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Impact of Social Jetlag and Circadian Patterns on Patients with Metabolic and Nocturnal Eating Syndromes

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Objective: Metabolic syndrome (MS) can result in many health hazards, including coronary heart disease, diabetes, fatty liver, and several types of cancer. Social jetlag is a discrepancy between biological and social timing. Circadian rhythm disruption is suggested to disturb the hypothalamus pituitary adrenal (HPA) axis. Disturbance of the HPA axis was reported to increase the risk of developing visceral obesity and MS. We hypothesized that social and circadian rhythm disruptions negatively impact patients with obesity and MS. This study aimed to detect the associations between obesity, MS, nocturnal eating syndrome, and social jetlag. **Methods:** One hundred obese patients were recruited (61 had MS). The patient group was compared to a healthy nonobese control group (n=50). Each studied patient was subjected to three questionnaires [Morningness Eveningness Questionnaire, Night Eating Questionnaire (NEQ), and Sleep Timing Questionnaire]; their anthropometric measures were taken, fasting lipid profile, liver, and kidney function tests, and fasting insulin were also assessed. **Results:** Patients with evening chronotype were mainly from the obese with MS group. NEQ total score was higher in obese patients with MS, and it showed a significant positive correlation with BMI. Total cholesterol, NEQ score, age, sleep latency, and awakening after sleep onset had significant associations with MS. **Conclusion:** Evening chronotype has a significant association with MS. Social jetlag negatively impacts obesity and MS, leading patients to have frequent nocturnal eating behaviors. Screening for sleep profile and social jetlag should be included in routine clinical practice of managing obesity.

Key Words: Metabolic syndrome; Obesity; Social jetlag; Chronotype, Night eating syndrome

INTRODUCTION

Metabolic syndrome (MS), initially described by Gerald Reaven in 1988 as "syndrome X" or "insulin resistance syndrome," is a collection of common irregularities, including resistance to insulin, impairment of glucose tolerance, central obesity, reduced high-density lipoprotein (HDL)-cholesterol levels, elevated triglycerides (TG), and hypertension. The condition reflects the sedentary lifestyle, over nutrition, and resultant excess adiposity

of the modern world [1]. The International Diabetes Federation (IDF) [2] released a global consensus definition for MS; this definition identified central obesity as an essential component of MS in addition to any two of the following four findings: 1) elevated serum TG: ≥150 mg/dL or history of medication administration for this hyperlipidemia; 2) low levels of HDL-cholesterol: <40 mg/dL in males and <50 mg/dL in females or medication administration for such reduced levels; 3) hypertension: with systolic blood pressure (DBP) ≥130 mm Hg or diastolic blood

pressure (DBP) ≥85 mm Hg, or administrating antihypertensive drugs; and 4) raised fasting blood glucose (FBG): ≥100 mg/dL or previously diagnosed type 2 diabetes mellitus (DM).

On the other hand, the Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) [3] defined MS as follows: 1) abdominal obesity in which waist circumference (WC) >102 cm in men, and >88 cm in women; 2) TG ≥150 mg/dL; 3) HDL-cholesterol <40 mg/dL in men and <50 mg/dL in women; 4) blood pressure (BP) ≥130/≥85 mm Hg; and 5) FBG ≥110 mg/dL.

The circadian rhythms are a sequence of endogenous autonomous oscillators created by the molecular circadian clock, which synchronizes internal time with the external environment in a 24-h daily cycle [4]. The interconnections between circadian rhythm disruption and metabolism clarify the significance of chronobiology in preventing and treating type 2 DM, obesity, and hyperlipidemia [5].

Chronotype is the tendency of a person to sleep at a particular time during the 24 hours. It is primarily regulated by the circadian clock but constrained by work obligations to a specific sleep schedule. The discrepancy between biological and social time can be described as social jetlag [6]; 69% of adults are documented to have at least 1 hour of social jetlag [7].

Social jetlag is the discrepancy in timing between the circadian and social clock [8]. Social jetlag represents the dissimilarity between sleeping and waking hours on free days (determined by individual predilection) and workdays (established by social and work obligations) [9]. Later chronotype and greater social jetlag were related to a higher body mass index (BMI) and obesity [10]. In a study including 792 individuals, there was an association between social jetlag and consumption of meals and snacks at delayed times of the day [11]. Furthermore, social jetlag was associated with the total calories consumed, particularly proteins, total fats, saturated fat, and cholesterol, all over the day, which proved the negative effect of circadian disturbance on food intake [11]. Uncoupling circadian-controlled activities like sleeping and eating from endogenous circadian rhythm negatively affect lipid and glucose metabolism, insulin regulation and may lead to obesity, such as seen in shift workers. In one experimental study, insulin sensitivity decreased, leptin secretion was suppressed, and the rhythm of cortisol was completely inverted in 10 adults following the uncoupling of circadian regulated behaviors from their biological rhythm [12].

The mechanism by which the social disturbances increase the susceptibility to developing MS is not fully understood; however, circadian rhythm disruption is suggested to disturb the suprachiasmatic nucleus, which controls the endogenous circadian rhythm and regulates the hypothalamus pituitary adrenal (HPA) axis [13]. Disturbance of the HPA axis was reported to increase the risk of developing visceral obesity and MS [14]. The activity of the sympathetic nervous system was reported to increase following sleep restriction or fragmentation [15]. Cortisol level showed significant elevation in the afternoon and evening periods following sleep restriction, which led to insulin resistance [16]. To our knowledge, no previous study combined detection and screening of the association between social jetlag, obesity, MS, and nocturnal eating syndrome (NES) in a single study. These multiple factors are thought to negatively affect the prognosis and management plan of target patients, which reflects the importance of the current research. We hypothesized that social and circadian rhythm disruption negatively impacts patients with obesity and MS. This study aimed to detect the associations between obesity, MS, NES, and social jetlag.

METHODS

Study subjects

This is a cross-sectional case-control study that was approved by the Institutional Review Board of the Faculty of Medicine, Mansoura University (Approval number MS/17.12.188). One hundred and fifty participants were recruited on a consequent base over one year from April 2019 to April 2020 after informed written consent to participate in the study and that on publishing the research, no personal data will be revealed. Participants were recruited from the obesity outpatient clinic at the Specialized Medical Hospital, Mansoura University. Participants included in this study were divided into three groups: obese with MS; obese subjects not fulfilling the criteria of MS; and nonobese group (the control group). Figure 1 summarizes the stepwise study methodology.

MS was diagnosed according to the IDF criteria updated in 2006 [2], which require central obesity plus two of the following: 1) TG ≥150 mg/dL or treated for raised TG; 2) HDL-cholesterol <40 mg/dL in men or <50 mg/dL in women, or on treatment for reduced HDL; 3) SBP ≥130 mm Hg, DBP ≥85 mm Hg, or on antihypertensive treatment; and 4) FBG ≥100 mg/dL or previously diagnosed type 2 DM.

We excluded patients who were older than 60 years old or younger than 22 years old (this age range was chosen to be excluded to avoid the impact of age on the circadian pattern and chronotype preference), patients with mental illness, patients with organ failure, patients using drugs that may affect sleep, and shift workers.

Each participant recruited in this study was subjected to history taking related to chronic illnesses and prescribed drugs. BP measurement using a manual sphygmomanometer, anthropometric measures, including weight, height, BMI, WC, and hip circumference (HC) were recorded.

During the collection of anthropometric data, participants were instructed to keep on only light clothes without shoes. Height and weight were measured to the nearest centimeter and kilogram, respectively. WC and HC were measured to the nearest 0.1 cm. Measurements were done via bypassing the measuring tape through the midpoint between the superior iliac crest and the lowest rib WC. HC was measured at the maximum protuberance [17]. BMI
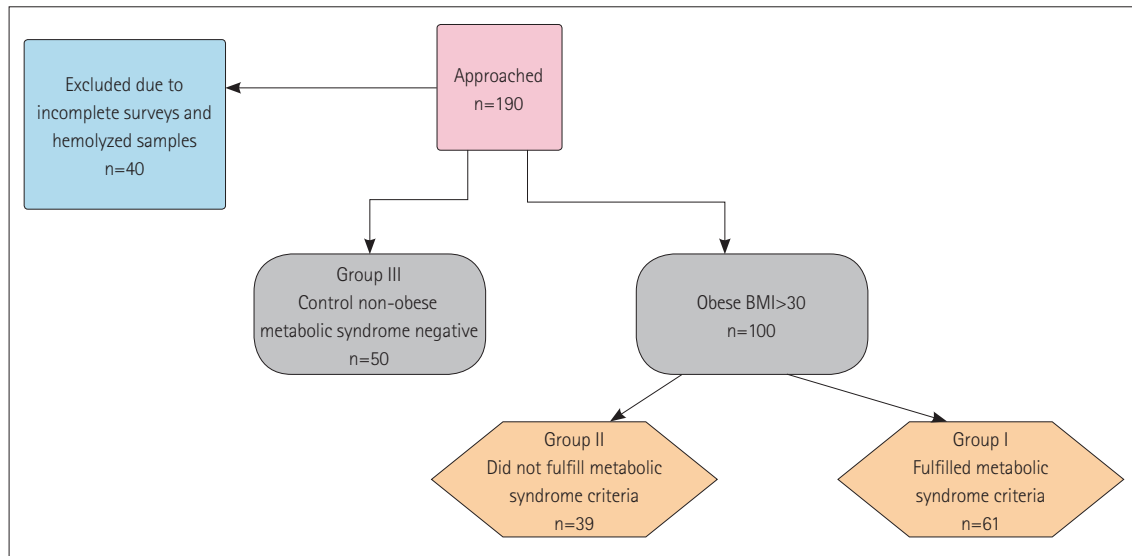
Figure 1. Stepwise study methodology.

was calculated using the Quetelet Index=body weight (kg) divided by height squared (m^2) [18].

Questionnaires

Assessment of circadian rhythm and the social pattern was obtained by applying the revised Morningness-Eveningness Questionnaire (MEQ) [19]. The MEQ total score was interpreted as morning-type (M-type: score 18–25), neither-type (N-type: score 12–17), and evening-type (E-type: score 4–11). We used the validated Arabic abridged shorter version [20].

All participants completed the Arabic translated and validated version of the Night Eating Questionnaire (NEQ) [21,22]. The NEQ is a 14-item questionnaire that assesses the behavioral and psychological symptoms of the NES. Questions 1, 4, and 14 are inversely scored. The total score included questions 1–12 and 14, while question 13 was not included in the total score but was used to exclude parasomnias. Also, question 15 was not added to the total score, but instead, it was used as an indicator of the course of symptoms. Questions 16 and 17 were used to confirm the presence of distress or impairment if the NES was present. The questions scored on a five-grade Likert's scale (scoring from 0 to 4), except for question 7. It was considered that individuals with a score of 25 or greater are suggested to have NES, and those with a score of 30 and above have strong evidence that they have NES [22].

Sleep Timing Questionnaire [23] includes 18 questions and provides an exact outline of an individual's typical sleep schedule like the time preferred for going to bed and wake up, frequency of night awakenings, and stability of sleep schedules [24]. We used the translated validated Arabic version [25].

Social jetlag was measured using the following steps, which were adopted from [11]. The participants were asked about the following parameters: When do you commonly go to sleep on weekdays? How long do you stay awake in bed before you go to sleep (after lights off) on weekdays? When did you commonly get up on weekdays? When do you commonly go to sleep at week-

ends? How long do you stay awake in bed before you go to sleep (after lights off) at weekends? When do you commonly get up at weekends? Lastly, social jetlag was determined by calculating the variance between mid-sleep time on weekends and weekdays, as the mid-sleep phase is the best phase presenter point for melatonin onset, which is an important circadian rhythm marker [26]. Those with a difference of more than one hour were considered suffering from social jetlag, while those with less than one-hour difference were considered free from social jetlag.

Laboratory measurements

FBG, fasting insulin, lipid profile, and liver and kidney function were measured. A fasting venous sample was collected from every participant in the study into a plain tube. The sample was left to clot for 20 minutes, then centrifuged at 3,000 rpm at room temperature; clear non-hemolyzed sera were separated and divided into two aliquots. One was used for the traditional lab investigation (liver function, serum creatinine, and lipid profile), and the other aliquot was left frozen at -20℃ till analysis of serum insulin. Serum insulin was assayed by ELISA kits supplied by ImmunoScape Corporation (Netherland).

Statistical analysis

The SPSS software (version 25.0; IBM Corp., Armonk, NY, USA) was used for data entry and analysis. Qualitative data were expressed as frequencies and percentages. Quantitative data were initially tested for normality using Kolmogorov-Smirnov and Shapiro-Wilk's test, with data being normally distributed if p>0.050. The presence of significant outliers (extreme values) was tested by examining boxplots. Quantitative data were expressed as the median and interquartile range, as the data was not normally distributed. Qualitative data for more than two groups (e.g., 2×3 table) were done by ANOVA and chi-square test (with Bonferroni method to adjust p values when comparing column proportions). For the quantitative data, the Kruskal-Wallis H test was used due to

the skewed distribution of data and significant outliers. Pairwise comparisons were used to properly compare each pair of data. Evaluation of the diagnostic presentation or the accuracy of a test to distinguish diseased from non-diseased cases was done using receiver operating characteristic (ROC) curve analysis. ROC curves were also used to compare the diagnostic performance of two or more diagnostic tests [27]. The likelihood of a diagnosis and associations were assessed using logistic regression analysis calculation of the crude odds ratio with its 95% confidence interval (CI).

RESULTS

Patients in obese with MS group were the eldest in the study sample (older than obese subjects not fulfilling the criteria of MS and controls), with a mean age of 52 years, which was statistically significant. In general, the percentages of males were higher than females (49.2% in obese subject with MS, 69.2% in obese subjects not fulfilling the criteria of MS, and 66% in controls). Table 1 shows that sex distribution was statistically significant, with a higher proportion of females among obese with MS. BMI, WC, and HC were statistically significantly higher in obese with and without MS compared to the controls. Waist hip ratio (WHR) had no statistically significant difference between the three groups. SBP, DBP, and mean arterial blood pressure (MBP) were all significantly higher in the obese with MS group compared to both the obese without MS and control groups. For the laboratory data of the participants, we found that FBG and TG were significantly higher in the obese with MS group compared to both the obese without MS and control groups. Low-density lipoprotein (LDL) was significantly higher in the obese with and without MS compared to the controls. There was no statistically significant difference between the three groups regarding serum creatinine, aspartate transaminase (AST), alanine transaminase (ALT), and AST/ALT ratio. Regarding albumin, a statistically significant difference existed only between the obese with MS group and the controls. HDL was significantly lower in obese with MS than obese without MS than control. Meanwhile, in regard to the chronotype profile of the study sample, it can be noticed that there is no statistically significant difference in the distribution of chronotypes in the three study groups. It also shows the scores of the NEQ among the sample of the study participants. A statistically significant difference in the distribution of the NEQ was seen in the three study groups. There was a higher NEQ score in obese with MS group compared to the other two study groups. This difference was statistically significant. As for the social jetlag, no statistically significant difference was detected in the distribution of social jetlag between the three study groups. These results are summarized in Table 1.

Table 2 presents the correlations between NEQ and social jetlag score and other parameters. There was a statistically significant positive correlation between the NEQ score and BMI (in the obese with MS group), sleep latency, and minutes staying awake on week-

days and weekends (in the obese with MS group), and a statistically significant negative correlation between the NEQ score and social jet lag (in both obese with and without MS groups). A statistically significant positive correlation was detected between social jetlag and TG (in the obese with MS group) and FBG (in the obese subjects with MS). Additionally, there was a statistically significant negative correlation between social jetlag and HDL (in the obese subjects without MS) and the total NEQ score (in both obese with and without MS groups). No statistically significant correlations were detected in all other tested parameters.

Table 3 presents the univariate analysis of the associations of the likelihood of occurrence of the MS in obese patients. The univariate regression analysis model showed that total cholesterol (TC), age, NEQ score, the sleep latency rank, and the rank of awakening after sleep were significantly associated with MS in obese patients. For everyone, a unit increase in TC, age, and NEQ score, obese patients have 1.012, 1.077, and 1.132 higher odds to exhibit MS, respectively.

Binomial logistic regression was performed to ascertain the effects of TC, age, NEQ score, and staying awake at weekends on the likelihood that participants have MS. The logistic regression model was statistically significant, $\chi^2(6)=43.125$, p<0.0005. The model correctly classified 77% of cases. Sensitivity was 82%, specificity was 69.2%, positive predictive value was 80.6%, and the negative predictive value was 71.1% (Supplementary Figure 1). Of the 6 associated variables, age ≥42.5 years and TC ≥139 mg/dL were statistically significant independent associations as shown in Table 4. Patients with age ≥42.5 years had 9.8 times higher odds to exhibit MS, and patients with TC ≥139 mg/dL had 6.7 times higher odds to exhibit MS.

DISCUSSION

In this study, we tried characterizing the chronobiology and eating habits in patients with MS in a trial to find further preventable risk factors, thus improving patient outcomes. The total scores of NEQ was also higher in study obese with MS. Social jetlag was positively associated with TG and FBG levels in obese subjects with MS and negatively associated with HDL and cholesterol in obese subjects not fulfilling the criteria of MS. These main findings of this study indicate that the MS can be worsened in a certain population who have social jetlag and are generally obese and that obesity is not only controlled by eating habits and physical exercise, but other risk factors can affect its severity and medical complications.

There are numerous mechanisms by which circadian rhythm disruptions can impact obesity and MS, as summarized in a review by Hernández-García et al [28]: 1) The adipose tissue, as a peripheral tissue, contains clock genes that regulate the rhythmic expression of adipokines (adiponectin, leptin, and resistin, among others) and therefore, is associated with the appearance of obesity and MS; 2) Clock genes are expressed in body fat, both the subcutaneous and visceral fat; 3) Adiponectin (ADIPOQ) and its re-

Table 1. The comparison of characteristics among three groups

Variable	Obese with MS (n=61)	Obese without MS (n=39)	Control (n=50)	KW/χ^2	p
Clinicodemographic variables					
Age (years)	52 (44−55)	41 (28−54)	45 (31−51)	19.927	0.03*
Sex, n (%)				8.967	0.04*
Males	30 (49.2)	27 (69.2)	33 (66)		
Females	31 (51.8)	12 (30.8)	17 (34)		
BMI	36.3 (32.4−40.3)	34.7 (31.6−38.1)	24.9 (22.8−27.3)	98.79	<0.0005*
WC (cm)	107 (85−121)	93 (78−109)	75.5 (65.7−82.5)	46.969	<0.0005*
HC (cm)	116 (89−134)	100 (88−127)	82 (70.75−97)	34.308	<0.0005*
WHR	0.94 (0.89−0.96)	0.92 (0.87−0.95)	0.93 (0.82−0.97)	2.435	0.296
SBP (mm Hg)	130 (120−140)	120 (110−130)	120 (110−120)	24.355	<0.0005*
DBP (mm Hg)	80 (70−80)	70 (70−80)	70 (70-80)	12.731	0.002*
MBP (mm Hg)	96.7 (90−100)	86.7 (83.3−93.3)	88.3 (83.3−93.3)	27.292	<0.0005*
Laboratory variables					
FBG (mg/dL)	168 (123−206)	101 (100−123)	89.5 (77−107)	22.946	<0.0005*
Creatinine (mg/dL)	0.8 (0.7−1.1)	0.9 (0.7−1)	0.8 (0.7−1)	1.816	0.403
Albumin (gm)	3.8 (3.4−4)	4 (3.5−4)	4 (3.8−4)	16.205	<0.0005*
AST (U/L)	16 (14−22)	15 (13−19)	15 (12−18)	5.608	0.061
ALT (U/L)	16 (14−21)	17 (14−21)	16 (15−18)	0.493	0.781
AST/ALT ratio	0.94 (0.84−1.18)	0.89 (0.8−1.04)	0.89 (0.86−0.9)	3.83	0.147
TC (mg/dL)	171 (143−207.5)	146 (110−179)	88.5 (77.7−99)	85.391	<0.0005*
LDL (mg/dL)	93.6 (73−121.4)	71.8 (41−112)	15.6 (8.9−27.2)	78.729	<0.0005*
TG (mg/dL)	166 (136.5−122)	100 (90−124)	90 (86.75−100)	56.534	<0.0005*
HDL (mg/dL)	41 (35−46)	51 (43−55)	55 (48−65)	52.889	<0.0005*
Psychometric questionnaires					
Chronotype				9.123	0.34
Defenitely morning	1 (1.6)	2 (5.1)	5 (10)		
Moderately morning	27 (44.3)	13 (33.3)	22 (44)		
Neither	26 (42.6)	21 (53.8)	18 (36)		
Moderately evening	5 (8.2)	3 (7.7)	5 (10)		
Defenitely evening	2 (3.3)	0 (0)	0 (0)		
Total MEQ score	17 (15−19)	16 (13−18.5)	18 (15−20)	2.663	0.264
Night Eating Questionnaire				26.057	<0.0005*
<25	30 (49.2)	32 (82.1)	45 (90)		
25−29	24 (39.3)	5 (12.8)	5 (10)		
>30	7 (11.5)	2 (5.1)	0 (0)		
Total score	25 (21−27)	22 (16−23)	11 (14.5−22)	37.528	<0.0005*
Social jetlag				0.312	0.856
Present	30 (49.2)	17 (43.6)	24 (48)		
Absent	31 (50.8)	22 (56.4)	26 (52)		

*statistically significant difference. BMI: body mass index, WC: waist circumferernce, HC: hip circumferernce, WHR: waist/hip ratio, SBP: systolic blood pressure, DBP: diastolic blood pressure, MBP: mean arterial blood pressure, FBG: fasting blood glucose, AST: aspartate transaminase, ALT: alanine transaminase, TC: total cholesterol, LDL: low-density lipoprotein, TG: triglyceride, HDL: high-density lipoprotein. Data expression: median (IQR) [compared by Kruskal-Wallis H Test]. Data expression: frequency (percentage). P: chi-square test (Monte Carlo significance). Comparisons of column proportions (adjusted p-value using Bonferroni method).

ceptors, ADIPOR1 and ADIPOR2, are considered a protective factor against obesity and MS. All of them showed a significant decrease of circadian rhythmicity in patients' adipose tissue with severe obesity. Finally, leptin, another adipokine, also displayed an association with circadian rhythmicity.

Our results revealed that age was higher in the obese with MS group compared to the other two groups. This coincides with De-

vers et al. [29] whose study showed that the prevalence of MS and the individual MS components increased with age. In this study, the level of serum albumin was lower in obese with MS compared to the other two groups. This was in contrast to the study conducted by Cho et al. [30], which revealed that higher serum albumin levels were associated with an increased prevalence of MS. This might be due to the cultural differences in the type of meals eaten

in the current study locality, where carbohydrates form the main component of the meals rather than proteins.

In the current study, chronotype did not show statistically significant differences between the three studied groups. This finding matches Cespedes Feliciano et al. [31] who showed no significant association between chronotype (assessed by MEQ) and obesity among males.

The association between NES and obesity has not been thoroughly evaluated. Our results showed that the total NEQ score was statistically significantly higher in the obese patients with MS group compared to the other two groups (p<0.0005). The prevalence of participants with a total NEQ score >30 was 11.5% of the obese group with MS and 5.1% of the obese group without MS, while 0% of the control group belonged to those with a total score >30. NES prevalence of 9.7% has been reported in diabetes, and participants with nocturnal eating symptoms were more likely to be obese [32]. Also, the studies by Yoshida et al. [33] and Islam et al. [34] agreed with our results as it showed a higher probability of developing MS among women with nocturnal eating habits. These current results contrast with Calugi et al. [35] whose study showed no difference in MS occurrence between participants with and without NES. This may be due to including patients with BMI ≥35 and defining the MS according to the modified Adult Panel Treatment-III.

The total NEQ score in our study was positively associated with BMI in the obese group with MS (p=0.049). This was in harmony with a research study examining the relationship between nocturnal eating habits (defined as dinner immediately before bed and snacks after dinner based on the conventional National Health and Nutrition Examination Survey) and components of MS and

found that people with both nocturnal eating habits had a higher probability of developing obesity [33]. Also, the study conducted by Allison et al. [22] investigating eating disorders in type 2 DM revealed that there was higher BMI in those with eating disorders group [using both NEQ for diagnosis of NES and Eating Disorder Examination-Questionnaire for diagnosis of binge eating disorder (BED)].

People with nocturnal eating habits were supposed to have higher TG levels and diminished insulin sensitivity. Low nocturnal insulin sensitivity leads to low lipoprotein lipase activity and causes higher circulating plasma TG levels [33]. Our study revealed different findings; it showed no statistically significant correlation between NEQ score and WC, HC, FBG, MBP, TC, TG, LDL, and HDL cholesterol. These results are coinciding with Calugi and colleagues [35,36] who stated that there is no association between NES and the components of MS (BP, blood glucose, WC,

Table 3. Crude associations of the likelihood of occurrence of metabolic syndrome in obese patients using a univariate binary logistic regression analysis

Variable	Crude odd ratio	95% CI (lower–upper)	p
Total cholesterol	1.012	1.002–1.021	0.014
Age	1.077	1.033–1.122	<0.0005
NEQ score	1.132	1.046–1.224	0.002
NEQ rank	3.001	1.380–6.525	0.006
Sleep latency (minutes)	1.017	0.997–1.038	0.101
Sleep latency rank	2.467	1.081–5.627	0.032
Awakening after sleep rank	1.63	1.220–2.177	0.001

NEQ: Night Eating Questionnaire, CI: confidence interval, P: binary standard logistic regression

Table 2. Correlations between the NEQ, social jetlag score, and other parameters

Variable	Associations with the NEQ				Associations with social jetlag			
	Obese with MS		Obese without MS		Obese with MS		Obese without MS	
	Coefficient	p	Coefficient	p	Coefficient	p	Coefficient	p
BMI	0.254	0.049	0.183	0.264	0.038	0.769	-0.281	0.081
WC	0.139	0.286	0.119	0.471	-0.014	0.914	-0.231	0.157
MBP	0.114	0.383	0.080	0.628	-0.069	0.590	0.010	0.950
FBG	0.100	0.442	0.222	0.175	0.320	0.012	0.003	0.989
TC	0.026	0.724	-0.072	0.664	0.111	0.393	-0.109	0.510
LDL	0.016	0.902	0.091	0.582	0.017	0.898	0.062	0.707
TG	0.095	0.464	-0.111	0.500	0.356	0.005	0.065	0.734
HDL	0.135	0.301	0.096	0.562	-0.025	0.852	-0.342	0.038
Total MEQ	-0.109	0.402	-0.304	0.060	0.017	0.897	-0.054	0.743
Sleep latency	0.405	0.001	0.146	0.375	-0.073	0.670	0.195	0.233
Social jetlag	-0.312	0.014	-0.429	0.006	NA	NA	NA	NA
Total NEQ	NA	NA	NA	NA	-0.312	0.014	-0.429	0.006
How many min patient stay awake in weekends	0.393	0.002	0.215	0.189	-0.115	0.378	0.172	0.296
How many min patient stay awake in weekdays	0.352	0.005	0.234	0.152	-0.065	0.666	0.126	0.445
HC	0.128	0.327	0.093	0.573	-0.030	0.821	-0.205	0.210
WHR	0.121	0.354	0.176	0.284	-0.024	0.857	0.001	0.996

p-value: Spearman's correlation. MS: metabolic syndrome, BMI: body mass index, WC: waist circumference, HC: hip circumference, WHR: waist to hip ratio, MBP: mean arterial blood pressure, FBG: fasting blood glucose, TC: total cholesterol, LDL: low-density lipoprotein, TG: triglyceride, HDL: high-density lipoprotein, MEQ: Morningness-Eveningness Questionnaire, NEQ: Night Eating Questionnaire

Table 4. Independent associations of the metabolic syndrome in obese patients

Variables	B	SE	Wald	p	OR	95% CI	
						Lower	Upper
Total serum cholesterol (<139 vs. ≥139 mg/dL)	1.90	0.63	9.1	0.003	6.69	1.94	23.10
Age (<42.5 vs. ≥42.5)	2.28	0.61	14.23	<0.0005	9.81	2.99	32.14
NEQ total score (<22 vs. ≥22)	0.71	0.58	1.48	0.220	2.04	0.64	6.46
Staying awake in the weekends (<25 vs. ≥25 min)	0.92	0.97	0.89	0.344	2.50	0.37	16.70
Sleep latency (<15 min vs. ≥15 min)	0.65	0.96	0.45	0.500	0.52	0.08	3.47
Awakening after sleep	0.29	0.21	1.97	0.160	1.34	0.89	2.04

Adjusted for age and sex. Cutoff values were depicted by ROC curve analyses (Supplementary Figure 1). NEQ: Night Eating Questionnaire, B: binary logistic regression coefficient, SE: standard error, OR: odds ratio, CI: confidence interval

HC, TG, and HDL cholesterol). Furthermore, Allison et al. [37] supported these findings by revealing that there were no differences between those with and without eating disorders (NES and BED) regarding WC, SBP, DBP, TG, and HDL cholesterol.

Social jetlag is the mismatch between biological and social timing; social jetlag has been measured as the discrepancy of midsleep time on weekdays and weekends. Social jetlag has been suggested to induce obesity and cardiometabolic abnormalities [34]. Our study revealed that the number of patients having social jetlag was higher in the obese group with MS compared to the other two groups, but there was no statistically significant difference. The current study results concur with a five-year (2007−2011) cohort study that aimed to determine the impact of circadian disruption on serum lipids, and there was also no significant association between MEQ score and HDL cholesterol [38]. The current study results agree to the study of Kanterman et al. [39] that used Munich Chronotype Questionnaire (designed by Roenneberg) [40] to assess chronotype in shift workers, but found no association between chronotype and and HDL cholesterol nor TG.

On the contrary, this differs from the New Hoorn Study, in which social jetlag increased the risk of MS in younger patients (<61 years) [41]. Additionally, some other researchers found no correlation between chronotype (using MEQ) and HDL cholesterol nor TG levels [31,42]. The results of previous studies are so contradictory and conflicting regarding this area. One study investigating the metabolic impact of evening chronotype in 101 middle-aged male workers with type 2 DM showed a significant correlation between MEQ and HDL cholesterol [43]. Also, Tomizawa et al. [38] revealed a significant association between MEQ and TG.

In the current study, social jetlag showed no statistically significant association with BMI, WC, HC, and WHR. These results were similar to [44]. However, this was unlike an alternative study, which showed that social jetlag was associated positively with BMI and WC [42]. Additionally, the New Hoorn Study revealed that those with greater social jetlag had higher WC [41]. Furthermore, our study revealed that social jetlag was positively correlated with FBG (p=0.012). An observational study reported earlier by the New Hoorn Study found that higher blood glucose level was associated with greater social jetlag [41].

This study further documented that obesity is not only related to overeating and decreased physical activity, but other alternative factors play a role in the metabolic profile. Unfavorable metabolic symptoms are usually associated with disrupted social rhythm and nocturnal eating. Additionally, we managed to compare obese patients with and without MS to a control group. We screened for nocturnal eating using a standardized objective questionnaire, and this eating pattern was rarely taken into account in other studies; this might indicate that we should consider chronobiological aspects when treating obesity and its metabolic complications.

This study has some limitations. First, the cross-sectional design did not help with the inference about the causality and follow up of metabolic profile. Second, the small sample size might limit the generalizability of results. Third, although the questionnaires are validated, they still are subjective and could depend on the patient's subjective feelings at the time of the interview, and objective measurement of caloric intake or sleep profile could have been more informative. Finally, we had no enough information about important confounding factors including physical activity, alcohol consumption, smoking, comorbidities (diabetes mellitus, hypertension, dyslipidemia) and concurrent medication (lipid lowering agents, glucose lowering agents, and others), which are highly associated with the development of MS.

MS (syndrome X) is a multiplex risk factor that arises from insulin resistance in addition to abdominal adiposity. TC, NEQ score, age, sleep latency rank, and awakening after sleep were significantly associated with MS in multivariate logistic regression.

Screening for circadian rhythm disruptions should be included as a routine assessment step with obese patients. Nocturnal eating behaviors are more common in obese patients with MS, and the role of chronotherapy should be further investigated in the management plan of such patients.

Supplementary Materials

Acknowledgments

with blood sample collection preservation and result collection.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

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REFERENCES

1. Obunai K, Jani S, Dangas GD. Cardiovascular morbidity and mortality of the metabolic syndrome. Med Clin North Am 2007;91:1169-1184.
2. Alberti G, Zimmet P, Shaw J, Grundy SM. The IDF consensus worldwide definition of the metabolic syndrome. Brussels: International Diabetes Federation 2006;23:469-480.
3. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). JAMA 2001;285:2486-2497.
4. Xie Y, Tang Q, Chen G, Xie M, Yu S, Zhao J, et al. New insights into the circadian rhythm and its related diseases. Front Physiol 2019;10:682.
5. Poggiogalle E, Jamshed H, Peterson CM. Circadian regulation of glucose, lipid, and energy metabolism in humans. Metabolism 2018;84:11-27.
6. Zhang Z, Cajochen C, Khatami R. Social jetlag and chronotypes in the Chinese population: analysis of data recorded by wearable devices. J Med Internet Res 2019;21:e13482.
7. Wittmann M, Dinich J, Merrow M, Roenneberg T. Social jetlag: misalignment of biological and social time. Chronobiol Int 2006;23:497-509.
8. Silva CM, Mota MC, Miranda MT, Paim SL, Waterhouse J, Crispim CA. Chronotype, social jetlag and sleep debt are associated with dietary intake among Brazilian undergraduate students. Chronobiol Int 2016;33:740-748.
9. Roenneberg T, Allebrandt KV, Merrow M, Vetter C. Social jetlag and obesity. Curr Biol 2012;22:939-943.
10. Yu JH, Yun CH, Ahn JH, Suh S, Cho HJ, Lee SK, et al. Evening chronotype is associated with metabolic disorders and body composition in middle-aged adults. J Clin Endocrinol Metab 2015;100:1494-1502.
11. Mota MC, Silva CM, Balieiro LCT, Fahmy WM, Crispim CA. Social jetlag and metabolic control in non-communicable chronic diseases: a study ad-

12. dressing different obesity statuses. Sci Rep 2017;7:6358.
12. Szosland D. Shift work and metabolic syndrome, diabetes mellitus and ischaemic heart disease. Int J Occup Med Environ Health 2010;23:287-291.
13. la Fleur SE, Kalsbeek A, Wortel J, Fekkes ML, Buijs RM. A daily rhythm in glucose tolerance: a role for the suprachiasmatic nucleus. Diabetes 2001;50: 1237-1243.
14. Gonnissen HK, Rutters F, Mazuy C, Martens EA, Adam TC, Westerterp-Plantenga MS. Effect of a phase advance and phase delay of the 24-h cycle on energy metabolism, appetite, and related hormones. Am J Clin Nutr 2012; 96:689-697.
15. Rao MN, Neylan TC, Grunfeld C, Mulligan K, Schambelan M, Schwarz JM. Subchronic sleep restriction causes tissue-specific insulin resistance. J Clin Endocrinol Metab 2015;100:1664-1671.
16. Buxton OM, Pavlova M, Reid EW, Wang W, Simonson DC, Adler GK. Sleep restriction for 1 week reduces insulin sensitivity in healthy men. Diabetes 2010;59:2126-2133.
17. Katz EG, Stevens J, Truesdale KP, Cai J, Adair LS, North KE. Hip circumference and incident metabolic risk factors in Chinese men and women: the People's Republic of China study. Metab Syndr Relat Disord 2011;9:55-62.
18. Keys A, Fidanza F, Karvonen MJ, Kimura N, Taylor HL. Indices of relative weight and obesity. J Chronic Dis 1972;25:329-343.
19. Adan A, Almirall H. Horne & Östberg morningness-eveningness questionnaire: a reduced scale. Pers Individ Differ 1991;12:241-253.
20. BaHammam AS, Almistehi W, Albatli A, AlShaya S. Distribution of chronotypes in a large sample of young adult Saudis. Ann Saudi Med 2011;31:183-186.
21. Elsadek AM, Hamid MS, Allison KC. Psychometric characteristics of the Night Eating Questionnaire in a Middle East population. Int J Eat Disord 2014;47:660-665.
22. Allison KC, Stunkard AJ, Thier SL. Overcoming night eating syndrome: a step-by-step guide to breaking the cycle. Oakland: New Harbinger Publications; 2004.
23. Monk TH, Buysse DJ, Kennedy KS, Pods JM, DeGrazia JM, Miewald JM. Measuring sleep habits without using a diary: the sleep timing questionnaire. Sleep 2003;26:208-212.
24. Klei L, Reitz P, Miller M, Wood J, Maendel S, Gross D, et al. Heritability of morningness-eveningness and self-report sleep measures in a family-based sample of 521 hutterites. Chronobiol Int 2005;22:1041-1054.
25. Mansour H, Tobar S, Fathi W, Ibrahim I, Wood J, Elassy M, et al. Arabic versions of the sleep timing questionnaire and the composite scale of morningness. Asian J Psychiatr 2015;13:48-51.
26. Umemura GS, Pinho JP, da Silva Brandão Gonçalves B, Furtado F, Forner-Cordero A. Social jetlag impairs balance control. Sci Rep 2018;8:9406.
27. Griner PF, Mayewski RJ, Mushlin AI, Greenland P. Selection and interpretation of diagnostic tests and procedures. Principles and applications. Ann Intern Med 1981;94(4 Pt 2):557-592.
28. Hernández-García J, Navas-Carrillo D, Orenes-Piñero E. Alterations of circadian rhythms and their impact on obesity, metabolic syndrome and cardiovascular diseases. Crit Rev Food Sci Nutr 2020;60:1038-1047.
29. Devers MC, Campbell S, Simmons D. Influence of age on the prevalence and components of the metabolic syndrome and the association with cardiovascular disease. BMJ Open Diabetes Res Care 2016;4:e000195.
30. Cho HM, Kim HC, Lee JM, Oh SM, Choi DP, Suh I. The association between serum albumin levels and metabolic syndrome in a rural population of Korea. J Prev Med Public Health 2012;45:98-104.
31. Cespedes Feliciano EM, Rifas-Shiman SL, Quante M, Redline S, Oken E, Taveras EM. Chronotype, social jet lag, and cardiometabolic risk factors in early adolescence. JAMA Pediatr 2019;173:1049-1057.
32. Morse SA, Ciechanowski PS, Katon WJ, Hirsch IB. Isn't this just bedtime snacking? The potential adverse effects of night-eating symptoms on treatment adherence and outcomes in patients with diabetes. Diabetes Care 2006; 29:1800-1804.
33. Yoshida J, Eguchi E, Nagaoka K, Ito T, Ogino K. Association of night eating habits with metabolic syndrome and its components: a longitudinal study. BMC Public Health 2018;18:1366.
34. Islam Z, Akter S, Kochi T, Hu H, Eguchi M, Yamaguchi M, et al. Association of social jetlag with metabolic syndrome among Japanese working population: the Furukawa Nutrition and Health Study. Sleep Med 2018;51:53-58.
35. Calugi S, Dalle Grave R, Marchesini G. Night eating syndrome in class II-III

obesity: metabolic and psychopathological features. Int J Obes (Lond) 2009; 33:899-904.

36. Dalle Grave R, Calugi S, Ruocco A, Marchesini G. Night eating syndrome and weight loss outcome in obese patients. Int J Eat Disord 2011;44:150-156.

37. Allison KC, Wadden TA, Sarwer DB, Fabricatore AN, Crerand CE, Gibbons LM, et al. Night eating syndrome and binge eating disorder among persons seeking bariatric surgery: prevalence and related features. Surg Obes Relat Dis 2006;2:153-158.

38. Tomizawa A, Nogawa K, Watanabe Y, Oishi M, Tanaka K, Sakata K, et al. Effect of circadian rhythm type on serum lipid levels in shift workers: a 5-year cohort study. Chronobiol Int 2019;36:751-757.

39. Kantermann T, Duboutay F, Haubruge D, Hampton S, Darling AL, Berry JL, et al. The direction of shift-work rotation impacts metabolic risk independent of chronotype and social jetlag--an exploratory pilot study. Chronobiol Int 2014;31:1139-1145.

40. Juda M, Vetter C, Roenneberg T. The Munich chronotype questionnaire for shift-workers (MCTQShift). J Biol Rhythms 2013;28:130-140.

41. Koopman ADM, Rauh SP, van't Riet E, Groeneveld L, van der Heijden AA, Elders PJ, et al. The association between social jetlag, the metabolic syndrome, and type 2 diabetes mellitus in the general population: the New Hoorn study. J Biol Rhythms 2017;32:359-368.

42. Wong PM, Hasler BP, Kamarck TW, Muldoon MF, Manuck SB. Social jetlag, chronotype, and cardiometabolic risk. J Clin Endocrinol Metab 2015;100: 4612-4620.

43. Iwasaki M, Hirose T, Mita T, Sato F, Ito C, Yamamoto R, et al. Morningness-eveningness questionnaire score correlates with glycated hemoglobin in middle-aged male workers with type 2 diabetes mellitus. J Diabetes Investig 2013; 4:376-381.

44. McMahon DM, Burch JB, Youngstedt SD, Wirth MD, Hardin JW, Hurley TG, et al. Relationships between chronotype, social jetlag, sleep, obesity and blood pressure in healthy young adults. Chronobiol Int 2019;36:493-509.
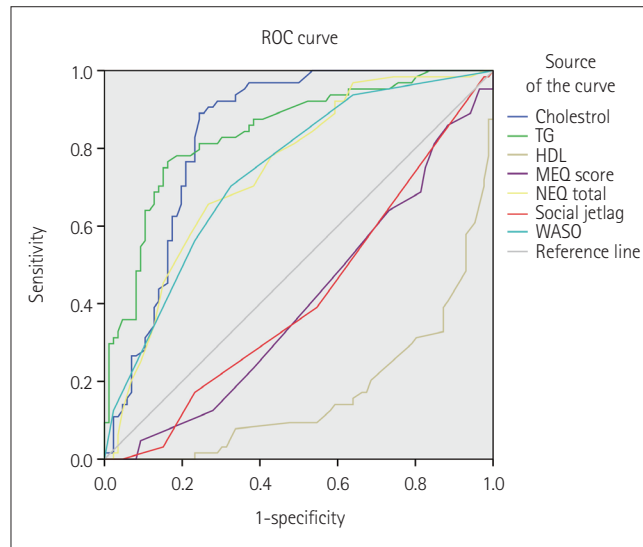
Supplementary Figure 1. ROC curve for risk factors of metabolic and night eating syndrome. ROC: receiver operating characteristic, TG: total cholesterol, HDL: high-density lipoprotein, MEQ: Morningness-Eveningness Questionnaire, NEQ: Night Eating Questionnaire, WASO: wake time after sleep onset.