The Impact of Obesity and Its Associated Sleep Disorders Either Alone or in Combination towards Systemic Diseases in Turkey

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Authors' contributions

*This work was carried out in collaboration among all authors. Author ZZU designed the study, wrote
the protocol and wrote the first draft of the manuscript. Author AUD performed the statistical analysis,
managed the analyses of the study. The other authors managed the literature searches. All authors
read and approved the final manuscript.*

Article Information

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ABSTRACT

Aims: Both obesity and sleep disorders represent an important public health problem. In this
study, the prevalence and consequences of obesity and associated sleep disorders were
investigated in the Turkish adult population.

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Methodology: Data were analyzed in 5019 subjects who had available body mass index (BMI) data from a population-based study interviewer-administered questionnaire (Turkish Adult Population Epidemiology of Sleep Disorders study: TAPES, original sample: 5521). Obesity was defined and classified by BMI into four groups as underweight (BMI<18 kg/m^2), normal (18≤BMI<25 kg/m^2), overweight (25≤BMI<30 kg/m^2), and obese (BMI >30 kg/m^2). Insomnia was defined according to the DSM-IV criteria, habitual snoring and risk for sleep-related breathing disorders (SDB) using the Berlin questionnaire, excessive daytime sleepiness with the Epworth sleepiness scale score, and restless legs syndrome (RLS) according to symptoms as per the International Restless Legs Syndrome Study Group criteria.

Results: The underweight, normal, overweight, and obesity rates were 2.9%, 40.5%, 34.3%, and 22.3%, respectively. Obesity was more common in women, and in the middle age, divorced/widow, lower education status, ex-smoker, low-income, and no regular exercise groups After the adjustment for age, gender, smoking status, educational status and income levels obesity was associated with the increased risk of SDB (OR: 13.03, 95%CI: 9.91-17.14), RLS (OR: 1.43, 95%CI: 1.01-2.02). The risk of heart disease, hypertension, diabetes mellitus, and hospitalization in the last year was higher in the obese population even after adjusting for age, sex, smoking status, educational status, and income levels [OR=2.06 (1.50-2.82), OR=3.45 (2.64-4.51), OR=2.93 (2.05-4.16), and OR=1.55 (1.22-1.98) respectively]. The risk of heart disease increased in subjects who were overweight and obese who had a high risk of SDB, and subjects with obesity who had RLS. The diabetes mellitus risk increased in subjects with obese who had a high risk of SDB or RLS.

Conclusion: Obesity was associated with a high risk of systemic diseases and obesity together with sleep disorders was associated with a higher risk of systemic diseases such as heart disease and diabetes. If confirmed with prospective longitudinal studies with objective measurements, screening for sleep-related symptoms could help to identify adults with obesity at high risk for heart disease and diabetes, and implementation of preventive measures and the proper management of these populations.

1. INTRODUCTION

According to the World Health Organization (WHO), obesity is a chronic condition defined by increased body mass index (BMI >30 kg/m^2). Obesity and its consequences represent a major public health problem. The prevalence of obesity has been increasing worldwide [1]. Epidemiologic studies from different parts of the world found the prevalence of obesity in a large range of 5-75% [2]. The prevalence of obesity is influenced by several environmental, sociodemographic and medical factors including sex, age, marital status, income, educational level, working status, and comorbidities including psychiatric, cardiovascular and pulmonary disorders [3-5].

There is growing research evidence for an association between sleep disorders and obesity [6-8]. Sleep disorders, especially sleep-related breathing disorders and insomnia, may also contribute to obesity or vice versa [9,10] Both have many mortal consequences, which are essential for the planning and implementation of public health policies [11-15].

This is the first population-based study in Turkey that aimed to: (1) investigate the prevalence of obesity and its sociodemographic and clinical correlates, (2) to explore whether any sleep disorders existed related to obesity in Turkey; and (3) to determine the risk of the systemic diseases such as hypertension (HT), diabetes mellitus (DM). lung disease, malignancy and rate of hospitalization in population with obesity and/or sleep disorders.

2. MATERIALS AND METHODS

The Research methods were described in a previous article [16]. Below we summarize the information related to our analysis.

2.1 Sampling

This study a sub-analysis of the Turkish Adult Population Epidemiology of Sleep Disorders (TAPES) study, which investigated a random sample of 5521 individuals designed through a multi-stage stratified sampling plan, representative of the general adult population in the entire country [16]. In this analysis, we included 5019 of sample the sample, who had available BMI measurements.

2.2 Definition of Obesity

Height and weight measurements were obtained when the subjects were in light clothes and without shoes, to the nearest 1 cm and 0.5 kg, respectively. Obesity is classified in terms of BMI (weight/height^2) into four groups as underweight (BMI <18/kg/m^2), normal (18≤BMI<25 kg/m^2), overweight (25≤BMI<30 kg/m^2), and obese (BMI>30 kg/m^2) [17].

2.3 Sleep Questionnaire

A questionnaire consisting of 132 questions was used as a data collection tool. The questions were determined by the Turkish Sleep Medicine Society (TSMS) Executive Board. The questionnaire included information on demographics, occupational history, educational and socioeconomic status, health problems, sleeping habits, depressive symptoms, sleep symptoms, and sleep disorders. Questions on sleep symptoms and disorders were selected by the "TAPES investigators" team. The Epworth Sleepiness Scale (ESS) was used to assess excessive daytime sleepiness (EDS). The ESS has been validated in Turkish [18]. Questions on restless legs syndrome (RLS) were adapted from the criteria proposed by the International Restless Legs Syndrome Study Group and used in a previous epidemiologic investigation of RLS in Turkey [19,20]. A draft questionnaire was revised after a pilot study including 86 participants applied in a range of hospitals in Istanbul, Ankara, Izmir, and Kayseri. Scales were tested for reliability and content validity (Chronbach's alpha >0.70). The Charlson Morbidity Index was used to assess the presence of physician-diagnosed systemic diseases.

2.4 Definition of Sleep Disorders

Questionnaire items used for these definitions are provided below.

2.4.1 Restless legs syndrome (RLS)

Having unpleasant feelings in one's legs like tingling, restlessness or throbbing when resting (e.g. sitting or lying) frequently (5-15 times a month) or almost every day (16 times a month or more), and affirming that: (i) this happens sometimes in one and sometimes in the other leg, (ii) it increases during the evening, (iii) moving leads to partial relief, and (iv) this condition hampers sleeping [19-21].

2.5 Insomnia

A "Yes" response to any of the following, as adapted from DSM–IV–TR:17

(1) Difficulty initiating sleep at least three times a week for a month or more.
(2) Difficulty maintaining sleep, fragmented sleep at least three times a week for a month or more.
(3) Early morning awakening at least once a week in the last month.

2.5.1 Risk of sleep-disordered breathing (SDB)

A positive score in at least two of the three categories in the Berlin Questionnaire, including questions on snoring, witnessed apnea, daytime sleepiness, hypertension, and measurement of BMI [22].

2.6 Habitual Snoring

Frequency of snoring described as "nearly every day" in response to the Berlin questionnaire.

2.7 Excessive Daytime Sleepiness

Scoring above 10 in the ESS, which has been validated in Turkish [18,23].

2.8 Poor Sleep Quality

Sleep quality was assessed using the Pittsburg Sleep Quality Index (PSQI), which has been translated and validated in Turkish [24,25]. The PSQI includes questions on sleep quality, sleep latency, sleep duration, drug usage, sleep habits, sleep disorders, drug use and daytime function in the last month. Scores equal to or higher than 6 were denoted as poor sleep quality.

2.9 Sample Size Calculation and Statistical Analysis

Prevalence of obesity, systemic diseases and sleep disorders were tabulated as percentages. Associations between predefined risk factors and obesity were compared by chi-square testing. Predefined factors included age in categories (years of age: 18-24, 25-44, 45-64 and 65+), smoking status (Nonsmoker, Ex-smoker and Current smoker), household monthly income level as converted to USD based on the currency as of the time of the study (<500 USD, 500–999

USD, 1000–1499 USD and ≥1500 USD), education status according to the question: "Which school did you graduate last?"(No education, Literate, Primary school (5 years), Secondary school (+3 years), High school (+3 years), University (+2 years or more)) and regular exercise (Exercising at least 5 times a week for a minimum of 30 min in each session). Subjects with missing information were few, and were not analyzed in the categories of this information. Multiple regression logistic regression models were constructed to assess the independent association between obesity and sleep disorders, and systemic diseases. Adjustments were made for the predefined risk factors. Regular exercise was not included in the models because it could be in the same causative change of systemic diseases with obesity. Odds ratios and 95% Confidence Intervals (95% CI's) were listed in the tables below the figures. P-values less than 0.05 were considered as significant in the two-tailed statistical testing. SPSS, 18 versions were used in the analysis.

Sample size calculation and Investigation of Interaction: In the TAPES survey, sample size calculation was based on prevalence estimations [16]. The sample size calculation was performed according to different prevalence estimates between 5% and 15%, and the margin of error between 0.625% and 1.25%, for 95% confidence intervals (CI). These assumptions yielded the sample size of 4671 for a prevalence estimate of 5% and margin of error of 0.625% (i.e. for 5% of prevalence estimate, a 95% CI of 4.3% to 5.6%). This number was corrected for a possible case response rate of 85-90%, to arrive at the final sample size of 5520. By using the sample size table for logistic regression analysis, with 1-beta 0.20, alpha 0.05, odds ratio 2, the sample size was calculated as 285 for univariate logistic regression analysis [26]. After the corrections for multivariate logistic regression analysis 1- ρ^2, where ρ is the multiple correlation coefficient relating to the specific covariate to the remaining covariates, the sample size was calculated as 313, 339 and 380, for ρ values of 0.3, 0.4 and 0.5, respectively.

We investigated the interaction between obesity and sleep disorders for the systemic diseases by repeating the analysis in the groups with and without that sleep disorder. This analysis was restricted to the systemic diseases, which showed significant association with obesity, determined as the 95%CI of OR excluding 1.

Interaction was considered according to the additive risk model, which means that the relative risk estimate (OR) in the group with sleep disorder minus that in the group without sleep disorder exceeded 1.

3. RESULTS

The prevalence rates of underweight, normal, overweight, and obesity were 2.9%, 40.5%, 34.3%, and 22.3%, respectively, in the TAPES study. Some 56.6% of the Turkish population has a BMI over 25 kg/m^2. Several personal characteristics were significantly different between participants who were obese, overweight, normal, and underweight (p<0.05). Obesity was more common in women, and the middle age, divorced/widow, lower education status, ex-smoker, lower-income, and no regular exercise groups (Table 1).

As shown in Table 2, obesity was more common those with any comorbidities such as heart disease, hypertension, lung disease and DM.

As shown in Table 3, all of the sleep variables in the present study were significantly different between the obesity groups (p<0.05). The obesity prevalence was higher in the population with diseases such as insomnia, RLS, SDB risk, sleepiness, and poor sleep quality.

The risks of heart disease, HT, and DM, were higher in the obese population. OR values were OR=2.06 (1.50-2.82), OR=3.45 (2.64-4.51) and OR=2.93 (2.05-4.16) for the risk of heart disease, HT and DM in the obese population in the logistic regression analysis model after adjusting for age, sex, smoking status, educational status, and income levels respectively. Hospitalization in the last year was higher in the obese population even after adjusting for age, sex, smoking status, educational status, and income levels [OR=1.55 (1.22-1.98)] (Fig. 1).

Fig. 2 shows the risk of sleep disorders and symptoms according to the BMI groups. Obesity was associated with a high risk of SDB, RLS, insomnia, and poor sleep quality, but after adjusting for age, sex, smoking status, educational status, and income levels, obesity was associated only with SDB and RLS. The risk of SDB and RLS was OR=13.03 (9.91-17.14) and OR=1.43 (1.01-2.02) in the obese population.

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Table 1. Association between BMI groups and personal characteristics

	n	Uwt% (SD)	Nm % (SD)	Owt % (SD)	Obs % (SD)	P
Total	5019	2.9 (0.2)	40.5 (0.7)	34.3 (0.7)	22.3 (0.6)	
Sex						
Male	2423	1.9 (0.3)	43.4 (1.0)	39.2 (1.0)	15.5 (0.7)	<0.001
Female	2596	3.8 (0.4)	37.9 (1.0)	29.8 (0.9)	28.5 (0.9)	
Age, yr						<0.001
18-24	742	9.0 (1.1)	68.5 (1.7)	18.3 (1.4)	4.2 (0.7)	
25-44	2388	2.7 (0.3)	44.6 (1.0)	34.1 (1.0)	18.6 (0.8)	
45-64	1468	0.6 (0.2)	24.5 (1.1)	39.9 (1.3)	35.1 (1.2)	
≥65	418	1.2 (0.5)	23.9 (2.1)	44.7 (2.4)	30.1 (2.2)	
Marital status						<0.001
Married	3733	1.7 (0.2)	35.4 (0.8)	37.5 (0.8)	25.4 (0.7)	
Single	930	7.7 (0.9)	66.3 (1.5)	20.6 (1.3)	5.3 (0.7)	
Divorced/widow	356	2.2 (0.8)	27.0 (2.4)	36.8 (2.6)	34.0 (2.5)	
Educational status						<0.001
No school	634	1.6 (0.5)	23.5 (1.7)	35.6 (1.9)	39.3 (1.9)	
Primary (5 yrs)	2112	1.7 (0.3)	32.3 (1.0)	38.0 (1.1)	28.0 (1.0)	
Secondary (8 yrs)	626	5.0 (0.9)	47.8 (2.0)	30.8 (1.8)	16.5 (1.5)	
High school (11 yrs)	1187	4.3 (0.6)	56.9 (1.4)	28.4 (1.3)	10.4 (0.9)	
University	459	3.7 (0.9)	49.7 (2.3)	35.9 (2.2)	10.7 (1.4)	
Smoking status						<0.001
Nonsmoker	2984	2.8 (0.3)	37.8 (0.9)	33.7 (0.9)	25.6 (0.8)	
Ex-smoker	346	1.2 (0.6)	26.6 (2.4)	42.8 (2.7)	29.5 (2.5)	
Current smoker	1689	3.4 (0.4)	48.2 (1.2)	33.6 (1.1)	14.8 (0.9)	
Household income*						<0.001
<750 TL	1852	2.6 (0.4)	35.6 (1.1)	35.5 (1.1)	26.3 (1.0)	
750-1000 TL	1212	3.5 (0.5)	37.5 (1.4)	34.2 (1.4)	24.8 (1.2)	
1000-1500 TL	1074	3.3 (0.5)	44.4 (1.5)	33.3 (1.4)	19.0 (1.2)	
1500-2000 TL	492	2.8 (0.7)	47.2 (2.3)	33.7 (2.1)	16.3 (1.7)	
>2000 TL	373	1.3 (0.6)	54.4 (2.6)	32.7 (2.4)	11.5 (1.7)	
Regular exercise						0.001
No	3617	2.8 (0.3)	39.2 (0.89)	34.3 (0.8)	23.7 (0.7)	
Yes	1402	3.2 (0.5)	43.9 (1.3)	34.3 (1.3)	18.6 (1.0)	

Uwt: underweight, Nm: Normal, Owt: overweight, Obs: Obese, TL: Turkish Liras
*: as for the time of the survey, categories of household income were <750 TL: <500 US dollars, 750-1000 TL: 500-666 US dollars, 1000-1500 TL: 667-1000 US dollars, 1500-2000 TL: 1001-1333 US dollars, >2000 TL: >1333 US dollars

The obese population with sleep symptoms and disorders had a higher risk of systemic diseases such as heart disease, HT, and DM. The interaction between obesity and sleep disorders for the risk of systemic diseases was assessed using logistic regression analysis models in the subgroups of sleep disorders. Interaction was defined as when the OR in the subgroup analysis was significant and higher than the OR in the all groups model. The results for heart disease and DM and are shown in Fig. 3. The risk of heart disease increased in subjects who were overweight and obese who had a high risk of SDB, and subjects with obesity who had RLS. The DM risk increased in subjects with obesity who had a high risk of SDB or RLS.

4. DISCUSSION

In this subgroup of the epidemiologic study of a sample representative of the adult population of Turkey, we investigated the prevalence, association, and consequences of obesity and sleep disorders including insomnia, RLS, EDS, and the risk of SDB using an interviewer-administered questionnaire. The four main findings of this study were as follows: (1) almost 56.6% of adults in Turkey had a BMI over 25 kg/m^2; (2) the prevalence of insomnia, RLS, EDS, the risk of SDB, and poor sleep quality were significantly more common in the obese population than in the non-obese population (3) obesity was associated with a higher prevalence of SDB and RLS; and (4) obesity, together with

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sleep disorders was associated with a higher prevalence of heart disease and DM. The most important finding of this study is that sleep disorders in the obese populationhave higher physician-diagnosed systemic diseases in Turkey.

Table 2. Association between BMI groups and systemic diseases and hospitalization in the last year

	n	Uwt% (SD)	Nm % (SD)	Owt % (SD)	Obs % (SD)	P
Comorbidities						
No	3736	3.4 (0.3)	46.5 (0.8)	33.4 (0.8)	16.7 (0.6)	<0.001
1	861	1.4 (0.4)	26.8 (1.5)	38.0 (1.7)	33.8 (1.6)	
2	289	1.7 (0.8)	18.7 (2.3)	35.6 (2.8)	43.9 (2.9)	
≥3	133	0 (0)	9.0 (2.5)	35.3 (4.1)	55.6 (4.3)	
Heart disease						<0.001
No	4661	3.1 (0.3)	41.9 (0.7)	34.1 (0.7)	20.9 (0.6)	
Yes	358	0 (0)	22.6 (2.2)	37.2 (2.6)	40.2 (2.6)	
DM						<0.001
No	4696	3.1 (0.3)	42.2 (0.7)	34.2 (0.7)	20.5 (0.6)	
Yes	323	0 (0)	15.8 (2.0)	36.8 (2.7)	47.4 (2.8)	
Hypertension						<0.001
No	4338	3.2 (0.3)	44.4 (0.8)	34.1 (0.7)	18.3 (0.6)	
Yes	681	0.9 (0.4)	15.7 (1.4)	35.7 (1.8)	47.7 (1.9)	
Lung disease						<0.001
No	4705	2.9 (0.2)	41.3 (0.7)	34.2 (0.7)	21.6 (0.6)	
Yes	314	2.9 (0.9)	29.3 (2.6)	35.7 (2.7)	32.2 (2.6)	
Cancer						0.02
No	4993	2.9 (0.2)	40.6 (0.2)	34.4 (0.7)	22.2 (0.6)	
Yes	26	7.7 (5.2)	23.1 (5.2)	26.9 (8.7)	42.3 (9.7)	
Hospitalization in the last year						<0.001
No	*4430*	2.9 (0.3)	41.6 (0.7)	34.7 (0.7)	20.8 (0.6)	
Yes	*579*	2.9 (0.7)	31.4 (1.9)	32.1 (1.9)	33.5 (2.0)	

Uwt: underweight, Nm: Normal, Owt: overweight, Obs: Obese
DM: diabetes mellitus

Table 3. Association between BMI groups and sleep disorders

	n	Uwt% (SD)	Nm % (SD)	Owt % (SD)	Obs % (SD)	P
Poor sleep quality						<0.001
No	*3925*	2.8 (0.3)	42.0 (0.8)	34.7 (0.8)	20.6 (0.6)	
Yes	*1094*	3.3 (0.5)	35.4 (1.4)	34.7 (1.4)	20.6 (1.2)	
Insomnia excluding RLS						0.001
No	*4177*	2.8 (0.3)	41.7 (0.8)	34.9 (0.7)	20.5 (0.6)	
Yes	*579*	3.8 (0.8)	39.0 (2.0)	30.2 (1.9)	26.9 (1.8)	
Sleepiness (ESS>10)						0.001
No	*4746*	2.8 (0.2)	40.8 (0.7)	34.6 (0.7)	21.7 (0.6)	
Yes	*273*	4.0 (1.2)	35.5 (2.9)	28.9 (2.7)	31.5 (2.8)	
RLS						<0.001
No	*4756*	3.0 (0.2)	41.4 (0.7)	34.4 (0.7)	21.3 (0.6)	
Yes	*263*	1.5 (0.7)	24.7 (2.7)	33.8 (2.9)	39.9 (3.0)	
Risk of SDB						<0.001
No	*4333*	3.2 (0.3)	45.2 (0.8)	36.3 (0.7)	15.2 (0.5)	
Yes	*686*	0.7 (0.3)	10.9 (1.2)	21.7 (1.6)	66.6 (1.8)	

Uwt: underweight, Nm: Normal, Owt: overweight, Obs: Obese
RLS: restless legs syndrome, SDB: sleep-disordered breathing, ESS: Epworth Sleepiness Scale
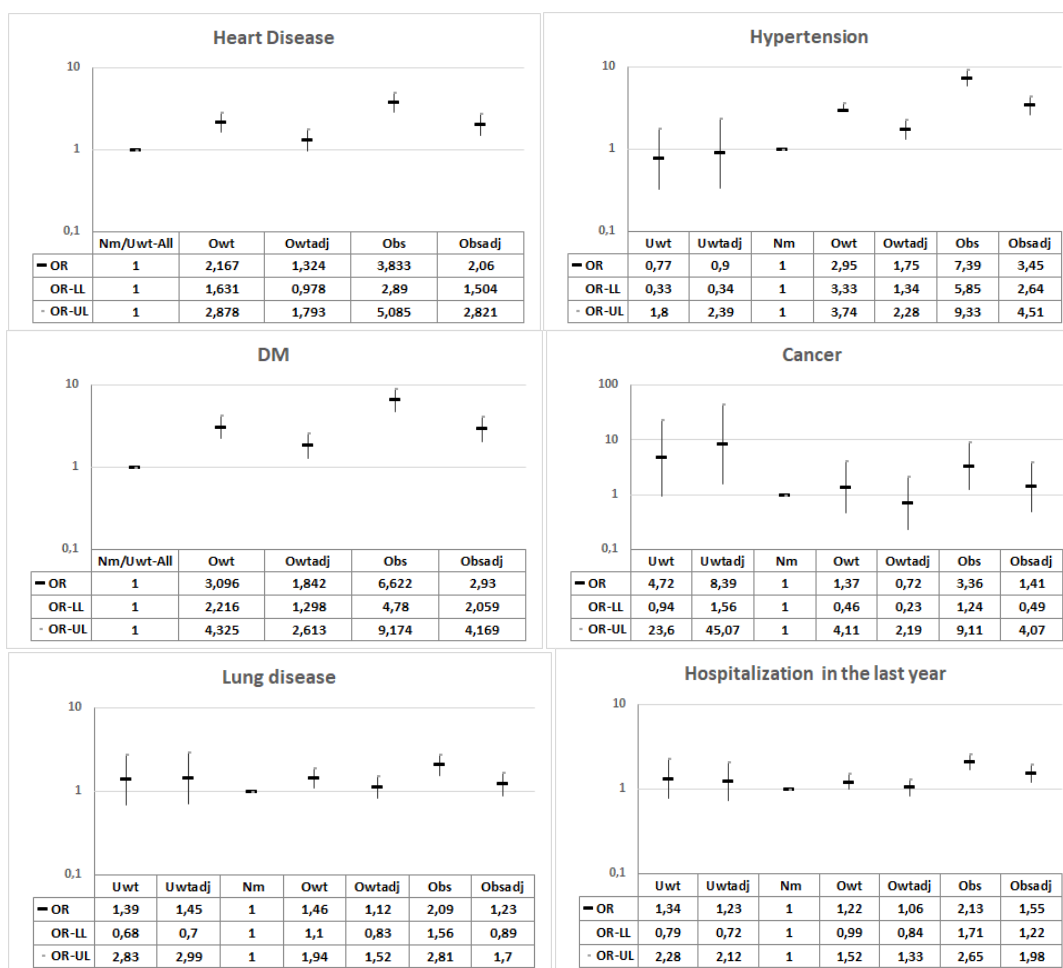
Fig. 1. Association between BMI groups and systemic diseases and hospitilization in the last year
Association between BMI groups and systemic diseases and hospitalization in the last year, crude and adjusted for age, sex, smoking status, educational status and income levels. Normal BMI group was the reference group. OR's and 95%CI's are provided in the figures.
Uwt: underweight, Nm: Normal, Owt: overweight, Obs: Obese, DM:diabetes mellitus, adj: adjusted as defined above
ORs cannot be calculated for the underweight group in heart disease and DM models

Heart Disease

	Nm/Uwt-All	Owt	Owtadj	Obs	Obsadj
OR	1	2,167	1,324	3,833	2,06
OR-LL	1	1,631	0,978	2,89	1,504
OR-UL	1	2,878	1,793	5,085	2,821

Hypertension

	Uwt	Uwtadj	Nm	Owt	Owtadj	Obs	Obsadj
OR	0,77	0,9	1	2,95	1,75	7,39	3,45
OR-LL	0,33	0,34	1	3,33	1,34	5,85	2,64
OR-UL	1,8	2,39	1	3,74	2,28	9,33	4,51

DM

	Nm/Uwt-All	Owt	Owtadj	Obs	Obsadj
OR	1	3,096	1,842	6,622	2,93
OR-LL	1	2,216	1,298	4,78	2,059
OR-UL	1	4,325	2,613	9,174	4,169

Cancer

	Uwt	Uwtadj	Nm	Owt	Owtadj	Obs	Obsadj
OR	4,72	8,39	1	1,37	0,72	3,36	1,41
OR-LL	0,94	1,56	1	0,46	0,23	1,24	0,49
OR-UL	23,6	45,07	1	4,11	2,19	9,11	4,07

Lung disease

	Uwt	Uwtadj	Nm	Owt	Owtadj	Obs	Obsadj
OR	1,39	1,45	1	1,46	1,12	2,09	1,23
OR-LL	0,68	0,7	1	1,1	0,83	1,56	0,89
OR-UL	2,83	2,99	1	1,94	1,52	2,81	1,7

Hospitalization in the last year

	Uwt	Uwtadj	Nm	Owt	Owtadj	Obs	Obsadj
OR	1,34	1,23	1	1,22	1,06	2,13	1,55
OR-LL	0,79	0,72	1	0,99	0,84	1,71	1,22
OR-UL	2,28	2,12	1	1,52	1,33	2,65	1,98

Several sociodemographic and medical factors are associated with obesity including sex, age, marital status, income, educational level, working status, and somatic or psychiatric conditions [3,4]. Obesity was more common in women, and the middle age, divorced/widow, lower education status, ex-smoker, lower-income, and no regular exercise groups in the present study. Lower educational status and socioeconomic status could be related to unhealthy dietary habits and obesity [3].

The prevalence of insomnia in patients with obesity (19.8±1.4%) was higher compared with non-obese patients (14±0.6%). Some recent studies suggested that sleep played an important role in obesity. No systematic reviews have specifically investigated the association between obesity and insomnia. A recent meta-analysis reviewed the past 10 years of findings on the association between insomnia and obesity, reporting that a small, significant cross-sectional correlation (r=0.06, p=0.03) was found between insomnia and BMI. Based on three studies, the odds of developing future insomnia among those who had obesity were not significantly greater than for those who were normal weight (OR=1.07, p=0.40) [27]. Contrary to these data,

we observed that the prevalence of insomnia was higher among the obese population. But at the same time similar to this data, obesity was not associated with insomnia after adjusting for age, sex, smoking status, educational status, and income levels in our study.

RLS has been reported to occur more frequently in obese individuals than in those with normal weight [28,29]. The prevalence rate of RLS in our study (9.5%) in patients with obesity, which was in the upper level of the rate of RLS in Turkey, was higher than in non-obese patients (4.0%), similar to these studies. One of the most important findings of the present study is that heart disease risk increased in subjects with

obesity who had RLS. Obesity and RLS are both associated with hypofunction of dopamine in the central nervous system. The United States cohorts, the Nurses' Health Study II, and the Health Professional Follow-up Study examined whether individuals who were obese had an increased risk of RLS [28]. An association between obesity and a higher RLS prevalence was seen in this and most studies, but not all [28,30-32]. The mechanisms through which obesity is associated with RLS are likely to be multiple. Cardiovascular diseases are associated with an increased risk of both obesity and RLS, and it has been suggested that vascular pathology may contribute to RLS [33,34]. Obesity and RLS could share some unknown common
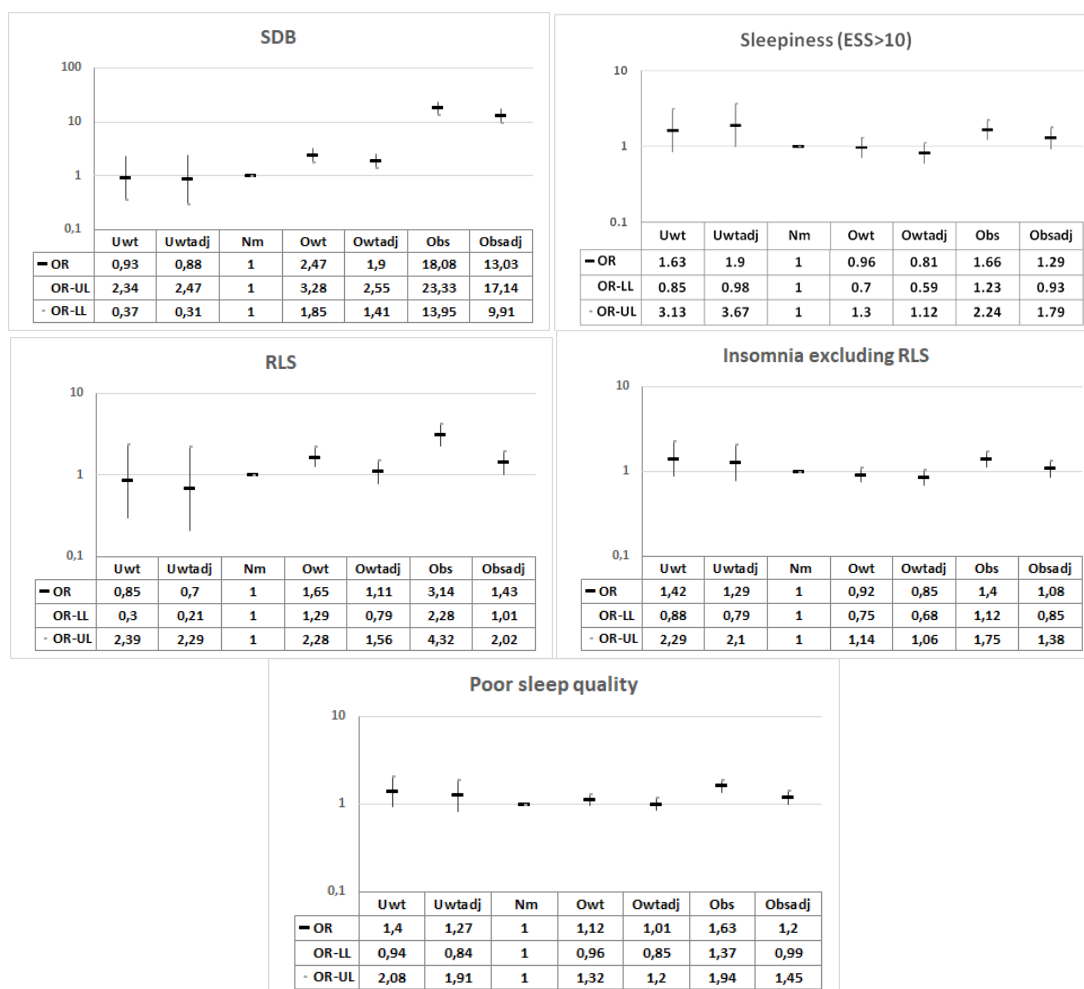
SDB

	Uwt	Uwtadj	Nm	Owt	Owtadj	Obs	Obsadj
OR	0,93	0,88	1	2,47	1,9	18,08	13,03
OR-UL	2,34	2,47	1	3,28	2,55	23,33	17,14
OR-LL	0,37	0,31	1	1,85	1,41	13,95	9,91

Sleepiness (ESS>10)

	Uwt	Uwtadj	Nm	Owt	Owtadj	Obs	Obsadj
OR	1.63	1.9	1	0.96	0.81	1.66	1.29
OR-LL	0.85	0.98	1	0.7	0.59	1.23	0.93
OR-UL	3.13	3.67	1	1.3	1.12	2.24	1.79

RLS

	Uwt	Uwtadj	Nm	Owt	Owtadj	Obs	Obsadj
OR	0,85	0,7	1	1,65	1,11	3,14	1,43
OR-LL	0,3	0,21	1	1,29	0,79	2,28	1,01
OR-UL	2,39	2,29	1	2,28	1,56	4,32	2,02

Insomnia excluding RLS

	Uwt	Uwtadj	Nm	Owt	Owtadj	Obs	Obsadj
OR	1,42	1,29	1	0,92	0,85	1,4	1,08
OR-LL	0,88	0,79	1	0,75	0,68	1,12	0,85
OR-UL	2,29	2,1	1	1,14	1,06	1,75	1,38

Poor sleep quality

	Uwt	Uwtadj	Nm	Owt	Owtadj	Obs	Obsadj
OR	1,4	1,27	1	1,12	1,01	1,63	1,2
OR-LL	0,94	0,84	1	0,96	0,85	1,37	0,99
OR-UL	2,08	1,91	1	1,32	1,2	1,94	1,45

Fig. 2. Association between BMI and sleep disorders
Association between BMI groups and sleep disorders, crude and adjusted for age, sex, smoking status, educational status and income levels. Normal BMI group was the reference group. OR's and 95%CI's are provided in the figures.
Uwt: underweight, Nm: Normal, Owt: overweight, Obs: Obese, RLS: restless legs syndrome, SDB: sleep-disordered breathing, ESS: Epworth Sleepiness Scale,adj: adjusted as defined above
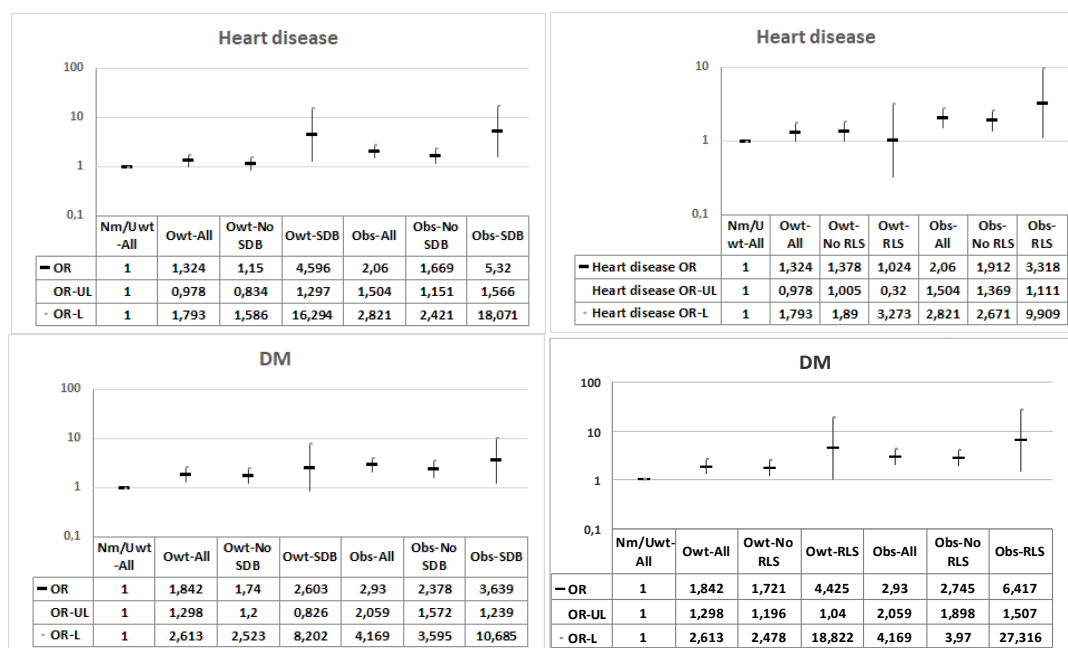
Fig. 3. Interaction between obesity and sleep disorders for DM and Heart disease
Association between BMI groups and Heart Disease and DM, adjusted for age, sex, smoking status, educational status and income levels. Normal and underweight BMI groupswereModels were constructed in groups with and without SDB and RLS, separately. OR's and 95%CI's in the subgroups of SDB and No-SDB, and RLS and No-RLD are provided in the figures. Additive interaction was found for DM between RLS and Owt, and between RLS and Obs; for Heart Disease between RLS and Obs, and between SDB and Owt, SDB and Obs
Nm/Uwt: Normaland underweight, Owt: overweight, Obs: Obese, DM:diabetes mellitus, RLS: restless legs syndrome, SDB: sleep- disordered breathing, All: The entire group

causes. Further experimental studies are needed to explore the biologic mechanisms underlying the potential roles of obesity in RLS.

Obesity has important health consequences, including an increased risk of a host of diseases including degenerative joint disease, type 2 diabetes, cardiovascular disease, and obesity-associated malignancies [5,35]. Risks of heart disease, HT, DM, and hospitalization in the last year were higher in the obese population in the present study, as expected, and consistent with the literature. An increased risk of coronary heart disease, heart disease, congestive heart failure, hypertension, stroke, and DM has been shown in patients with SDB in previous studies [11-13]. Obesity was associated with a high risk of systemic diseases, and obesity together with sleep disorders was associated with a higher risk of systemic diseases such as heart disease and diabetes in the present study. To our knowledge, this is the first study to report an increased risk of DM in subjects with obesity who have RLS; a very limited conflicting paper reported increased heart disease risk in subjects with obesity who had a high risk of SDB and RLS. Although the

mechanisms are not clear yet, RLS is associated with many systemic diseases, including obesity, diabetes and cardiovascular diseases, [28,36-39]. In a study obesity was evaluated as a possible risk factor for RLS and the presence of RLS was correlated with obesity and vascular risk factors at a significant level [29]. The Nagahama study evaluated the impact of obesity on diabetes and hypertension and reported that the associations of obesity with diabetes or hypertension were indirectly mediated by SDB (24.0% and 21.5%, respectively) [40]. The authors of another study hypothesized that obesity would increase the effect of nocturnal hypoxemia on the risk of incident cardiovascular disease [41]. In adults with suspected obstructive sleep apnea, the highest cardiovascular risk was found in obese patients with nocturnal oxygen desaturation; however, the effect of these two factors together did not exceed the effect of each factor considered individually in that study.

Obesity together with SDB was associated with higher risk of diabetes in this study. The relationship between SDB and diabetes is bidirectional. SDB-induced intermittent hypoxia

and arousals may result in decreased insulin sensitivity, sympathetic excitation, and systemic inflammation, eventually leading to diabetes. At the same time, uncontrolled glucose may desensitize the carotid body and pharyngeal dilator muscle, which promotes SDB. Obesity and diabetic neuropathy may worsen SDB disease severity. The Systematic Literature Review and Meta-Analysis of Metabolic Consequences of Obstructive Sleep Apnea in Adolescents with obesity concluded that obesity led to increased metabolic risk, and OSA appeared to independently increase metabolic impairment. The authors stated that adolescents with obesity should be frequently screened for OSA to determine the need for treatment and reduce this metabolic burden [42].

There are several strengths to this study. First, the sample was a random, nationally representative population sample, which makes the findings generalizable for the general adult population of Turkey. Second, the larger sample size allowed us to control for several confounders for obesity. However, our study also has several limitations. First, the lack of polysomnography) for the diagnosis of SDB, and objective assessments of blood pressure, systemic diseases, and cardiovascular risk factors such as hyperlipidemia are limitations of the study. Second, because of the cross-sectional design of the study, it is difficult to interpret the causality of the associations found. We tried to use the term obesity together with sleep disorders instead of sleep-related obesity or obesity-related sleep disorders. Therefore, longitudinal studies with objective measurements such as PSG are necessary to establish a cause-effect relationship.

5. CONCLUSION

These findings would help in the assessment of the health burden of obesity and sleep disorders, especially SDB and RLS, and address risk groups for the planning and implementation of healthcare and treatment guidelines. A causal relationship between sleep and obesity still has to be confirmed through prospective longitudinal studies with objective measurements, and whether treatment of one of the disorders would ameliorate the other has to be confirmed in well-controlled interventional trials. If confirmed, screening for sleep-related symptoms could help to identify adults with obesity at high risk for heart disease and diabetes, and implementation of

preventive measures and the proper management of these populations.

CONSENT

Informed consent was given by the participants.

ETHICAL APPROVAL

Ethical approval was obtained from the Scientific Research Assessment Commission of Hacettepe University (HEK 10/34-25).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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