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Urinary 6-Sulfatoxymelatonin Excretion and Metabolic Parameters in Adolescents with Overweight and Obesity

Fazla Kilolu ve Obez Adölesanlarda İdrar 6-Sülfatoksimelatonin Atılımı ve Metabolik Parametreler

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Abstract

Objective: Adolescent overweight and obesity are associated with insulin resistance and adverse lipid profiles. Melatonin has been implicated in metabolic regulation, but data on urinary melatonin excretion in adolescents are limited. This study aimed to compare first-morning urinary 6-sulfatoxymelatonin/creatinine ratio (aMT6s/Cr) levels between adolescents with overweight/obesity and normal-weight controls and to examine their relationship with metabolic parameters.

Methods: This cross-sectional study included 120 adolescents aged 12–18 years, 67 with overweight/obesity and 53 normal-weight controls. Anthropometric measurements, fasting glucose, insulin, and lipid parameters were recorded. Insulin resistance was assessed by HOMA-IR. Integrated overnight melatonin secretion was estimated using first-morning urinary aMT6s normalized to creatinine. Multivariable linear regression was performed within the overweight/obesity group.

Results: Age and sex distributions were similar between the groups. Body mass index (BMI), triglyceride levels, and HOMA-IR were higher in the overweight/obesity group ($p < 0.01$). Urinary aMT6s/Cr levels did not differ between groups ($p = 0.72$). Within the overweight/obesity group, urinary aMT6s/Cr was inversely correlated with HOMA-IR ($r = -0.287$, $p = 0.019$), fasting insulin ($r = -0.320$, $p = 0.009$) and triglyceride levels ($r = -0.308$, $p = 0.013$). In multivariable linear regression, age and sex remained associated with urinary aMT6s/Cr, whereas fasting insulin, HOMA-IR, triglycerides, HDL-cholesterol, and BMI were not significant.

Conclusion: Urinary aMT6s/Cr did not differ by weight status. Although lower urinary melatonin excretion was associated with unfavorable metabolic parameters in univariable analyses in the overweight/obesity group, these associations did not remain significant after adjustment. Age and sex were independently associated with urinary aMT6s/Cr.

Keywords: Adolescent ; Obesity; 6-Sulfatoxymelatonin

Öz

Amaç: Adölesan dönemde fazla kilololuk ve obezite, insülin direnci ve olumsuz lipid profili ile ilişkilidir. Melatoninin metabolik düzenlemede rol oynadığı düşünülmekle birlikte, adölesanlarda üriner melatonin atılımına ilişkin veriler sınırlıdır.

Bu çalışmada, fazla kilolu/obez adölesanlar ile normal kilolu kontroller arasında sabah ilk idrarda ölçülen 6-sülfatoksimelatonin/kreatinin oranı (aMT6s/Cr) düzeylerinin karşılaştırılması ve aMT6s/Cr ile metabolik parametreler arasındaki ilişkinin incelenmesi amaçlandı.

Yöntem: Bu kesitsel çalışmaya 12-18 yaş aralığında 120 adölesan dahil edildi; 67'si fazla kilolu/obez, 53'ü normal kiloluydu. Antropometrik ölçümler, açlık glukozu, insülin ve lipid parametreleri kaydedildi. İnsülin direnci homeostatik model değerlendirmesi ile (HOMA-IR) hesaplandı. Gece boyunca melatonin sekresyonu, sabah ilk idrarda ölçülen aMT6s/Cr ile değerlendirildi. Fazla kilolu/obez grupta çok değişkenli lineer regresyon analizi yapıldı.

Bulgular: Gruplar yaş ve cinsiyet açısından benzerdi. Beden kitle indeksi (BKİ), trigliserid düzeyleri ve HOMA-IR fazla kilolu/obez grupta daha yüksekti ($p < 0.01$). Üriner aMT6s/Cr düzeyleri gruplar arasında farklılık göstermedi ($p = 0.72$). Fazla kilolu/obez grupta üriner aMT6s/Cr ile HOMA-IR ($r = -0.287$, $p = 0.019$), açlık insülini ($r = -0.320$, $p = 0.009$) ve trigliserid düzeyleri ($r = -0.308$, $p = 0.013$) arasında negatif korelasyon saptandı. Çok değişkenli lineer regresyonda yaş ve cinsiyetin üriner aMT6s/Cr ile bağımsız ilişkili kalırken, açlık insulini, HOMA-IR, trigliseridler, HDL-kolesterol ve BKİ anlamlı bulunmadı.

Sonuç: Üriner aMT6s/Cr düzeyleri kilo durumuna göre farklılık göstermedi. Fazla kilolu/obez adölesanlarda daha düşük üriner melatonin atılımı, tek değişkenli analizlerde olumsuz metabolik parametrelerle ilişkili görünse de, bu ilişkiler çok değişkenli düzeltme sonrası bağımsız anlamlılığını korumadı. Yaş ve cinsiyet, üriner aMT6s/Cr ile bağımsız ilişkili bulundu.

Anahtar Kelimeler: Adölesan; Obezite; 6-Sülfatoksimelatonin

Introduction

Obesity is a major global public health concern, with a steadily increasing prevalence among children and adolescents [1-3]. The prevalence of overweight and obesity among adolescents has risen significantly over recent decades, a trend observed across both high-income and middle-income nations [4-8]. Adolescent obesity often persists into adulthood and is associated with increased risk of metabolic syndrome, type 2 diabetes, and cardiovascular disease [2-7]. Understanding biological mechanisms linking excess adiposity to early metabolic impairment during adolescence is therefore essential.

Melatonin is a neurohormone primarily secreted by the pineal gland during the dark phase and is best known for its role in circadian timing and sleep-wake rhythms [9]. In addition to its chronobiologic role, melatonin has been implicated in glucose homeostasis, insulin secretion, lipid metabolism, oxidative stress and inflammatory pathways [10-12]. Experimental, genetic, and clinical studies suggest that altered melatonin secretion or signaling may be involved in impaired metabolic regulation; in particular, *MTNR1B* polymorphisms have been associated with impaired β-cell function, elevated fasting plasma glucose, and increased risk of type 2 diabetes, supporting a role for melatonin pathways in insulin resistance and cardiometabolic risk [13,14].

Human studies evaluating melatonin in pediatric obesity remain limited and have reported inconsistent findings. Some reports have described altered nocturnal melatonin profiles in children or adolescents with obesity, whereas others have not demonstrated clear differences according to weight status [15-17]. For instance, one study reported higher salivary melatonin levels after sleep onset in adolescents with obesity compared to controls [15], whereas another study observed lower nocturnal melatonin concentrations in those with insulin resistance [17]. Differences in study design, biologic sample type, sampling time, and participant characteristics may partly explain these inconsistent findings.

Urinary 6-sulfatoxymelatonin (aMT6s), the major metabolite of melatonin, is a practical and non-invasive marker of integrated nocturnal melatonin secretion. Although urinary aMT6s does not directly define circadian phase, it may be useful for evaluating overall nocturnal melatonin secretion in clinical studies. Data on urinary aMT6s and its metabolic correlates in adolescents with overweight and obesity remain limited [17,18].

Therefore, the aim of this cross-sectional study was to compare first-morning urinary aMT6s/Cr levels between adolescents with overweight/obesity and normal-weight controls and to examine the relationship between urinary aMT6s/Cr and metabolic parameters, particularly insulin resistance and lipid profile markers.

Materials And Methods

Study design and participants

This cross-sectional study was conducted between October 2023 and October 2024 at the Pediatric Outpatient Clinic of Giresun University Maternity and Children Training and Research Hospital. Adolescents presenting for routine clinical care were consecutively screened for eligibility. The study protocol adhered to the principles of the Declaration of Helsinki and was approved by the Giresun University Clinical Research Ethics Committee (Decision no: 17.01.2023/1). Written informed consent was obtained from the parents or legal guardians of all participants.

Grouping and eligibility criteria

Participants were classified according to age- and sex-specific BMI percentiles based on established pediatric growth references [19]. Adolescents with a BMI between the 5th and 84th percentiles were assigned to the normal-weight group, whereas those with a BMI at or above the 85th percentile were assigned in the overweight/obesity group. The overweight/obesity group included both adolescents with overweight (BMI, 85th to < 95th percentile) and adolescents with obesity (BMI, ≥ 95th percentile).

Exclusion criteria were defined to reduce potential confounding factors affecting melatonin secretion or metabolic measurements.

Adolescents with chronic systemic disease, thyroid dysfunction, chronic liver disease, psychiatric disorders, or use of medications known to affect serotonin or melatonin metabolism were excluded. Participants with vitamin D deficiency (serum 25-hydroxyvitamin D < 12 ng/mL) were excluded in accordance with pediatric consensus recommendations [20].

Sample size

Sample size was estimated using G*Power version 3.1. Based on an effect size of 0.502 derived from pediatric melatonin study [21], with 80% power and a two-sided alpha of 0.05, at least 50 participants were required in each group. Participants were enrolled consecutively until the target sample size was reached.

Data collection and anthropometric measurements

Sociodemographic characteristics and medical histories were obtained using a standardized questionnaire. Clinical evaluation included blood pressure measurement and anthropometric measurements. Standing height was recorded using a stadiometer, and body weight was measured using a Tanita TC380 device with participants wearing light clothing and no shoes. BMI was calculated as weight in kilograms divided by height in meters squared (kg/m²). Anthropometric measurements and BMI percentiles were evaluated according to Turkish pediatric reference data described by Neyzi et al. [19], and weight status was classified using age- and sex-specific pediatric BMI percentile categories based on established growth references [22].

Biochemical analyses and melatonin analyses

Following an overnight fast, venous blood samples were collected between 08:00 and 10:00. Laboratory parameters, including fasting glucose, insulin, creatinine, and a complete lipid profile (total cholesterol, LDL-C, HDL-C, and triglycerides), were analyzed using Roche Cobas e602 and c502 analyzers. Insulin resistance was evaluated using the homeostasis model assessment for insulin resistance (HOMA-IR) index, calculated as: fasting insulin (µIU/mL) x fasting glucose (mg/dl) / 405 [23]. Integrated nocturnal melatonin secretion was estimated by measuring urinary aMT6s in first-morning urine samples and normalizing the values to urinary creatinine (aMT6s/Cr). The creatinine-adjusted ratio is a validated, non-invasive marker of integrated nocturnal melatonin secretion; however, this measure does not provide information on circadian phase of dim light melatonin on set [24-26]. Urine aliquots were stored at –80° C until analysis. Urinary aMT6s concentrations were determined using a commercial ELISA kit (BUHLMANN Laboratories AG, Switzerland), while urinary creatinine was measured using the Roche Cobas c502 analyzer.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation or median (interquartile range), according to data distribution, and categorical variables were presented as number and percentage (%). Normality of continuous variables was assessed using the Kolmogorov- Smirnov test.

Comparisons between the normal-weight and overweight/obesity groups were performed using the independent-samples t-test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables. Categorical variables were compared using the chi-square test.

Correlations between urinary aMT6s/Cr levels and metabolic parameters were evaluated using Pearson or Spearman correlation coefficients, as appropriate. These analyses were performed in the overall study population and separately within the normal-weight and overweight/obesity groups. A two-way analysis of variance was used to examine the effects of sex and weight-status group on urinary aMT6s/Cr levels. A p value of less than 0.05 was considered statistically significant.

In identify factors independently associated with urinary aMT6s/Cr levels, two separate multivariable linear regression models were constructed within the overweight/obesity group. Urinary aMT6s/Cr was entered as the dependent variable. BMI was entered as a continuous variable (kg/m2). In the first model, age, sex, BMI, fasting insulin, triglycerides, and HDL-C were included. In the second model, age, sex, BMI, HOMA-IR, triglycerides, and HDL-C were included. Fasting insulin and HOMA-IR were not entered into same model because of conceptual overlap.

Results

Participant characteristic and metabolic findings

A total of 120 adolescents were included in the study, comprising 67 participants (55.8%) in the overweight/obesity group and 53 (44.2%) in the normal-weight group (Table 1). Age and sex distributions were comparable between the groups (p = 0.620 and p = 0.180, respectively). The overweight/obesity group had significantly higher BMI values than controls (p < 0.001). No significant differences were observed between groups in systolc and diastolic blood pressure or fasting glucose levels (Table 1).

Analysis of metabolic parameters revealed that triglyceride levels were significantly higher in the overweight/obesity group (p=0.041), whereas HDL-C showed a nonsignificant downward trend (p=0.080). HOMA-IR values were also significantly higher in the overweight/obesty group (p=0.002) (Table 1).

Table 1. Demographic, clinical, and biochemical characteristics of adolescents with overweight/obesity and normal-weight.

Variable	Total (n=120)	Overweight/Obesity (n=67)	Normal-Weight (n=53)	p
Age (years)	14.88 ± 1.66	14.81 ± 1.77	14.98 ± 1.52	0.620
Sex, n (%)				0.180
Female	67 (55.8)	41 (61.2)	26 (49.1)	
Male	53 (44.2)	26 (38.8)	27 (50.9)	
BMI (kg/m²)	27.30 ± 7.60	32.55 ± 5.46	20.40 ± 3.23	**<0.001**
Systolic BP (mmHg)	115.9 ± 11.8	117.8 ± 11.6	113.4 ± 10.7	0.090
Diastolic BP (mmHg)	66.8 ± 10.6	68.1 ± 10.9	65.2 ± 9.8	0.150
Fasting glucose (mg/dL)	98.4 ± 16.2	100.1 ± 16.8	96.2 ± 15.1	0.210
Triglycerides (mg/dL)	118.6 ± 57.5	129.4 ± 60.1	105.1 ± 51.2	**0.041**
HDL-C (mg/dL)	45.2 ± 10.4	43.7 ± 9.8	47.1 ± 10.7	0.080
aMT6s/Cr	43.03 ± 20.18	43.61 ± 21.10	42.29 ± 19.13	0.720
HOMA-IR	6.81 ± 6.87	8.32 ± 7.15	4.18 ± 2.04	**0.002**

BMI: body mass index; HOMA-IR: homeostasis model assessment for insulin resistance; HDL-C: high-density lipoprotein cholesterol; aMT6s/Cr: 6-sulfatoxymelatonin/creatinine ratio. Data are presented as mean ± SD or n (%). A p-value < 0.05 was considered statistically significant.

Melatonin Secretion Patterns

Urinary aMT6s/Cr ratios did not differ significantly between groups (p = 0.720). Absolute aMT6s concentrations were numerically higher in the overweight/obesity group; however, this difference was not statistically significant and was attenuated after normalization to urinary creatinine.

Correlation Analyses

Within the overweight/obesity group, urinary aMT6s/Cr was inversely correlated with HOMA-IR (r = –0.287, p = 0.019), fasting insulin (r = –0.320, p = 0.009), and triglycerides (r = –0.308, p = 0.013) (Figure 1-3).

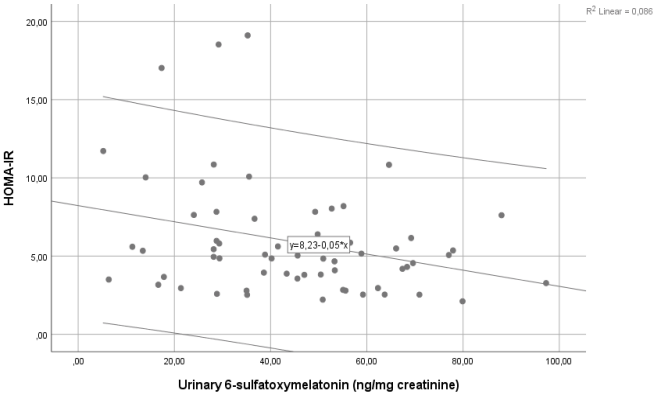

Figure 1. Correlation between urinary aMT6s/Cr and HOMA-IR

Scatter plot showing the inverse correlation between urinary aMT6s/Cr and HOMA-IR in adolescents with overweight/obesity (r = -0.287, p = 0.019).

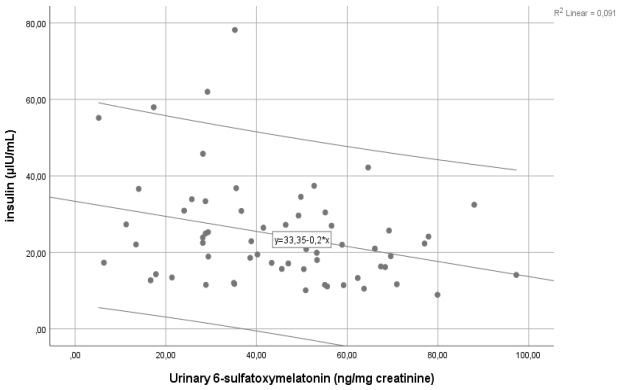

Figure 2. Correlation between urinary aMT6s/Cr and fasting insulin

Scatter plot showing the inverse correlation between urinary aMT6s/Cr and fasting insulin in adolescents with overweight/obesity (r = -0.320, p = 0.009).

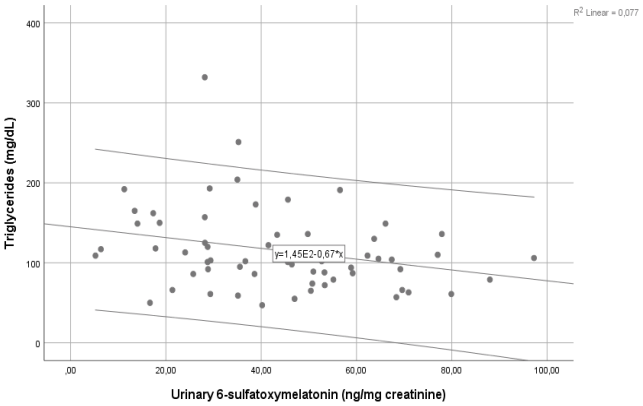

Figure 3. **Correlation between urinary aMT6s/Cr and triglyceride**

Scatter plot showing the inverse correlation between urinary aMT6s/Cr and triglyceride levels in adolescents with overweight/obesity (r = -0.308, p = 0.013).

Multivariable linear regression analyses in the overweight/obesity group

In multivariable linear regression analyses performed within the overweight/obesity group, both models were statistically significant overall. In the model including fasting insulin, the model explained 35.3% of the variance in urinary aMT6s/Cr (R^2= 0.353, adjusted R^2= 0.284, $F(6,57) = 5.173$, $p < 0.001$). Age (B = -3.964, β = -0.335, p = 0.006) and sex (B = -19.744, β = -0.468, p < 0.001) remained independently associated with urinary aMT6s/Cr, whereas fasting insulin, triglycerides, HDL-C, and BMI were not indepently significant (Table 2, Model 1).

In the model including HOMA-IR, the model explained 34.7% of the variance in urinary aMT6s/Cr (R^2 = 0.347, adjusted R^2 = 0.279, $F(6,57) = 5.054$, $p < 0.001$). Again, age (B = -3.957, β = -0.334, p = 0.006) and sex (B = -19.446, β = -0.461, p < 0.001) remained independently associated with urinary aMT6s/Cr, whereas HOMA-IR, triglycerides, HDL-C, and BMI were not independently significant. Collinearity diagnostics did not indicate problematic multicollinearity (VIF range: 1.077-1.363). Given the sex coding used in the analysis (1 = female, 2 = male), the negative regression coefficient indicates lower urinary aMT6s/Cr levels in males than in females (Table 2, Model 2).

Table 2. Multivariable linear regression models for urinary aMT6s/Cr in adolescents with overweight/obesity

Model 1: Fasting insulin included

Variable	B	SE	Standardized β	p	95% CI for B
Constant	156.349	29.098		**<0.001**	98.082 to 214.616
BMI (kg/m2)	-0.364	0.405	-0.099	0.373	-1.175 to 0.447
Fasting insulin	-0.291	0.180	-0.190	0.113	-0.652 to 0.070
Triglycerides	-0.040	0.050	-0.097	0.433	-0.141 to 0.061
HDL-C	-0.047	0.223	-0.026	0.833	-0.495 to 0.400
Age	-3.964	1.375	-0.335	**0.006**	-6.717 to -1.212
Sex	-19.744	5.199	-0.468	**<0.001**	-30.155 to -9.333
Model summary: R^2 = 0.353, adjusted R^2 = 0.284, F(6,57) = 5.173, p < 0.001 BMI was entered as a continuous variable (kg/m2), sex was coded as 1= female and 2= male. **Abbreviations:** aMT6s/Cr: 6-sulfatoxymelatonin/creatinine ratio, HDL-C: high-density lipoprotein cholesterol.					

Model 2: HOMA-IR included

Variable	B	SE	Standardized β	p	
Constant	155.657	29.226		**<0.001**	97.133 to 214.181
BMI (kg/m2)	-0.390	0.407	-0.106	0.342	-1.205 to 0.425
HOMA-IR	-0.968	0.666	-0.170	0.152	-2.300 to 0.365
Triglycerides	-0.045	0.050	-0.111	0.367	-0.145 to 0.055
HDL-C	-0.042	0.224	-0.023	0.853	-0.491 to 0.407
Age	-3.957	1.385	-0.334	**0.006**	-6.730 to -1.184
Sex	-19.477	5.226	-0.461	**<0.001**	-22.913 to -8.982
Model summary: R^2 = 0.347, adjusted R^2 = 0.279, F(6,57) = 5.054, p < 0.001 BMI was entered as a continuous variable (kg/m2) , sex was coded as 1= female and 2= male. **Abbreviations:** aMT6s/Cr: 6-sulfatoxymelatonin/creatinine ratio, HDL-C: high-density lipoprotein cholesterol, HOMA-IR: homeostasis model assessment for insulin resistance.					

Interaction Analysis

A two-way ANOVA, was performed to examine the potential confounding effect of sex. A significant main effect of sex on aMT6s/Cr levels was observed ($F_{(1,116)}$ = 6.471, p = 0.012). There was no significant main effect of obesity status ($F_{(1,116)}$ = 0.770, p = 0.380) and no significant sex x obesity interaction ($F_{(1,116)}$ = 3.375, p = 0.069).

Discussion

The present study investigated the association between nocturnal melatonin secretion, obesity, and metabolic parameters in adolescents. Urinary aMT6s/Cr, used as an index of integrated nocturnal melatonin secretion, did not differ significantly between adolescents with overweight/obesity and normal-weight peers. Within the overweight/obesity group, lower urinary aMT6s/Cr levels were associated with higher fasting insulin, HOMA-IR, and triglyceride levels in univariate analyses. However, in multivariable linear regression analyses adjusted for BMI, age, sex, and lipid parameters, age and sex remained independently associated with urinary aMT6s/Cr, whereas BMI, fasting insulin, HOMA-IR, triglycerides, and HDL-C were not independently significant.

The absence of a significant difference in urinary aMT6s/Cr levels between adolescents with normal weight and those with overweight/obesity suggests that total overnight melatonin secretion may not be determined by weight status alone during adolescence. This finding is in line with the heterogeneous pediatric literature, in which results regarding melatonin secretion in obesity have been inconsistent [15]. Such discrepancies may be related to differences in pubertal maturation, study populations, and sampling strategies across studies. Although experimental evidence suggests that adipose-derived signals may modulate pineal function [27], excess adiposity alone may not be sufficient to produce a measurable reduction in nocturnal melatonin output in adolescents. In interpreting these findings, it should be noted that urinary aMT6s/Cr reflects integrated overnight secretion rather than circadian phase, and that unmeasured factors such as sleep habits and evening light exposure could influence these results.

A methodological strength of this study is the use of first-morning urinary aMT6s as a non-invasive marker of cumulative nocturnal melatonin secretion. This approach is particularly practical in pediatric populations because repeated nocturnal blood sampling is invasive, may disrupt sleep, and is often difficult to implement in adolescents. Urinary aMT6s has been shown to correlate with overnight plasma melatonin secretion and is considered a reliable indicator of cumulative nocturnal pineal output [24-26]. However, urinary aMT6s reflects total overnight melatonin secretion rather than circadian phase or rhythm. Therefore, the present findings should not be interpreted as evidence regarding dim light melatonin onset, circadian timing, circadian misalignment, or other markers of circadian phase. Rather, they should be understood as reflecting integrated nocturnal melatonin secretion.

In univariable analyses, urinary aMT6s/Cr was inversely correlated fasting insulin, HOMA-IR, and triglyceride levels suggesting a possible relationship between melatonin secretion and metabolic regulation in adolescents with overweight/obesity. This finding is biologically plausible, as melatonin has been implicated in glucose homeostasis, insulin signaling, and lipid metabolism through MT1 and MT2 receptor-mediated pathways, and altered melatonin signaling has been associated with insulin resistance and dyslipidemia in previous studies [6,13,14,16,28]. However, these associations did not remain independently significant in multivariable linear regression models after adjustment for age, sex, and BMI. Therefore, our findings do not support an independent association between urinary aMT6s/Cr and metabolic risk markers in this cohort. Rather, the observed univariable relationships may reflect the influence of demographic, developmental, or adiposity-related factors that were not fully captured in unadjusted analyses. Given the cross-sectional design of the study, these findings should be interpreted as associations rather than evidence of a causal role for melatonin in the development of insulin resistance or dyslipidemia.

Age was independently and inversely associated with urinary aMT6s/Cr levels in both multivariable regression models. In addition, sex remained an independent correlate, with lower urinary aMT6s/Cr levels observed in males than in females. This finding is consistent with the significant main effect of sex identified in the two-way ANOVA, supporting the presence of sex-related differences in nocturnal melatonin secretion during adolescence. Together, these results suggest that urinary melatonin excretion may be influenced by age-and sex-related biological variation. However, Tanner stage data were not available in the present study; therefore, pubertal maturation could not be formally evaluated as a potential confounder. Given the substantial hormonal and developmental changes that occur during adolescence, the observed associations with age and sex should be interpreted cautiously, and future studies incorporating pubertal staging are needed to clarify these relationships.

This study has several strengths. Sample collection was standardized to routine school days, minimizing the potential influence of social jet lag. Participants were recruited from a single geographic region, which may have reduced variability in environmental light exposure.

Several limitations should be acklowledged. First, this was a cross-sectional study; therefore, causal relationships cannot be inferred. Second, Tanner stage data were not available, which is important because pubertal maturation may influence insulin resistance, lipid metabolism, and melatonin secretion. Third, objective sleep-related and behavioral variables—including sleep duration, chronotype, evening light exposure, and screen use— were not assessed. These factors may substantially affect melatonin secretion and may partly explain interindividual variation in urinary aMT6s/Cr. Fourth, First-morning urinary aMT6s/Cr reflects integrated nocturnal secretion but does not capture circadian phase.

Finally, the study was conducted at a single center, which may limit generalizability.

Despite these limitations, the present study provides additional evidence regarding nocturnal melatonin secretion in adolescents with overweight/obesity. The absence of a significant difference in urinary aMT6s/Cr levels between weight-status groups, together with the lack of independent associations between urinary aMT6s/Cr and metabolic risk markers after adjustment, suggests that melatonin excretion may be influced more by developmental and biological factors than by adiposity-related metabolic abnormalities alone.

The use of first-morning aMT6s/Cr as a non-invasive biomarker and the inclusion of a normal-weight comparison group strengthen the clinical relevance of the findings. Further longitudinal studies incorporating pubertal staging, sleep characteristics, light exposure, chronotype, and validated circadian phase measures are needed to better define the role of melatonin in adolescent metabolic health.

Conclusion

Urinary aMT6s/Cr levels were not significantly different between adolescents with overweight/obesity and normal-weight controls. Although, urinary aMT6s/Cr inversely correlated with insulin resistance markers and triglyceride levels in univariable analyses within the overweight/obesity group, these associations were not independently significant after multivariable adjustment. Age and sex were independently associated with urinary aMT6s/Cr levels. These findings suggests that developmental factors may contribute more strongly to variation in melatonin excretion during adolescence than metabolic abnormalities alone. Further longitudinal studies incorporating pubertal assessment and sleep-related variables are needed to clarify the determinants and clinical significance of melatonin secretion in adolescence.

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