

## Frequency of night eating syndrome and melatonin levels in the urine of adolescents

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

**Aim.** The aim is to study the frequency of night eating syndrome (NES) and its correlation with melatonin levels in the daily urine of adolescents.

**Materials and methods.** Primary screening of 486 adolescents (15–18 years) with complaints of eating disorders, overweight, obesity, which included a survey (test “Depressive Disorders in Adolescents”, Night Eating Questionnaire (NEQ), Dutch Eating Behaviour Questionnaire (DEBQ) and anthropometry (BMI) was conducted. In the second stage, a sample of 56 adolescents (11.5 %) who met the NES criteria of DSM-5 (main group) and 50 adolescents who did not have NES (comparison group) was formed. The urine concentration of 6-sulfatoxymelatonin (6-COMT) was determined by enzyme immunoassay (Buhlmann 6-Sulfatoxymelatonin ELISA Kit, Switzerland).

**Results.** Deficit of body weight had 3 (8.8 %) of adolescent boys, 20 (58.8 %) were overweight, 1 (2.9 %) – obese and only 10 (29.4 %) had the average normative values of body weight; among female adolescents, 1 (4.5 %) – body weight deficit and obesity, 10 (45.5 %) – overweight and average normative indicators. According to the DEBQ, restrictive eating behaviors were identified in 15 (26.8 %) adolescents; in 30 (53.6 %) adolescents – emotional and in 11 (19.6 %) adolescents – external. The mean score of the NEQ was  $28.4 \pm 2.2$  and positively correlated with BMI ( $r = +0.62$ ,  $P < 0.05$ ). Participants who exceeded the screening threshold for NES ( $n = 56$ , 11.5 %) had increased BMI ( $P < 0.01$ ), likelihood of overweight/obesity ( $P = 0.001$ ), consumption of sugary drinks ( $P < 0.001$ ), daytime sleep less than twice a week ( $P < 0.01$ ), shorter sleep duration ( $P < 0.01$ ), high and moderate levels of depression, lower levels of melatonin, which were inversely correlated with the results of the NEQ ( $r = -0.68$ ,  $P < 0.05$ ).

**Conclusions.** The prevalence of NES among teenagers was 11.5 %. Among the types of eating behavior, the most common was the emotional type (53.6 %). Adolescents with NES had a significantly higher total depression score ( $96.7 \pm 8.06$ ,  $P < 0.001$ ) and a lower level of 6-COMT ( $22.89 \pm 3.44$ ,  $P < 0.001$ ), which was inversely correlated with the degree of NES ( $r = -0.68$ ,  $P < 0.05$ ), BMI ( $r = -0.74$ ;  $P < 0.01$ ) and depression level ( $r = -0.65$ ;  $P < 0.01$ ).

### Key words:

adolescents, night eating syndrome, melatonin.

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## Частота синдрому нічного переїдання та рівень мелатоніну в сечі підлітків

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Проблеми порушень харчової поведінки в сучасній медицині та психології належить особливе місце.

**Мета роботи** – вивчити частоту синдрому нічного переїдання та його кореляцію з рівнем мелатоніну в добовій сечі в підлітків.

**Матеріали та методи.** Здійснили первинний скринінг 486 підлітків віком 15–18 років зі скаргами на порушення харчової поведінки, надлишок маси тіла, ожиріння. Скринінг передбачав опитування, застосували тест «Депресивні розлади у підлітків» (ДРП), опитувальник нічного прийому їжі (Night Eating Questionnaire, NEQ), Нідерландський опитувальник харчової поведінки (DEBQ), а також антропометрію (індекс маси тіла, ІМТ). На другому етапі сформувавши вибірку з 56 підлітків, які відповідали критеріям синдрому нічного переїдання за DSM-5 (основна група), та 50 підлітків, у яких не було ознак синдрому (група порівняння). Визначили концентрацію метаболіту мелатоніну – 6-сульфатоксимелатоніну (6-COMT) у сечі методом імуноферментного аналізу за допомогою тест-набору Buhlmann 6-Sulfatoxymelatonin ELISA Kit (Швейцарія).

**Результати.** У 3 (8,8 %) підлітків-хлопців виявили дефіцит маси тіла, у 20 (58,8 %) – надлишкову масу тіла, у 1 (2,9 %) – ожиріння, тільки в 10 (29,4 %) осіб зареєстрували середні нормативні значення маси тіла. Серед підлітків-дівчат визначили по 1 (4,5 %) випадку з дефіцитом маси тіла й ожирінням, по 10 (45,5 %) – із надлишком маси тіла та середніми нормативними показниками. Згідно з опитувальником DEBQ, обмежувальний тип харчової поведінки виявили у 15 (26,8 %) підлітків, емоційний – у 30 (53,6 %), екстернальний – у 11 (19,6 %) випадках. Середній бал опитувальника NEQ становив  $28,4 \pm 2,2$ , позитивно корелював з ІМТ ( $r = +0,62$ ,  $p < 0,05$ ). Учасники, що перевищили поріг скринінгу для синдрому нічного переїдання ( $n = 56$ , 11,5 %), мали збільшений ІМТ ( $p < 0,01$ ), підвищену ймовірність надлишкової ваги/ожиріння ( $p = 0,001$ ), понаднормово споживали цукровмісні напої ( $p < 0,001$ ), мали денний сон менше ніж двічі на тиждень ( $p < 0,01$ ), меншу тривалість сну ( $p < 0,01$ ), а також у них виявили високий і середній рівень депресії за тестом ДРП, нижчий рівень мелатоніну, що зворотно корелював з результатами опитувальника NEQ ( $r = -0,68$ ,  $p < 0,05$ ).

**Висновки.** Поширеність NES у підлітків становить 11,5 %. Серед типів харчової поведінки найчастіше виявляли емоційний тип (53,6 %). Підлітки з синдромом нічного переїдання мали вірогідно вищий загальний бал депресії ( $96,7 \pm 8,06$ ,  $p < 0,001$ ) і нижчий рівень 6-COMT ( $22,89 \pm 3,44$ ,  $p < 0,001$ ), що зворотно корелював зі ступенем синдрому нічного переїдання ( $r = -0,68$ ,  $p < 0,05$ ), ІМТ ( $r = -0,74$ ;  $p < 0,01$ ) та рівнем депресії ( $r = -0,65$ ;  $p < 0,01$ ).

### Ключові слова:

підлітки, синдром нічного переїдання, мелатонін.

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The problem of eating disorders in modern medicine and psychology has a special place [1]. Every year, in Ukraine, the number of people with various variants of eating behavior is slowly but steadily growing, the number of requests for medical and psychological help is also growing [2]. Today, the issue of behavioral disorders in adolescence is one of the most pressing problems in the world [3,4]. It attracts the attention of psychologists and psychiatrists.

Eating disorders require close attention, as they can lead to severe mental and physical consequences [5–8], in particular, to the “Night Eating Syndrome” (NES). This syndrome was described in 1955 by A. J. Stunkard, W. J. Grace, H. G. Wolff [9] and was characterized by morning anorexia, evening hyperphagia and insomnia. In 2013, the Diagnostic and Statistical Manual of Mental Disorders, 5<sup>th</sup> Edition (DSM-5) was published [10], in which the NES was first reflected in the section “Other specified nourishment disorders or eating disorders” (307.59, F50.8), that was recommended by the Ministry of Health of Ukraine for implementation in 2016 [11].

The prevalence of NES in different samples usually ranges from 0.3 % to 94.0 % [12–15]. Current NES diagnostic criteria include: nocturnal meals and/or evening hyperphagia at least twice a week, initial insomnia, and nocturnal awakenings. In addition, at least three of the following symptoms should be involved: morning anorexia, a strong desire to eat between dinner-to-bed time, insomnia, a belief that one needs to eat in order to get to sleep, and a worsened mood in the evening.

The relationship between NES and depressed mood and/or depression has been emphasized in the literature [16]. Some authors view the NES as a “circadian delay in food intake”. People with nocturnal eating disorders may suffer from hormonal imbalances, including melatonin dysfunction, because melatonin induces and supports sleep [17]. Studies [18] have shown that in children, there is a delay in the peak of melatonin levels, which is associated with more fragmented sleep during the night and suggested that melatonin plays an important role in the development of sleep-wake rhythm.

Taking into account the insufficient number of studies on the prevalence of NES among adolescent children, in particular in Ukraine, the wide range of its fluctuations, which may be due to the use of different diagnostic criteria, the presence of only separate studies on the possible role of melatonin in strengthening violations of the circadian regime of food consumption, especially in adolescence age, the study on the level of this hormone in persons with eating disorders is relevant.

## Aim

The aim of this study was to examine the frequency of nocturnal overeating syndrome and its correlation with the level of melatonin in daily urine in adolescents.

## Materials and methods

A sample of children was formed in stages. Primary screening (486 adolescents aged 15–18 years, who were selected on an outpatient basis according to the results of appeals to specialists of the Chernivtsi Regional Children’s

Clinical Hospital regarding complaints of eating disorders, overweight, obesity), included a survey (all participants filled out a socio-demographic questionnaire, the Depressive Disorders in Adolescents (DDA) test, developed on the basis of ATQ (The Automatic Thoughts Questionnaire for Children) [19], the Night Eating Questionnaire (NEQ) [20,21] containing 14 questions, from of which, all participants completed the first nine questions of the questionnaire, questions 10–12 were filled out by participants who woke up at night, and questions 13 and 14 were filled out by participants who snack before bed. With the exception of the seventh item of the questionnaire, all others were rated on a five-point Likert scale from 0 to 4. The seventh item asked for mood swings during the day and those who did not notice them rated this item as 0. Ukrainian study of validity and reliability was conducted by F. Laniush, A. Urbanovych [22]. The study was conducted using the Dutch Food Behavior Questionnaire (DEBQ), which contained subscales for emotional, external and limited food intake and anthropometry (determined by Body Mass Index (BMI)).

In the second stage, a sample of 56 (34 boys and 22 girls) was formed of adolescents who met the NES criteria inclusion: 15–18 years, NES according to DSM-5 (main group) and 50 adolescents (15–18 years old, 25 boys and 25 girls) who did not have NES (comparison group).

Exclusion criteria were serious physical or emotional illness, including diabetes and other endocrine disorders; use of psychotropic drugs, steroids, diuretics or hypnotics; concomitant eating disorders; participation in a weight loss program. Tobacco, caffeine and drug use were not evaluated.

Determination of the urine concentration of melatonin metabolite – 6-sulfatoxymelatonin (6-COMT) was performed (Ukrainian-German laboratory “Bukintermed”, Chernivtsi). To do this, the first morning portion of urine was collected (06:00) in sterile containers. Quantitative determination of urine 6-COMT was performed by ELISA using a set of reagents Buhlmann 6-Sulfatoxymelatonin ELISA Kit (Switzerland) on an analyzer ImmunoChem-2100, HTI, USA.

Statistical processing of the results obtained was carried out on a personal computer ACER Intel® Core™ i3-7020 CPU @ 2.30GHz in the Windows 10 operating system using the programs “Microsoft Office Excel” and “Statistica 10” with standard methods of variational statistics. Quantitative and ordinal indicators were presented as an average value (M) ± standard deviation (s), qualitative – in the form of an absolute number of observations and a share (in %) of the total number of patients in the sample as a whole or in the corresponding group. A significance of the results was determined by the Student’s t-test (with a parametric data distribution) and the Mann-Whitney test (with a non-parametric data distribution). The normality of the distribution was determined by the Shapiro–Wilk test. The non-parametric Pearson test ( $\chi^2$ ) was used to check the significance of the overall relationship measure. The Fisher’s exact method was used to compare percentage data. Correlation analysis was performed using Spearman’s coefficients (r). Results were presented as M ±  $\sigma$ . Differences were considered statistically significant at P < 0.05.

Patient studies were conducted in accordance with the provisions of the 1975 Declaration of Helsinki, revised and amended in 2002, by the directives of the National Re-

search Ethics Committees. During the tests, all participants received informed consent and all measures were taken to ensure the anonymity of the participants.

## Results

The subjects were divided into subgroups by age and sex (Table 1). At the initial examination, BMI was determined (Fig. 1). BMI in adolescents of the main group was  $27.5 \pm 2.5$  kg/m<sup>2</sup>, and in adolescents of the control group –  $27.2 \pm 3.9$  kg/m<sup>2</sup>. Among male adolescents, significantly higher rates of deviations from the normative mean values were found.

Thus, a deficit of body weight was in 8.8 %, overweight – in 58.8 %, obesity – in 2.9 % and the average normative values of body weight – only in 29.4 %. A slightly different distribution of BMI indicators was found among female respondents, in particular, 4.5 % – body weight deficit and obesity, 45.5 % – overweight and average normative indicators.

According to the DEBQ questionnaire, restrictive eating behaviors were identified in 15 adolescents; this type of eating behavior was characterized by deliberate efforts to achieve or maintain the desired weight through self-restriction in nutrition. Emotional type of eating behavior was identified in 30 adolescents; with this type of eating behavior, the desire to eat arises in response to negative emotional states. External type of eating behavior was identified in 11 adolescents; with this type of eating behavior, the desire to eat was stimulated not by a real feeling of hunger, but by the appearance of food, its smell, texture or contemplation of how others eat.

The distribution of adolescents by type of eating disorders depending on sex is presented in Fig. 2.

When analyzing the results of the questionnaire, it was found that eating disorders occurred in almost all adolescents with overweight or obesity. In the group of adolescents without excess body weight, eating disorders were found in 27.8 % of respondents. A combination of several types of eating disorders occurred in 61 % of overweight adolescents.

In total, according to the NEQ questionnaire, 56 adolescents (11.5 %) met the NES criteria (main group). The threshold value for the diagnosis of NES according to the NEQ was >25 points (the total score ranged from 0 to 52). The mean score of the questionnaire was  $28.4 \pm 2.2$  and moderately positively correlated with BMI ( $r = +0.62$ ,  $P < 0.05$ ) (Fig. 3).

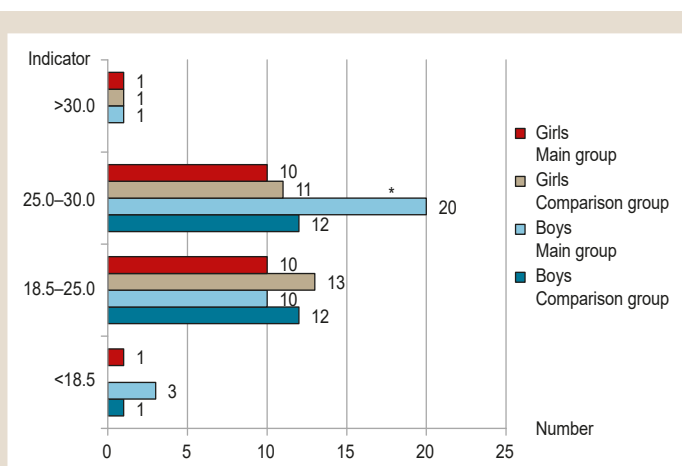
The amount of food consumed by adolescents in the main and comparison groups differed only moderately. Those who ate at night had  $8.4 \pm 0.6$  episodes of food in 24 hours compared with  $4.4 \pm 0.3$  in adolescents of the control group ( $P < 0.001$ ).

The analysis included assessment on the following scales: eating at night (mean score  $8.5 \pm 1.1$ ), evening hyperphagia (mean score  $9.4 \pm 1.6$ ), morning anorexia ( $7.8 \pm 1.8$ ) and disorders of mood and sleep (mean score  $6.3 \pm 1.1$ ).

Adolescents in the main group, woke up at night significantly more often ( $3.7 \pm 1.1$  times) than adolescents in the comparison group ( $0.30 \pm 0.09$  times,  $P < 0.001$ ). In 84 % of cases, waking up at night in the main group of adolescents was related to eating. Among adolescents in the comparison

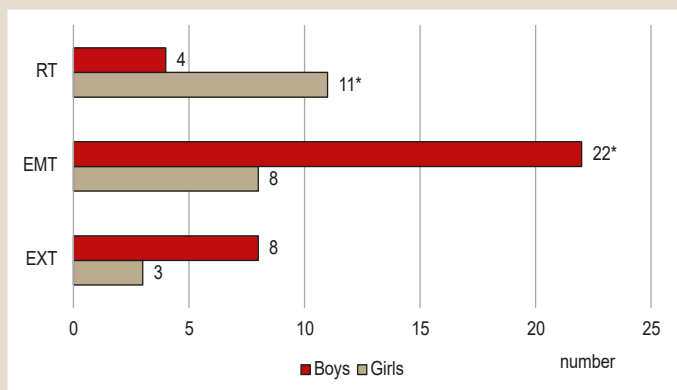
**Table 1.** Distribution of surveyed adolescents by sex and age

Age	Boys (n = 59)		Girls (n = 47)		Total, n/%
	Main group, n/%	Comparison group, n/%	Main group, n/%	Comparison group, n/%	
15	6/17.6	4/16.0	4/18.2	6/24.0	20/18.9
16	8/23.5	7/28.0	6/27.3	7/28.0	28/26.4
17	9/26.5	8/32.0	5/22.7	5/20.0	27/25.5
18	11/32.4	6/24.0	7/31.8	7/28.0	31/29.2
Total	34/100.0	25/100.0	22/100	25/100	106/100



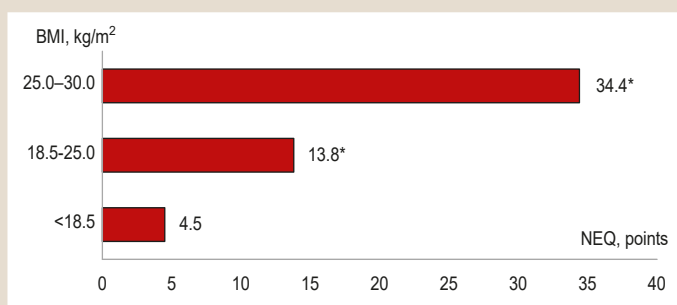
**Fig. 1.** Distribution of respondents by BMI.

\*:  $P < 0.05$ .



**Fig. 2.** Distribution of adolescents by type of eating disorders depending on sex.

EXT: external type of eating behavior; EMT: emotional type of eating behavior; RT: restrictive type of eating behavior; \*:  $P < 0.05$ .



**Fig. 3.** Night Eating Questionnaire scores based on Body Mass Index.

\*:  $P < 0.05$ .

**Table 2.** Indicators of 6-sulfatoxymelatonin in the urine of adolescents

6-COMT, ng/ml (n = 106)			
Boys (n = 59)		Girls (n = 47)	
Comparison group (n = 25)	Main group (n = 34)	Comparison group (n = 25)	Main group (n = 22)
47.23 ± 3.62	23.51 ± 4.16*	45.22 ± 2.91	22.34 ± 4.21*

\*: the difference is significant,  $P < 0.01$ .

**Table 3.** Indicators of 6-sulfatoxymelatonin in the urine of adolescents with NES

NEQ, points	6-COMT, ng/ml	
	Boys (n = 34)	Girls (n = 22)
0–10, (n = 5)	31.51 ± 3.11, (n = 3)	30.44 ± 3.91, (n = 2)
11–25, (n = 20)	25.14 ± 2.12, (n = 10)	24.25 ± 2.77, (n = 10)
26–52, (n = 31)	14.17 ± 2.09*, (n = 21)	13.09 ± 2.11*, (n = 10)

\*:  $P < 0.01$

group, 64.0 % reported snacks after dinner, while 92.8 % of adolescents in the main group reported snacks after dinner and at bedtime ( $\chi^2 = 6.34$ ,  $P < 0.001$ ). Morning anorexia was reported by 21.4 % of those who ate at night and 16 % of those who did not eat at night ( $\chi^2 = 2.23$ ,  $P > 0.05$ ).

NES was significantly associated with sleep duration ( $\chi^2 = 6.77$ ,  $P < 0.01$ ). Adolescents with NES reported less sleep time and had a higher overall DDA score ( $96.7 \pm 8.06$ ) than adolescents in the comparison group ( $25.3 \pm 2.4$ ,  $P < 0.001$ ).

Participants who exceeded the screening threshold for NES (n = 56, 11.5 %) had increased BMI ( $\chi^2 = 6.68$ ,  $P < 0.01$ ), likelihood of overweight / obesity ( $\chi^2 = 25.23$ ,  $P = 0.001$ ), consumption of sugary drinks ( $P < 0.001$ ), daytime sleep less than twice a week ( $\chi^2 = 7.11$ ,  $P < 0.01$ ), shorter sleep duration ( $\chi^2 = 7.11$ ,  $P < 0.01$ ). Among adolescents in the main group, 5 people (8.9 %) had a score on the DDA  $102.6 \pm 11.2$ , which corresponded to a high level of depression, 31 people (57.1 %) –  $46.4 \pm 5.9$  points, which corresponded to the average level of depression, the remaining 19 (33.9 %) had an average score corresponding to a low level of depression ( $23.3 \pm 3.2$ ).

People with nocturnal eating disorders may suffer from hormonal imbalances. In particular, the level of melatonin, a hormone that helps regulate sleep, can change dramatically during the night in such people. According to the results of our studies, the urine level of 6-COMT in the adolescents with NES, both overweight and normal weight, was significantly lower ( $22.89 \pm 3.44$ ) than in the comparison group ( $46.44 \pm 4.26$ ,  $P < 0.001$ ) (Table 2).

A moderate inverse relationship was established between melatonin and BMI in children with excess body weight ( $r = -0.74$ ;  $P < 0.01$ ) and the level of depression ( $r = -0.65$ ;  $P < 0.01$ ).

It should be noted that the urine level of 6-COMT in the adolescents depended on the degree of eating disorder. Thus, according to the NEQ results, the greater the number of points was scored by a teenager, the lower the 6-COMT was (Table 3).

An inverse correlation between melatonin and BMI in overweight children was established ( $r = -0.7436$ ;  $P < 0.01$ ).

There was no difference between the comparison group and main group in terms of the estimated time of falling asleep ( $\chi^2 = 2.34$ ,  $P > 0.05$ ), caloric content of the diet ( $\chi^2 = 2.23$ ,  $P > 0.05$ ) and a significant correlation between these indicators and the level of melatonin ( $\chi^2 = 2.41$ ,  $P > 0.05$ ).

## Discussion

NES is associated with adverse health effects. NES is a form of eating disorder and can often coexist with the symptoms of other eating disorders [23–25]. The prevalence of NES is quite variable among adolescents and university students: from 2.9 % to 5.7 % among US college students to 13.8 % among Turkish university students [26–29], and studies [30,31] indicate an even greater NES prevalence in connection with COVID-19 infection. In this study, the prevalence of NES was 11.5 %, which is slightly higher than in other studies [32,33]. The difference can be explained by the fact that adolescents have higher levels of stress and more sleep problems than other age groups.

We evaluated the relationship between NES severity, body weight, depression, and melatonin in adolescent urine. The NES was first studied in a cohort of children aged 8–10 years [34] using the NEQ. In addition to the main symptoms (excessive evening snacks and night meals), other important clinical symptoms were identified: morning anorexia, insomnia, depressed mood, strong desire to eat in the evening and at night, the belief that one needs to eat in order to get to sleep [35].

Studies [36] have shown that American university students, due to eating disorders, had a high prevalence of anorexia nervosa, risk of self-harm, alcoholism, history of psychiatric disorders, and attention-deficit/hyperactivity disorder in the last year before the study. Individuals with NES were significantly more likely to have a history of underweight than overweight. Another study reported that individuals with NES showed increased anxiety about body shape and weight compared with the healthy control group. Adolescents who demonstrated the criteria for both overeating disorder and NES had a higher risk of eating and mood disorders than those who had a single disorder, and this may indicate the possibility of some synergy between these conditions. Studies demonstrated that NES had similar characteristics to other known eating disorders, including bulimia nervosa and overeating disorders [37]. Adolescents with common comorbidities such as depression, sleep disorders, other eating disorders, and those in periods of increased stress should be screened by the NEQ. Nocturnal meals are of interest because of the possible role in the development and maintenance of obesity [38,39] and the association with pathologies such as overeating, psychological distress [40,41], sleep disorders [42] and diabetes [43].

In our study, adolescents with NES symptoms also had the higher overall score on the depressive disorder scale, shorter sleep duration ( $P < 0.01$ ), elevated BMI ( $P < 0.01$ ), and the higher probability of obesity ( $P = 0.001$ ). Our previous studies [44] found decreased melatonin levels in overweight children. Another study indicated increased melatonin levels in obese people [45]. The authors attributed this to the fact that melatonin, which is involved in antioxidant and anti-inflammatory protection, may be activated in the context of obesity as a compensatory mechanism. The body will start producing it to increase drowsiness and promote behaviors aimed at getting time to sleep, or to counteract the pro-inflammatory and oxidative stress effects of obesity and sleep deprivation. It is known that melatonin plays an important role in the development of sleep-wake rhythm [46].



A number of studies have shown that melatonin and melatonergic agents are effective in treating wakefulness because they can accelerate the onset of sleep, increase sleep duration, and slightly alter sleep patterns [47]. Melatonin agonists [48,49] have been approved by the EU and the US for the treatment of wakefulness and resynchronization of circadian rhythms. In this regard, it is possible to assume that melatonin plays a role in the development of NES. In our study, urinary melatonin levels in adolescents with NES were significantly lower than in adolescents without NES and correlated negatively with the severity of NES symptoms and BMI. Attenuation of nocturnal elevations in melatonin may be associated with the effects of corticotropin-releasing hormone (CRH), which inhibits melatonin secretion [50]. We did not measure CRH, but the results [51] indicated that CRH levels were increased.

Despite the fact that the NES remains an understudied condition, there is quite enough information about the identified comorbidities and complications that can be prevented in later life. Understanding the best treatment for patients who develop NES can be critical to preventing significant morbidity and potentially helping to halt its progression.

## Conclusions

1. The prevalence of NES among adolescents is 11.5 %.
2. The results suggest a link between Body Mass Index, depression and melatonin levels in adolescents with NES.

**Prospects for further research.** Despite great efforts to find an effective diagnosis of this syndrome, further research is needed to distinguish between Night Eating Syndrome and other eating disorders, as well as the use of a multidisciplinary approach as a more promising management of these conditions.

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