship between metabolic syndrome and OSA seems to be bidirectional. While the evidence gathered in the present study shows a high prevalence of OSA in MetS patients, there is equal strong evidence suggesting this relationship in the other direction with high prevalence of MetS in OSA patients. In some of the contemporary studies reviewed by us that explored the prevalence of MetS in OSA patients, it has been reported to vary from 51.4% to 81.8%[22-25] in different studies thus showing a strong correlation and coexistence of the two entities.

The basic relationship between metabolic syndrome and OSA is primarily guided by the obesity owing to which the pharyngeal airway collapses thus resulting in a restrictive pharyngeal pathway that contributes to the apneic episodes and the resulting repetitive arousals[26]. It is believed that different factors contributing to metabolic syndrome directly or indirectly contribute to obesity.

Coexistence of these two entities has even been reported in various cross-sectional studies. In their study, Parish *et al.*[27] reported the prevalence of OSA and MetS in a select population to be 76.3% and 53.1% patients respectively and found coexistence of two in 43%, thus showing that 81.0% of MetS patients had OSA too. The combined presence of MetS and OSA is often termed as Syndrome Z and has been reported to be highly frequent with its prevalence ranging from 19.2% to 50%[28-29] and in context with relative proportion of MetS patients having OSA it comes out in range 54.4% to 71.4%[28,29].

In the present study, we found prevalence of OSA to be 20% in Controls. Although there are no contemporary studies built around a case-control studies, however, evidence from cross-sectional studies evaluating prevalence of syndrome Z show the prevalence of OSA in non-MetS subjects to range from 6.8% to 36%[27-29]. These findings suggest that while OSA is a major issue in MetS patients, however, it is an equally important emerging health related issue in a non-MetS population.

In the present study, prevalence of mild, moderate and severe OSA was 10%, 22% and 26% respectively in MetS cases and 12%, 6% and 2% respectively in non-MetS cases. OSA patients tended to have significantly higher proportion of cases with moderate and severe OSA as compared to non-MetS controls. Darger*et al.*[17] in their study among MetS patients diagnosed 60.2% cases with moderate or higher severity of OSA as per criteria used in the present study. Moideen*et al.*[18] also found that more than half (71.9%) of their patients had moderate to severe OSA. In the study of Dubey *et al.*[19]too 86% patients had moderate/severe OSA. All these findings correspond with the observations made in the present study and depict that in patients with MetS not only the risk of developing OSA higher but it also is related with higher severity.

In the present study we found a significant association between number of metabolic syndrome factors and prevalence of OSA in overall study population as well as in cases however, this relationship could not be extended to controls. As far as relationship of number of MetS components and OSA risk is concerned, it is primarily driven by cumulative effect of multiple risk factors contributing to burden of OSA. With respect to absence of this association in controls, it could be owing to the limitation of presence of not more than two metabolic syndrome factors (except for one case). The pathogenesis of OSA is complex and is marked by presence of several comorbid conditions and in such a scenario multiplicity of cardio-metabolic factors in terms of multiple MetS components seems to have a direct impact on OSA prevalence. Sureja and Bhambani[21] in their study similar to our study found a significant increase in severe OSA prevalence with increasing number of metabolic syndrome patients. Neumann *et al.*[30] too also found a significant relationship between number of metabolic components and severe sleep disordered breathing (SDB). The findings of the present study are thus in agreement with these reports.

The findings of the present study showed that syndrome Z (coexistence of Metabolic Syndrome and OSA) is a ground reality and is being ignored extensively. The cross-relationship between OSA and MetS indicates the need to evaluate the patients simultaneously for both the entities even if being diagnosed for one of them. The health impacts of coexisting MetS and OSA also need to be studied. Further studies on a larger sample size are also recommended.

Conclusion:-

The findings of the present study showed that there was a high prevalence of OSA among metabolic syndrome patients. It was also seen that increasing number of metabolic syndrome factors had a direct association with increasing prevalence of metabolic syndrome and its severity. The findings of the present study showed that MetS patients as compared to controls had almost 2.9 times higher risk of OSA and an almost 6 times higher risk of moderate-to-severe OSA.

The findings of the present study signify syndrome Z (coexistence of Metabolic Syndrome and OSA) as a ground reality which is being ignored extensively. The findings highlight the need to screen the metabolic syndrome patients for presence of OSA at a regular interval, especially in patients having more than 3 metabolic syndrome factors. The findings of the study also highlight the need to target control of OSA and its severity as an essential target of metabolic syndrome management strategy.

Table 1:- Comparison of Demographic Profile and Clinical Characteristics of Cases and Controls.

SN	Characteristic	Cases (n=50)	Controls (n=100)	Statistical significance
1.	Mean age±SD (Range) in years	50.80±10.16 (30-70)	50.24±11.20 (30-70)	't'=0.298; p=0.766
2.	Sex			
	Male	40 (80.0%)	80 (80.0%)	χ^2=0.000; p=1.000
	Female	10 (20.0%)	20 (100.0%)	
3.	BMI (kg/m^2)	34.53±5.84	30.48±4.59	t=4.638; p<0.001
4.	Waist circumference (cm)	117.18±13.57	96.64±14.05	t=8.534; p<0.001

5.	SBP (mmHg)	132.92±13.37	125.34±9.23	t=4.060; p<0.001
6.	DBP (mmHg)	87.58±9.60	79.96±7.74	t=5.223; p<0.001
7.	FBS (mg/dl)	118.68±18.65	92.16±9.67	t=11.49; p<0.001
8.	TG (mg/dl)	187.20±56.79	136.35±8.95	t=8.767; p<0.001
9.	HDL (mg/dl)	38.34±10.22	45.63±7.71	t=-4.881; p<0.001
10.	Number of metabolic syndrome factors			
	None	0	22 (22.0%)	**χ^2=145.800; p<0.001**
	One	0	47 (47.0%)	
	Two	0	30 (30.0%)	
	Three	14	1 (1.0%)	
	Four	17	0	
	Five	19	0	

Table 2:- Comparison of Cases and Controls for OSA screening outcome, OSA prevalence and severity.

SN	Characteristic	Cases (n=50)	Controls (n=100)	Statistical significance
1.	OSA Screen Positive (Berlin Questionnaire High risk category)	29 (58.0%)	20 (20.0%)	χ^2=21.88;p<0.001
2.	OSA severity (AHI)			
	No OSA (AHI <5)	21 (42.0%)	80 (80.0%)	χ^2=34.00;p<0.001
	Mild (AHI 5-15)	5 (10.0%)	12 (12.0%)	
	Moderate (AHI 16-30)	11 (22.0%)	6 (6.0%)	
	Severe (AHI >30)	13 (26.0%)	2 (2.0%)	

Table 3:- Association between number of components of metabolic syndrome with OSA and its severity.

Number of Metabolic syndrome components present	Total No. of cases	No OSA		Mild		Moderate		Severe	
		No.	%	No.	%	No.	%	No.	%
Overall population									
None	15	14	93.3	0	0.0	1	6.7	0	0.0
One	33	28	84.8	3	9.1	2	6.1	0	0.0
Two	51	38	74.5	8	15.7	3	5.9	2	3.9
Three	15	8	53.3	4	26.7	3	20.0	0	0.0
Four	17	5	29.4	2	11.8	7	41.2	3	17.6
Five	19	8	42.1	0	0.0	1	5.3	10	52.6
Chi-square		χ^2=78.346; p<0.001							
Cases									
Three	14	8	57.1	3	21.4	3	21.4	0	0.0
Four	17	5	29.4	2	11.8	7	41.2	3	17.6
Five	19	8	42.1	0	0.0	1	5.3	10	52.6
Chi-square		χ^2=19.729; p=0.003							
Controls									
None	15	14	93.3	0	0.0	1	6.7	0	0.0
One	33	28	84.8	3	9.1	2	6.1	0	0.0
Two	51	38	74.5	8	15.7	3	5.9	2	3.9
Three	1	0	0.0	1	100.0	0	0.0	0	0.0
Chi-square		χ^2=12.480; p=0.188							

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