# A Prospective Study Evaluating the Correlation of Sleep Pattern, Melatonin Secretion and Obesity

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## ABSTRACT

Background: The present study aims to assess correlation of sleep patterns, melatonin secretion, and obesity.

Materials and Methods: One hundred and twenty-two subjects in age ranged 11-17 years of both genders were subjected to fasting blood glucose, insulin level, uric acid, lipid profile and renal function test measurement. Insulin resistance and level of melatonin with enzyme-linked immunosorbent assay (ELISA) were determined.

Results: There were 30 males and 22 females without insulin resistance (IR) and 40 males and 30 females with IR. There were 6 prepubertal, 12 pubertal, and 34 postpubertal subjects without IR and 8 prepubertal, 15 pubertal, and 47 postpubertal subjects with IR. The mean Body Mass Index (BMI) (Kg/m2) was 29.1 and 34.2, Systolic Blood Pressure (SBP) (mm Hg) was 128.6 and 134.2, Diastolic Blood Pressure (DBP) (mm Hg) was 66 and 72, total cholesterol (TC) (mg/dl) was 160.2 and 164.8, triglyceride (TG) (mg/dl) was 70 and 104.2, High Density Lipoprotein (HDL) (mg/dl) cholesterol was 54.2 and 46.8 and Low-density lipoprotein (LDL) (mg/dl) cholesterol was 92 and 98 in subjects without IR and in subjects with IR respectively. The mean uric acid was 5.3 mg/dl in subjects without IR and 5.9 mg/dl in subjects with IR. The mean MT6s:Cr (Melatonin 6s: Creatinine) ratio was 31.4 in subjects without IR and 27.4 in subjects with IR. The difference between both groups was found to be significant (P< 0.05).

Conclusion: There was reduced night melatonin secretion, impaired energy metabolism in subjects with obesity.

Keywords: Sleep, obesity, melatonin.

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## INTRODUCTION

Obesity is a non-communicable disease earlier considered to be highly prevalent in developed countries, but now it is alarmingly increasing in developing countries also.[1] There is a remarkable rise in the number of overweight and obese children from 4% to 18% in the last 45 years.[2] According to the World health organization (WHO), both genders are affected and in the year 2016, the prevalence was 19% in boys and 18% in girls. The disparity between energy consumption and expenditure leads to obesity and overweight.[3]

Multiple factors influence the disease, among which lifestyle, genetics and environmental factors play the significant role. WHO warned the world about rising in deaths due to non-communicable diseases and the main reason being obesity.[4] The prevalence was found to be 38.2% in children less than 5 years of age in the year 2019. The increasing number has been estimated in Asia. In India, this disease has spread in rural as well as urban societies due to sedentary life style, westernization, and urbanization.[5]

The relation between obesity and sleeping pattern has been established in the literature.[6] The pineal gland secrete melatonin hormone which controls sleep pattern which is directly controlled by the suprachiasmatic nucleus of the hypothalamus.[7] The level of melatonin is more among children and then starts decreasing till puberty and with advanced age.[8] At night time, secretion is more than day time. The circadian rhythm of sleep starts falling due to regression of the pineal gland as age advances.[9,10] Considering this, we attempted the present study to assess the correlation of sleep patterns, melatonin secretion, and obesity.

## MATERIALS & METHODS

A sum total of one hundred and twenty two subjects in age ranged 11-17 years of both genders were involved in the study. The approval for this cross-sectional study was taken from the institutional review committee with vide number as, "EC/TRG/2019/955/27356". The written consent was taken from the parents of subjects who were enrolled in the study.

Socio-demographic profile was recorded in case history proforma. Patients were kept on overnight fasting and a 5 ml venous blood was obtained. Parameters such as lipid profile including TG, TC, HDL and LDL, fasting blood sugar, uric acid, and insulin level was determined. Renal function tests were measured. Insulin resistance was measured using the homeostasis model assessment of insulin resistance (HOMA-IR). The first-morning sample of urine taken with full aseptic conditions was used for the estimation of 6-sulfatoxymelatonin (MT6s), the major metabolite of melatonin, and normalized to urinary creatinine levels to account for the urinary concentration. McMullan CJ et al in their study demonstrated that MT6s to creatinine ratio (MT6s:Cr) ratio correlates well with the cumulative nocturnal melatonin secretion.[11] Therefore, all the subjects were instructed to bring a sample from the first-morning urine (between 06.30 and 07.00 am) on the day of examination, which was a regular school day. Regular physical activity other than school sport as well as eating habits during daily electronic media consumption (television, computer, tablet or smartphone) was also evaluated.

To determine the chronotype, the midpoint of sleep on workdays (MSW) and the midpoint of sleep on free days (MSF) were estimated.[3] Chronotype (MSFst) was defined as MSF corrected for sleep time acquired during workdays. The social jet lag which is the discrepancy between biological and social timing was estimated as the time difference between MSF and MSW.[11] Taking an account on the number of free and working days we calculated the weekly average sleep duration as sleep duration during the week and during the weekend $((SDw \times WD + SDf \times (7 - WD))/7)$ (SDw- Sleep duration for typical work, WD- Number of workdays, SDf- Sleep duration for free days). Results were compiled, clubbed, and spread along the MS excel sheet. Statistical analysis was performed using SPSS version 19.0. The mean value and standard deviation was calculated and 't' test was applied for comparison on independent samples. Beta coefficient was calculated to see the correlation between the two variables. The p value <0.05 was considered as significant.

## RESULTS

**Table 1: Subject distribution based on gender [Data Tabulated as Number (Percentage)]**

| Gender | Without IR in | With IR | P value |
|--------|---------------|---------|---------|
| Male | 30 (57.7%) | 40 (57.1) | 0.68 |
| Female | 22 (42.3%) | 30 (42.9) | 0.71 |

There were 30 (57.7%) males and 22 (42.3%) females without insulin resistance and 40 (57.1) males and 30 (42.9) females with insulin resistance. The difference was non-significance (P>0.05) [Table 1].

**Table 2: Distribution based on age [Data Tabulated as Number (Percentage)]**

| Age group | Without IR | With IR | P value |
|---|---|---|---|
| Prepubertal | 6 (11.6%) | 8 (11.4%) | 0.52 |
| Pubertal | 12 (23.0%) | 15 (21.4%) | 0.69 |
| Postpubertal | 34 (65.4%) | 47 (67.2%) | 0.12 |

**Table 3: Comparison of parameters [Data Tabulated as Mean ± SD]**

| Parameters | Without IR | With IR | P value |
|---|---|---|---|
| BMI (Kg/m$^2$) | 29.1 ± 2.17 | 34.2 ± 2.64 | 0.03** |
| SBP (mm Hg) | 128.6 ± 6.71 | 134.2 ± 8.82 | 0.04* |
| DBP (mm Hg) | 66 ± 5.14 | 72 ± 7.49 | 0.03* |
| Total cholesterol (mg/dl) | 160.2 ± 11.26 | 164.8 ± 12.37 | 0.73 |
| Triglycerides (mg/dl) | 70 ± 8.72 | 104.2 ± 10.89 | 0.01* |
| HDL cholesterol (mg/dl) | 54.2 ± 6.61 | 46.8 ± 4.41 | 0.03* |
| LDL cholesterol (mg/dl) | 92 ± 7.75 | 98 ± 8.63 | 0.05* |

**Table 4: Assessment of uric acid and melatonin secretion [Data Tabulated as Mean ± SD]**

| Parameters | Without IR | With IR | P value |
|---|---|---|---|
| Uric acid (mg/dl) | 5.3 ± 1.12 | 5.9 ± 1.57 | 0.03* |
| MT6s:Cr ratio | 31.4 ± 3.69 | 27.4 ± 2.29 | 0.04* |

**Table 5: Association of media consumption with chronobiology and melatonin secretion [Regression analysis: Sex, age, and pubertal status were introduced as cofactors. Linear regression model. B = unstandardized regression coefficient.]**

| Parameters | Variables | B coefficient | P value | 95% Confidence Interval |
|---|---|---|---|---|
| Chronotype (MSFst) | Media consumption after 10 pm | 1.02 | 0.042 | 0.79-1.28 |
| | Duration of media consumption | 1.08 | 0.03 | 0.86-1.43 |
| | 3–6 h vs. <3 h | 0.72 | 0.04 | 0.49-0.91 |
| | >6 h vs. <3 h | 1.125 | 0.01 | 0.82-1.46 |
| Melatonin secretion | Media consumption after 10 pm | 0.778 | 0.014 | 0.71-0.94 |
| | Duration of media consumption | 1.039 | 0.01 | 0.84-1.23 |
| | 3–6 h vs. <3 h | 0.392 | 0.18 | 0.12-0.53 |
| | >6 h vs. <3 h | 1.065 | 0.023 | 0.84-1.40 |
| Social jetlag | Media consumption after 10 pm | 0.231 | 0.184 | 0.09-0.33 |
| | Duration of media consumption | 0.189 | 0.58 | 0.13-0.29 |
| | 3–6 h vs. <3 h | -0.413 | 0.74 | -0.28--0.62 |
| | >6 h vs. <3 h | -0.509 | 0.31 | -0.24-0.77 |

There were 6 (11.6%) prepubertal, 12 (23.0%) pubertal, and 34 (65.4%) postpubertal subjects without IR and 8 (11.4%) prepubertal, 15 (21.4%) pubertal, and 47 (67.2%) postpubertal subjects with IR. The difference was non-significance (P>0.05) [Table 2].

The mean Body mass index (BMI) (Kg/m2) was $29.1 \pm 2.17$ and $34.2 \pm 2.64$, Systolic blood pressure (SBP) (mm Hg) was $128.6 \pm 6.71$ and $134.2 \pm 8.82$, Diastolic blood pressure (DBP) (mm Hg) was $66 \pm 5.14$ and $72 \pm 7.49$, total cholesterol (mg/dl) was $160.2 \pm 11.26$ and $164.8 \pm 12.37$, triglyceride (mg/dl) was $70 \pm 8.72$ and $104.2 \pm 10.89$, HDL cholesterol (mg/dl) was $54.2 \pm 6.61$ and $46.8 \pm 4.41$ and LDL cholesterol (mg/dl) was $92 \pm 7.75$ and $98 \pm 8.63$ in subjects without IR and in subjects with IR respectively. The difference between both groups was found to be significant (P< 0.05) [Table 3].

The mean uric acid was $5.3 \pm 1.12$ mg/dl in subjects without IR and $5.9 \pm 1.57$ mg/dl in subjects with IR. The mean Melatonin 6s: Creatinine (MT6s:Cr) ratio was $31.4 \pm 3.69$ in subjects without IR and $27.4 \pm 2.29$ in subjects with IR. The difference between both groups was found to be significant (P<0.05) [Table 4].

Melatonin secretion showed no association with the daytime or duration of media consumption. There were significant associations of media consumption in the late evening and the duration of media consumption with chronotype and social jetlag (P<0.05) [Table 5].

**DISCUSSION**

The individual melatonin level in young adults plays an essential role in controlling the duration and time of sleep behavior in addition to genetic, environmental, and hormonal factors called chronotypes.[10,11] There is a shifting of sleep-wake behavior from pubertal development to late chronotypes resulting in misalignment of biological and social clocks among individuals.[12] This is known as social jetlag and is linked to enhanced risk for the progression to obesity, impaired mental health, and metabolic disorders.[13] Melatonin is considered to be the association between sleep deficiency and metabolic diseases controlling metabolism and body weight.[14,15] We attempted the present study to assess the correlation between sleep patterns, melatonin secretion, and obesity.

In our study, there were 30 males and 22 females without insulin resistance and 40 males and 30 females with insulin resistance. Overberg et al,[16] conducted a study on 149 adolescents with obesity. It was found that 101 subjects with insulin resistance had significantly lower nocturnal melatonin levels in contrast to unimpaired insulin secretion. It was further found that triglyceride and elevated uric acid levels revealed significant associations with melatonin secretion. Patients with late chronotype showed a higher incidence of insulin resistance.

We observed that the mean BMI (Kg/m2) was 29.1 and 34.2, SBP (mm Hg) was 128.6 and 134.2, DBP (mm Hg) was 66 and 72, total cholesterol (mg/dl) was 160.2 and 164.8, triglyceride (mg/dl) was 70 and 104.2, HDL cholesterol (mg/dl) was 54.2 and 46.8 and LDL cholesterol (mg/dl) was 92 and 98 in subjects without IR and in subjects with IR respectively. Rojdgmark et al,[17] found that in obese subjects there is some alteration in the function of pinealocytes. The study consist of 9 healthy and 8 obese individuals and the nocturnal melatonin (MT) secretion was determined. The results found no difference in groups. The obese groups were reinvestigated following two days of fasting. After two days, the level of body weight decreased up to 2.6 kgs and blood glucose levels decreased to 0.2 mmol/L. There was no alteration in the level of serum cortisol. We found that the mean uric acid was 5.3 mg/dl in subjects without IR and 5.9 mg/dl in subjects with IR. The mean MT6s:Cr ratio was 31.4 in subjects without IR and 27.4 in subjects with IR.

Agil A et al did an experimental study on rats in which melatonin was added in the drinking water. A statistically significant ($p<0.05$) reduction in weight was observed in melatonin treated rats as compared to the other group. Besides this, apparent reduction in systolic blood pressure was also seen. A significant improvement in dyslipidemia was also noticed, with a reduction in hypertriglyceridemia from 580±40 to 420.6±40.9mg/dL ($P<0.01$). Melatonin raised high-density-lipoprotein (HDL) cholesterol from 81.6±4.9 to 103.1±4.5mg/dL, $P<0.01$ and significant reduction in low-density-lipoprotein (LDL) cholesterol from 5.20±0.4 to 4.14±0.3 mg/dL ($P<0.05$) but had no effect on total cholesterol levels.[14]

Mc Mullan et al aimed to investigate the association of endogenous nocturnal melatonin secretion with insulin resistance in humans. A cross-sectional study was done on 1,075 US women without diabetes, hypertension, or malignancy. Higher nocturnal melatonin secretion was found which was inversely associated with insulin levels and insulin resistance. They suggested that nocturnal melatonin secretion is independently and inversely associated with insulin resistance.[13]

In this study it was observed that melatonin secretion showed no association with the daytime or duration of media consumption. There were significant associations of media consumption in the late evening and the duration of media consumption with chronotype and social jetlag ($P< 0.05$). A few studies showed that subject treated with melatonin revealed marked fall in bodyweight and oxidative stress and improvement of lipid levels, insulin sensitivity, and hepatic parameters.[18,19]

**Limitations**

The present study can give better results if the sample size may be increased. Moreover, genetic studies done for the evaluation of alterations in melatonin receptors may better suggest the relation between melatonin and insulin resistance. In addition to this, the present study assesses the secretion of melatonin by measuring its main metabolite MT6s in the urine samples withdrawn in the morning and thereafter normalizing it to urine creatinine levels which didn't predict any information on the amplitude or timing of its secretion.

**CONCLUSION**

It was found that there was reduced night melatonin secretion, impaired energy metabolism in subjects with obesity. The present study also gives a lead about the relationship between melatonin secretion, its chronotype, and social jetlag, and therefore it might be important in formulating techniques or strategies to reduce social jetlag by adapting a better and sound sleeping behavior with the individual chronotype into multimodal lifestyle therapy of adolescents with obesity. Moreover, this implies changes in media consumption time particularly in the evening late hours, exposure to daylight, and alignment of environmental factors (like daily school start time) with the age-dependent chronotype.

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