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Case Report

Moving beyond the metabolic syndrome: syndrome Z in Indian subcontinent: a case report and review of literature

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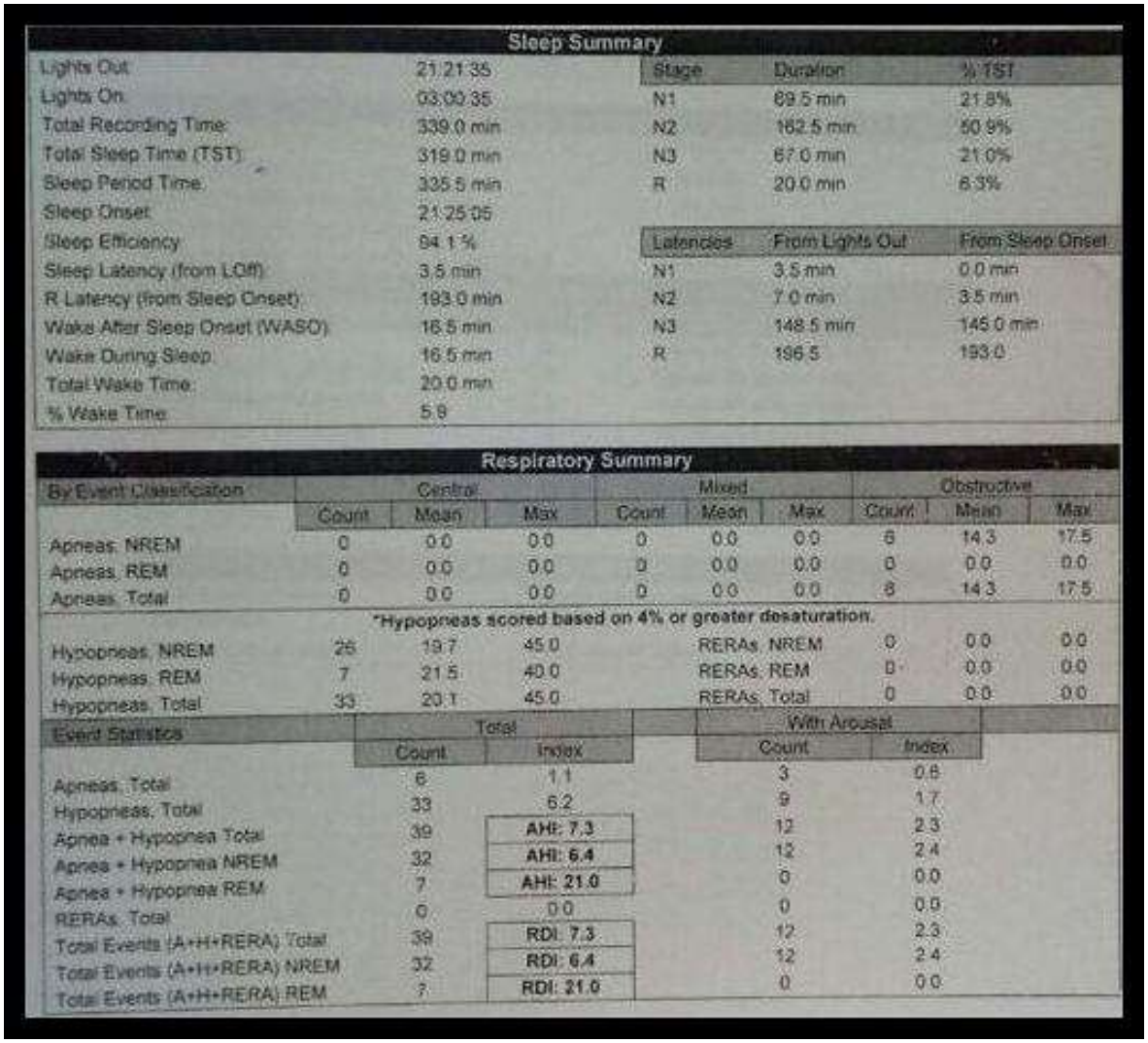
ABSTRACT

Conventionally the combination of obstructive sleep apnea (OSA) and the metabolic syndrome (syndrome X) has been described as syndrome Z. With the dawn of modern era while there has been a rapid upsurge in the incidence of syndrome Z there has also been a paradigm shift in its topographical distribution. Syndrome Z earlier a disease predominantly of the developed world is now rapidly acquiring the magnitude of an epidemic in the developing nations as well. Coexisting OSA and metabolic syndrome also have a synergistic impact in increasing the risk for cardiovascular diseases. Hence, we present here a case report of syndrome Z and review of literature from the Indian subcontinent to essentially prime the physicians regarding this syndrome with significant social and economic impact, so that early health measures can be initiated to identify and treat the syndrome Z epidemic.

Keywords: Syndrome Z, OSA, Metabolic syndrome, Syndrome X, AHI

INTRODUCTION

The metabolic syndrome (syndrome X or insulin resistance syndrome) consists of a constellation of metabolic abnormalities including central obesity, hypertriglyceridemia, low levels of high density lipoprotein (HDL) cholesterol, hyperglycemia and hypertension.[1] The diagnosis of OSA can be made when the AHI is >5 in a patient with excessive daytime sleepiness.[2] The combination of OSA and metabolic syndrome has been referred to as "syndrome Z". There is paucity of information on the exact prevalence of syndrome Z in the Indian subcontinent community and the factors associated with it.[3] Although, in India a community based survey had reported the prevalence of OSA as 9.3% and that of obstructive sleep apnea syndrome (OSAS) as 2.8%.[4] These figures are similar to those reported in the western population.[5] The past few decades have seen a growing recognition of the presence of various types of metabolic dysfunction in subjects with OSA, which have further highlighted the association of metabolic syndrome and OSA.[6] Obstructive sleep apnea (OSA) has been linked to increased cardiovascular morbidity and mortality from both coronary heart disease and stroke.[7] Sleep disorders are common among the general population.[7,8] Sleep related breathing disorders (SRBD) can impair academic and occupational performance, cause work-related and road accidents, and disturb mood and social adjustment disrupting personal life and relationships. Also, sleep-related breathing disorders may lead to or exacerbate serious medical, neurological and psychiatric problems.[9] This clearly signifies the personal, social and economic impact of syndrome Z on human society. Still only a few studies in India have studied the prevalence of syndrome Z which clearly underscores the unmet need of research in this direction. Hence, we report here a case of syndrome Z to put a spotlight on this severe systemic disease with appalling health effects.



Sleep Summary

Lights Out	21:21:35
Lights On	03:00:35
Total Recording Time	339.0 min
Total Sleep Time (TST)	319.0 min
Sleep Period Time	335.5 min
Sleep Onset	21:25:05
Sleep Efficiency	94.1 %
Sleep Latency (from LOff)	3.5 min
R Latency (from Sleep Onset)	183.0 min
Wake After Sleep Onset (WASO)	16.5 min
Wake During Sleep	16.5 min
Total Wake Time	20.0 min
% Wake Time	5.9

Stage	Duration	% TST
N1	69.5 min	21.8%
N2	162.5 min	50.9%
N3	67.0 min	21.0%
R	20.0 min	6.3%

Latencies	From Lights Out	From Sleep Onset
N1	3.5 min	0.0 min
N2	7.0 min	3.5 min
N3	148.5 min	145.0 min
R	196.5	193.0

Respiratory Summary

By Event Classification	Central			Mixed			Obstructive		
	Count	Mean	Max	Count	Mean	Max	Count	Mean	Max
Apneas, NREM	0	0.0	0.0	0	0.0	0.0	6	14.3	17.5
Apneas, REM	0	0.0	0.0	0	0.0	0.0	0	0.0	0.0
Apneas, Total	0	0.0	0.0	0	0.0	0.0	6	14.3	17.5

*Hypopneas scored based on 4% or greater desaturation.

Hypopneas, NREM	26	19.7	45.0	RERAs, NREM	0	0.0	0.0
Hypopneas, REM	7	21.5	40.0	RERAs, REM	0	0.0	0.0
Hypopneas, Total	33	20.1	45.0	RERAs, Total	0	0.0	0.0

Event Statistics	Total		With Arousal	
	Count	Index	Count	Index
Apneas, Total	6	1.1	3	0.6
Hypopneas, Total	33	6.2	9	1.7
Apnea + Hypopnea Total	39	AHI: 7.3	12	2.3
Apnea + Hypopnea NREM	32	AHI: 6.4	12	2.4
Apnea + Hypopnea REM	7	AHI: 21.0	0	0.0
RERAs, Total	0	0.0	0	0.0
Total Events (A+H+RERA) Total	39	RDI: 7.3	12	2.3
Total Events (A+H+RERA) NREM	32	RDI: 6.4	12	2.4
Total Events (A+H+RERA) REM	7	RDI: 21.0	0	0.0

Figure 1: Polysomnography–sleep and respiratory summary.

CASE REPORT

A 45 year old female presented to us with a history of excessive day time sleepiness since 4 years which was associated with habitual loud snoring and excessive weight gain in the recent past. This all led to impaired concentration, decreased sleep latency and eventually had severely affected her quality of life. She was a diagnosed case of hypothyroidism and systemic hypertension since 10 years and 5 years respectively and was on regular medication since then. In past, she had also underwent endoscopic sinus surgery and cholecystectomy in the year 1998 and 1993 respectively. On examination, she was obese with body mass index (BMI) of 39.26 (obesity class II), height of 148 cm and weight of 86 kg. Her waist circumference was 117 cm, hip circumference was 121 cm, neck circumference was 36 cm and neck length was 7 cm. Her waist to hip ratio was 0.967. Her blood pressure was 160/90 mm Hg, respiratory rate was 18 cycles/ minute with a pulse rate of 82 beats/minute.

On investigation, her hemoglobin was 9.3 gm%, fasting blood sugar (FBS) was 130 mg% and post prandial (PP) blood sugar was 287 mg%. Fasting lipid profile showed total cholesterol of 241 mg%, HDL of 32 mg%, LDL of 166 mg%, VLDL of 43 mg% and triglyceride of 213 mg%. Her HbA1c was 7.38 mg% and serum TSH was 3.2 mIU/L while her arterial blood gas analysis was within normal limits.

Overnight polysomnography study with 319 minutes of sleep recording showed apnea index 1.1, hypopnea index 6.2 and total apnea hypopnea index (AHI) of 7.3/hr of sleep which was suggestive of mild obstructive sleep apnea, while AHI individually for NREM and REM was 6.4/hr and 21.0/hr respectively with CPAP titration of 8 cm of water. Modified Berlin Questionnaire reflected high risk while Epworth Sleepiness Score (ESS) was 17/24. She also had metabolic syndrome according to NCEP ATP criteria. She was thus diagnosed with OSA along with metabolic syndrome hence fulfilling the criteria for syndrome Z.

Subsequently, apart from the supportive and symptomatic care the patient was started on metformin to benefit the insulin resistance, statin, was put on CPAP in the night during the course of admission (was not affordable enough to buy a portable CPAP machine for use at home), the medications for patient's chronic diseases were continued and she was counselled regarding various options available for weight reduction. She principally agreed to undergo bariatric surgery and was thereby transferred under the care of a bariatric surgeon. The patient is yet to come in follow-up.

REVIEW OF LITERATURE AND DISCUSSION

Agrawal et al in their study had showed that the prevalence of metabolic syndrome was four times higher in patients of OSA than controls and the prevalence increased with increasing severity of OSA.[10] Therefore, patients with metabolic syndrome should be investigated for OSA and vice versa, as early detection and correction of these conditions may result in significant decrease in morbidity and mortality. Mishra et al had also earlier reported that the development and presentation of sleep disordered breathing and its frequent association with metabolic syndrome and type 2 diabetes reflect that the underlying pathophysiologies are certainly linked and treating one disorder ameliorates the symptoms of the related conditions.[11] Hasan et al had also concluded that the obstructive sleep apnea syndrome is strongly associated with the metabolic syndrome, hypothyroidism, and recent or current smoking.[12] Khot et al reported that the prevalence of syndrome Z is high in T2DM, and increases with age and duration of diabetes. Hypertension is an independent risk factor.[13] Syndrome Z has a positive correlation with BMI, hypertriglyceridemia, and increased waist circumference. Iyer also found evidence favoring a possible role of sleep disorders as risk factors for metabolic abnormalities and concluded that there is a close relationship between sleep, circadian rhythm, obesity, insulin resistance, hypertension and cardiovascular disorders which needs to be dissected and managed and also suggested a causal role of OSA in development of metabolic syndrome and eventually their compounded adverse effects on human health.[14] Thus, all these studies highlight the severity and adverse effects of syndrome Z as a systemic disease and therefore call for instituting aggressive measures for preventing and treating syndrome Z at an early stage.

Soneja et al in a large placebo controlled, double blind, randomized, crossover study with a longer duration of follow-up observed that the metabolic abnormalities are responsive to CPAP therapy.[15] The same was reiterated by Sharma et al who found that 3 months of CPAP therapy lowers blood pressure and partially reverses metabolic abnormalities.[16] Hence, as was done in this case CPAP therapy should be recommended in all patients with syndrome Z more so in patients who can afford portable machines to administer home based CPAP therapy.

Dubey et al in their study had validated polysomnography as a valuable tool to access non symptomatic sleep disordered breathing at an early stage in patients with metabolic syndromes.[17] Iyer et al also observed that the association of sleep disorders with obesity and metabolic syndrome demands sleep history to be recorded and polysomnography performed in these patients.[18] Diagnosis of sleep disordered breathing will pave the way for better management and possibly reversal of metabolic errors. Pandharipande et al in line with these findings suggested therefore that every patient with the metabolic syndrome should be screened for OSA, at the very least by taking a sleep history and using the Epworth sleepiness scale.[19] If results are positive, a diagnostic sleep study should be performed. In fact the metabolic syndrome itself could serve as a marker of OSA as these two syndromes often go hand in hand in the form of syndrome Z. Based on our experience in this case we too strongly recommend the same for early identification and better management of syndrome Z.

Ravindran et al while reporting a case of syndrome Z had also emphasized upon the significant correlation of syndrome Z with CAD and the need for early diagnosis and treatment of this condition to prevent cardiovascular morbidity and mortality.[20] We also by means of this case report intend to sensitize the medical community regarding the magnitude of the syndrome Z epidemic and the urgent need to institute public health measures in this regard.

CONCLUSION

To conclude we can say that by means of the above reported case we want to lay stress on the dire consequences of syndrome Z so that further prospective and interventional studies, with adequate sample sizes and longer follow-up, rigorous control for confounding factors and ideally, randomization and control for any therapeutic intervention, can be encouraged to estimate the exact incidence & prevalence and explore the other not yet identified ill health effects of syndrome Z in order to initiate goal directed community health measures to curb this rising epidemic.

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