

Gastroesophageal Reflux, Laryngopharyngeal Reflux and Sleep Quality in Adult Population

Yetişkin Nüfuslarda Gastroözofageal Reflü, Laringofaringeal Reflü ve Uyku Kalitesi

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ABSTRACT Objective: This study was conducted to determine the interrelationships of gastroesophageal reflux, laryngopharyngeal reflux and sleep quality in adults. Sleep quality in adults is important for health protection in terms of physiological and psychological and increasing performance. Recent studies have emphasized a strong association between sleep disorders and gastrointestinal disorders. **Material and Methods:** This cross-sectional study was carried out with 400 individuals who are >18 years old who were registered family health centers from east, west, north, and south of Elazığ province between April and June 2018. A Personal Information Form, Gastroesophageal Reflux Disease Questionnaire, Reflux Symptom Index, and the Pittsburgh Sleep Quality Index were used as data collection tools. **Results:** The results of simple linear regression indicate that Pittsburgh Sleep Quality Index global score was associated with Gastroesophageal Reflux Disease Questionnaire, Reflux Symptom Index, age, gender, educational status, marital status, working status, monthly income perception, health perception and the person living together. By the multiple regression analysis, Reflux Symptom Index, Gastroesophageal Reflux Disease Questionnaire, the employment status and being widow are the most correlated variables on the Pittsburgh Sleep Quality Index global score and explained 27% of the total variance. **Conclusion:** In addition to being a significant relationship between reflux and sleep quality, it can be asserted that some socio-demographic variables besides reflux is the important parameters required while evaluating the sleep-related problems.

ÖZET Amaç: Bu çalışma, erişkinlerde gastroözofageal reflü, laringofaringeal reflü ve uyku kalitesinin ilişkilerini belirlemek amacıyla yapılmıştır. Yetişkinlerde uyku kalitesi, fizyolojik ve psikolojik açıdan sağlığın korunması ve performansın artması açısından önemlidir. Son çalışmalar, uyku bozuklukları ve gastrointestinal bozukluklar arasında güçlü bir ilişki olduğunu vurgulamaktadır. **Gereç ve Yöntemler:** Bu kesitsel çalışma, Nisan ve Haziran 2018 tarihleri arasında Elazığ ilinin doğu, batı, kuzey ve güneyinden aile sağlığı merkezlerine kayıtlı 18 yaş ve üzeri 400 kişi ile gerçekleştirildi. Veri toplama araçları olarak Kişisel Bilgi Formu, Gastroözofageal Reflü Hastalığı Anketi, Reflü Semptom İndeksi ve Pittsburgh Uyku Kalitesi İndeksi kullanıldı. **Bulgular:** Basit doğrusal regresyon sonuçları, Pittsburgh Uyku Kalitesi İndeksi skorunun Gastroözofageal Reflü Hastalığı Anketi, Reflü Semptom İndeksi, yaş, cinsiyet, eğitim durumu, medeni durum, çalışma durumu, aylık gelir algısı, sağlık algısı ve birlikte yaşama ile ilişkili olduğunu göstermektedir. Çoklu regresyon analizi ile Reflü Semptom İndeksi, Gastroözofageal Reflü Hastalığı Anketi, istihdam durumu ve dul olma Pittsburgh Uyku Kalitesi İndeksi skorunda en çok ilişkili değişkenler olup toplam varyansın %27'sini açıklamıştır. **Sonuç:** Reflü ile uyku kalitesi arasında anlamlı bir ilişki olmasının yanı sıra reflü dışında bazı sosyodemografik değişkenlerin de uyku ile ilgili sorunları değerlendirirken gerekli olan önemli parametreler olduğu söylenebilir.

Keywords: Sleep quality; gastroesophageal reflux disease; laryngopharyngeal reflux

Anahtar Kelimeler: Uyku kalitesi; gastroözofageal reflü; laringofaringeal reflü

Sleep is considered as a significant variable of health, which substantially affects the quality of life and well-being of the individual, because it is an important process with physiological, psychological and

social dimensions which prepare the individual for the new day by enabling the body to be refreshed, the brain functions to be adjusted and the cells to be repaired. The quality of sleep, which is an important as-

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pect of this process, refers to the fact that the individual feels fit and rested, at his best in terms of body functions, ready for the next day and relaxed after waking up.^{1,2} According to studies, the incidence rate of poor sleep quality in adult individuals varies between 40% and 80%.^{3,4} Gastrointestinal diseases are known to be among the chronic diseases that negatively affect the quality of sleep.⁵⁻⁷ In fact, this situation is a cycle; while gastrointestinal diseases may lead to sleep disturbance, sleep disturbance may cause exacerbation of the gastrointestinal symptoms.⁸ Due to physiological changes during sleep, especially the incidence rate of reflux, which is a gastrointestinal disease, is high. It has been found out in the studies that there is a significant correlation between reflux and sleep problems, and the risk of reflux-related sleep disorders increases, resulting in low sleep quality.^{6,9}

Reflux can occur in two ways. The first is the gastroesophageal reflux caused by the passage of the acidic gastric contents into the esophagus or beyond and the oral cavity without any force, and the mucosal damage in the esophagus, the second is the atypical picture of laryngopharyngeal reflux, in which laryngopharyngeal symptoms are prominent, resulting from the effect of the gastric contents in the larynx and pharynx apart from the esophagus.⁵⁻⁷ It is known that both types of reflux lead to sleep problems and sleep problems trigger these diseases.⁸ Even though there is a relationship between sleep and reflux, it is quite difficult to determine the causes and effects of this condition.¹⁰ Sleep may change the physical mechanism of the esophagus by causing a deterioration in the normal esophageal acid clearance. As a result of the decrease in swallowing during sleep, a decrease also occurs in the primary peristaltic movements that are responsible for the reflux clearance volume in the esophagus. With the reduction in the salivary flow to the distal portion of the esophagus, and also in the salivary secretion during sleep, acid reflux occurs with decreased alkalization.¹¹ Along with the primary peristaltic movements, secondary peristaltic movements are also particularly effective in reducing salivary secretion throughout the night. The decreased secondary peristaltic response in people with sleep disorders disrupts the esophageal

acid clearance and leads to reflux.¹² With the significant decrease in basal pressure in the upper esophageal sphincter, the risk of aspiration increases. In addition, an increase in the gastric acid secretion and a decrease in gastric discharge occur during the night.¹¹ Sleep causes a change in the normal acid clearance of the esophagus and is more associated with the objective acid reflux parameters.¹³ Some studies indicate that the incidence rate of gastroesophageal reflux disease is 20% in the society.^{14,15} In our country, this rate has been detected as 27.5%.¹⁶ Diagnosing laryngoesophageal reflux is more difficult since its symptoms do not resemble those of classic gastroesophageal reflux disease, and therefore, it is sometimes defined as 'silent reflux'.⁵ The presence of laryngoesophageal reflux was detected in 10% of the patients who applied to the otolaryngology department.¹⁷ In the literature, there are many studies that investigate the correlation between gastroesophageal reflux disease and sleep.^{14,17-19} On the other hand, there are also studies that often examine the relationship between laryngoesophageal reflux and obstructive sleep apnea syndrome.^{5,20} When we have a look at the literature, studies that investigate the relationship between the presence of gastroesophageal reflux and laryngopharyngeal reflux (LPR) and sleep quality are quite limited even though there are many studies that separately examine the relationship between the presence of gastroesophageal reflux and LPR and individuals' sleep quality.^{13,16,21-25} In this context, this study was conducted to determine the effect of the presence of gastroesophageal reflux disease (GERD) and LPR on the sleep quality of individuals aged over 18 years in society, as well as other socio-demographic determinants.

MATERIAL AND METHODS

DESIGN AND PARTICIPANTS

This cross-sectional study was conducted between April and June 2018. The sample size of the study comprised individuals aged 18 and older who registered in family health centers (FHC) in the city center of Elazığ, Turkey. In order to determine the number of samples to be reached, stratified sampling method was used to represent the population well and

four FHC were selected from the east, west, south and north of Elazığ province. Each FHC was identified as a stratum and individual selection was made by considering the proportion of these four stratum in the population (stratum volume) to be proportional by observing less units from the stratum which less variation, much units from much variation and also considering the sampling cost. For this, the formula “ $n/N = \text{sample volume} / \text{population volume}$ ” was used and the result was found to be 400. Verbal informed consent was obtained from the individuals included in the study. The study protocol was approved by the Firat University Non-invasive Trials Ethics Committee (decree code: 171179, 16/11/2016) and complied with the principles of the Declaration of Helsinki.

DATA COLLECTION

The personal information form, GERD-Questionnaire (GERD-Q), Reflux Symptom Index (RSI), and Pittsburgh Sleep Quality Index (PSQI) were used as data collection tools.

Personal Information: The personal information form included information about the participant’s age, education status, marital status, employment status, perception of monthly income, health insurance, perception of health, and cohabitants. We assessed the perception of monthly income and health using a self-rating scale, which was a continuous scale anchored by three verbal descriptions ranged from very poor to very well.

Gastroesophageal Reflux Disease Questionnaire: The study of the Turkish validity and reliability of the GERD-Q was conducted by Mungan et al. The GERD-Q is a self-reported instrument and is used for diagnosing and managing GERD. It is useful for guiding treatment decisions by distinguishing between the patients who have frequent symptoms and occasional symptoms. The GERD-Q is 3-point Likert-type scale and consists of six items in total: four items about symptoms and two items about the effects of the disease. The frequency of symptoms in the previous week is assessed. Each item equates to a 0-3 score, with ascending scoring for items 1-2 and 5-6 (from 0 to 3), but with descending scoring for items 3-4 (from 3 to 0). The total score is obtained by adding the scores given for each item (0-18).¹⁸

In addition, the sum of the scores obtained from items 5 and 6 is the impact score (0-6). An impact score of 3 or more indicates that the individual is highly influenced by gastroesophageal reflux. The total score and impact score are used to calculate the overall GERD-Q score. A total score with a mean of 0-7 interprets a *low reflux probability*; a total score of 8-10 and an impact score of less than 3 or a total score of 11-18 and an impact score of less than 3 indicates an *inconveniencing GERD*; and a total score of 8-10 and an impact score of 3 or more or a total score of 11-18 and an impact score of 3 or more is considered as *disrupting GERD*.²⁶

Reflux Symptom Index: The RSI, which was developed by Belafsky et al. is an index consisting of nine questions that can be answered by patients and that allows the detection of LPR.²⁷ Each item scores between no problem (0) and severe problem (5), with a maximum total score of 45. In scoring, a total score of 13 or more is considered to indicate LPR.²⁸ In this study, the RSI was used by translating it into Turkish. Previously, a Turkish validity and reliability study of the RSI was not conducted, but it was stated in the literature that it could be used to diagnose patients.²⁸ The Cronbach alpha of the scale for this study was found to be 0.86 (Validity and reliability Cronbach’s alpha values of the scale could not be found).

Pittsburgh Sleep Quality Index: The PSQI, developed by Buysse et al., is a self-reporting scale used to evaluate the sleep quality and sleep disorder of individuals.²⁶ The Turkish adaptation of the scale was validated with a Cronbach’s alpha score of 0.80 by Agargün et al. The PSQI comprises 19 questions and contains seven domains: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, and sleep disturbances, use of sleep medication, and daytime dysfunction over the previous month. Each item on the scale is scored as 0-3 points, and the total score taken from the scale varies between 0 and 21, with a score of >5 indicating worse sleep quality. A higher score indicates a worse sleep quality. The first nine items of the PSQI contribute to the total score, but item 10, which is evaluated by the client’s bedmate or roommate, does not contribute to the PSQI score.²⁸ The Cronbach alpha of the scale for this study was found to be 0.81.

DATA ANALYSIS

We used SPSS for Windows version 21.0 for the statistical analysis of the research data. Normality of distribution of the data was evaluated using skewness and kurtosis values. Percentage, mean, and standard deviation (SD) were used for reporting demographic data of the participants, independent samples t-test and ANOVA were used for comparing the continuous data averages. For correlation analyses, Pearson's correlation test was performed. Binary logistic regression was used to obtain odds ratios (ORs) with 95% confidence interval (CI) to assess the associations between factors analyzed in the study and poor sleep quality. We considered participants with scores of ≤ 5 to have good sleep quality and those with scores of > 5 to have a poor sleep quality. The significance level was accepted as $p < 0.05$.

Ethical Consideration: An approval to conduct the research was obtained from the Ethics Committee of the Elazığ University Non-interventional Clinical Research, in addition to the necessary permissions obtained from the related institutions. The research was conducted in accordance with the Helsinki Declaration Principles

RESULTS

Table 1 shows that the participants had a mean age of 47.9 years (SD=15.8). Of these, 55.3% were male, 20.3% were illiterate, 71.5% were married, 3.7% lived alone, and 62.5% were unemployed. The majority of the participants had moderate level income and health perception, with 55.7 % and 43.5 % respectively. Study participants mostly had good sleep quality (60.7%), low reflux probability (67.3) and did not have indication of LPR (76.0).

Table 2 illustrates that there was a statistically significant difference in GERD-Q score according to age, educational level, marital status, working status, and health perception ($p < 0.05$), whereas there was no significant difference according to gender, cohabitants, and income perception level ($p > 0.05$). Additionally, we observed a significant difference in RSI scores according to age, educational level, marital status, working status, and income perception ($p < 0.05$, Table 2), but we found no significant difference in RSI scores and gender, co-

TABLE 1: Sociodemographic and sleep-related characteristics of participants.

Variables	n (%)
Age	
Young adults (<39)	133 (33.3)
Middle-aged adults (40-59)	163 (40.8)
Old adults (>60)	104 (26.0)
Educational level	
Illiterate	81 (20.3)
Elementary	156 (39.0)
High school	82 (20.5)
Bachelor	81 (20.2)
Gender	
Female	179 (44.7)
Male	221 (55.3)
Marital status	
Married	286 (71.5)
Single	71 (17.7)
Widow	43 (10.8)
Cohabitants	
Alone	15 (3.7)
Spouse or children	385 (96.3)
Working status	
Employed	150 (37.5)
Unemployed	250 (62.5)
Income perception	
Low	84 (21.0)
Moderate	223 (55.7)
High	93 (23.3)
Health perception	
Low	122 (30.5)
Moderate	174 (43.5)
High	104 (26.0)
Sleep quality	
Poor	157 (39.3)
Good	243 (60.7)
GERD-Q	
Low reflux probability	269 (67.3)
Inconveniencing GERD	120 (30.0)
Disrupting GERD	11 (2.8)
RSI	
Negative	304 (76.0)
Positive	96 (24.0)

GERD-Q: Gastroesophageal Reflux Disease Questionnaire; RSI: Reflux Symptom Index.

habitants, and health perception ($p > 0.05$, Table 2). Furthermore, we found that Global PSQI score had a statistically significant difference according to gender, marital status, working status, income perception [least significant difference (LSD) post hoc test: low > moderate and high] and health perception (LSD post

TABLE 2: The mean Global PSQI, GERD-Q, and RSI scores according to sociodemographic characteristics of participants.

Variables	GERD-Q Mean±SD	RSI Mean±SD	PSQI Mean±SD
Age*			
Young adults (<39)	3.23±3.83	7.56±8.94	5.26±3.23
Middle-aged adults (40-59)	4.36±4.12	6.90±7.73	5.15±3.15
Old adults (>60)	5.84±5.30	10.76±7.71	6.45±4.00
F/p value	10.317/0.00	6.680/0.00	5.122/0.06
Educational level			
Illiterate	6.37±5.36	11.29±10.21	6.06±3.64
Elementary	4.68±4.38	8.01±7.82	5.74±3.74
High school	3.59±3.99	7.77±9.10	5.17±3.16
Bachelor	2.52±2.99	6.54±6.57	4.88±2.85
F/p value	12.109/0.00	6.084/0.00	2.116/0.10
Gender			
Female	5.05±4.97	8.82±9.72	6.08±3.64
Male	3.80±3.91	7.55±7.89	5.05±3.22
t-test/p value	2.809/0.05	1.438/0.15	2.994/0.03
Marital status			
Married	4.47±4.39	8.20±8.82	5.40±3.22
Single	2.66±3.55	5.77±7.00	4.80±3.22
Widow	6.41±5.23	11.39±10.00	7.44±4.54
F/p value	10.268/0.00	5.680/0.00	8.675/0.00
Cohabitants			
Alone	4.67±4.75	10.20±12.15	6.67±2.99
Spouse or children	4.35±4.46	8.04±8.62	5.47±3.47
t-test/p value	0.271/0.77	0.683/0.51	1.318/0.19
Working status			
Employed	3.17±3.40	6.05±7.95	4.31±2.52
Unemployed	5.07±4.85	9.36±9.01	6.23±3.72
t-test/p value	-4.206/0.00	-3.707/0.00	-5.590/0.00
Income perception			
Low	4.79±4.49	9.44±8.60	6.90±4.43
Moderate	4.39±4.44	8.45±9.06	5.34±3.15
High	3.89±4.46	6.12±7.91	4.66±2.71
F/p value	0.920/0.40	3.550/0.03	10.336/0.00
Health perception			
Low	3.09±3.76	6.76±9.07	4.89±3.04
Moderate	4.67±4.36	8.26±8.56	5.45±3.30
High	5.34±5.05	9.47±8.61	6.36±3.98
F/p value	8.126/0.00	2.741/0.07	5.326/0.01

*[23]; PSQI: Pittsburgh Sleep Quality Index; GERD-Q: Gastroesophageal Reflux Disease Questionnaire; RSI: Reflux Symptom Index; SD: Standard deviation.

hoc test: low moderate <high) ($p < 0.05$, Table 2), however, did not have any statistically significant difference in respect of educational level and cohabitants ($p > 0.05$, Table 2).

As depicted in Table 3, we present Pearson correlations among Global PSQI, GERD-Q and RSI scores. The Global PSQI, GERD-Q and RSI scores were found to be 5.52 (SD=3.4; range=0-18), 4.3 (SD=4.46;

range=0-18), and 8.12 (SD= 8.77; range=0-45), respectively. It is shown that Global PSQI score was positively correlated with GERD-Q ($r=0.380^{**}$) and RSI scores ($r=0.414^{**}$). Additionally, GERD-Q score recorded significantly positive correlation with RSI score ($r=0.458^{**}$). There is a positive correlation between poor sleep quality and reflux. The higher the score on the sleep quality scale, the higher the risk of reflux.

TABLE 3: Means, standart deviations and correlations with confidence interval among Global PSQI, GERD-Q and RSI scores.

Variables	M	SD	1	2
1. PSQI	5.52	3.46		
2. GERD-Q	4.37	4.46	0.380** [0.22, 0.37]	
3. RSI	8.12	8.77	0.414** [0.13, 0.20]	0.458** [0.19, 0.28]

***Correlation is significant at the 0.01 level (2-tailed); PSQI: Pittsburgh Sleep Quality Index; GERD-Q: Gastroesophageal Reflux Disease Questionnaire; RSI: Reflux Symptom Index.

Looking at [Table 4](#), in the logistic regression analysis, five factors were significantly associated with poor sleep quality of the participants (Method=Enter): RSI

score (OR, 1.07; 95% CI, 1.04 to 1.10), GERD-Q score (OR, 1.11; 95% CI, 1.04 to 1.17), gender (OR, 1.68; 95% CI, 1.01 to 2.80 for female), perceived income level (OR, 3.03; 95% CI, 1.42 to 6.43 for moderate; OR 2.25; 95% CI, 1.19 to 4.24 for low), and perceived health (OR, 0.55; 95% CI, 0.31 to 0.98 for low).

In the study, it was found that being a woman, low and middle income among socio-demographic characteristics are factors that negatively affect sleep quality.

DISCUSSION

GERD and LPR have different symptoms; whereas LPR patients are generally daytime reluxers, patients

TABLE 4: Logistic regression for evaluation of the variables affecting the sleep quality in the study participants.

Variable Category	B	SE	OR	95% CI	p value
RSI	0.065	0.016	1.07	1.04-1.10	0.00
GERD-Q	0.101	0.030	1.11	1.04-1.17	0.00
Age					
Young adults (<39) (reference)			1.00		
Middle-aged adults (40-59)	-0.074	0.403	0.93	0.42-2.05	0.86
Old adults (>60)	-0.181	0.342	0.83	0.43-1.63	0.60
Educational level					
Illiterate (reference)			1.00		
Elementary	-0.573	0.437	0.56	0.24-1.33	0.19
High school	-0.540	0.344	0.58	0.30-1.14	0.12
Bachelor	-0.089	0.363	0.92	0.45-1.86	0.81
Gender					
Male (reference)			1.00		
Female	0.519	0.262	1.68	1.01-2.80	0.05
Marital Status					
Married (reference)			1.00		
Single	-0.012	0.430	0.99	0.43-2.30	0.98
Widow	-0.146	0.529	0.86	0.31-2.44	0.78
Cohabitants					
Spouse or children (reference)			1.00		
Alone	0.796	0.657	2.22	0.61-8.03	0.23
Working status					
Employed (reference)			1.00		
Unemployed	0.301	0.290	0.74	0.42-1.30	0.30
Income perception					
High (reference)			1.00		
Moderate	0.107	0.385	3.03	1.42-6.43	0.00
Low	0.809	0.323	2.25	1.19-4.24	0.01
Health perception					
High (reference)			1.00		
Moderate	0.269	0.319	0.76	0.41-1.43	0.40
Low	0.599	0.293	0.55	0.31-0.98	0.04

B: Regression coefficient; SE: Standard error; OR: Odds ratio; CI: Confidence interval; GERD-Q: Gastroesophageal Reflux Disease Questionnaire; RSI: Reflux Symptom Index.

with GERD are nocturnal refluxers.^{21,26} It is already known that reflux affects the sleep quality of individuals by causing them to wake up throughout the night.¹⁷ This paper examined the influence of LPR as well as GERD and some sociodemographic factors in sleep quality among individuals aged 18 years or older. The study showed that the prevalence of poor sleep quality, GERD and LPR is common in the participants aged 18 years and older, with 39.3%, 32.8%, and 24.0 respectively. We found that global PSQI score differed according to some sociodemographic factors such as marital status, working status, perceived health and income status. However, logistic regression analysis showed that GERD, LPR, gender, and perceived income status were the most powerful risk factors for poor sleep quality.

According to the international literature, the prevalence of poor sleep quality in people aged 18 and over differ from 9% to 78%.^{3,17,28} Similarly, being widowed, unemployed and perceived poor health was identified as the factors associated with poor sleep quality in the literature.^{29,30} Unlike the results of our study, Berhanu et al. found that men and middle age adults had poor sleep quality and being middle age and low-income level were more common risk factors for being poor sleeper.³ In this study, we assessed the participants' perceived income level and determined the perception of medium or low-income level was a significant factor for poor sleep quality. Additionally, whereas some studies stated that being a female was certainly associated with poor sleep similar to the findings of this study, the others did not find a significant difference between female and male in different age groups.^{4,31-33}

The results of our study were similar with a previous study illustrating a positive impact of GERD on sleep quality.¹⁷ In the study conducted in Japan showed that the prevalence of sleep disorders was higher in those with GERD than those without the disease in adults, and there was a significant correlation between the presence of gastroesophageal reflux and sleep disorders.¹⁸ Unlike the findings of this present study, PSQI scores did not significantly correlate with GERD-Q scores according to the study conducted by Jeon (2017) in Korea.¹⁹ There is bidirectional relationship between GERD and poor sleep

quality (Jung et al., 2010; Oh 2016) and individuals with GERD are likely to experience almost three times more sleep problem.¹⁴

Gouveia et al. reported the mean of the RSI score of participants with or without obstructive sleep apnea as 8.4 like the findings of the present study.²² In a study conducted in the USA, the result of RSI score was one of the significantly associated factors with sleep quality.³⁴ Although nighttime refluxers have more likelihood of experiencing sleep problem compared to daytime refluxers, GERD patients with LPR symptoms, they are more likely to be poor sleeper.²⁶

This paper contributes to the literature in the way of assessing the impact of self-reported GERD and LPR as well as sleep-related sociodemographic factors on the sleep quality of people aged 18 years and older. In this study, sleep quality was evaluated subjectively with the PSQI. Not assessing the objective sleep parameters, GERD, LPR can be considered a limitation of this study. It is recommended that the correlation between GERD, LPR and sleep parameters objectively investigated in future studies.

CONCLUSION

Consequently, there is a significant correlation between GERD, LPR and poor sleep quality. Also, being a female 1.7 times, perceived moderate- or low-income level 3.1 and 2.3 times respectively, increase the probability of being poor sleeper. According to the results in this study, it can be asserted that GERD and LPR are the important parameters that needs to be examined while evaluating sleep-related problems in adults. Evaluating the presence of GERD and LPR is also recommended in treatment approaches for sleep disorders.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or mem-

bers of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: İlknur Dolu, Maral Kargin; **Design:** Maral Kargin, İlknur Dolu, Evrim Çelebi; **Control/Supervision:** Maral

Kargin, İlknur Dolu; **Data Collection and/or Processing:** Maral Kargin, Evrim Çelebi; **Analysis and/or Interpretation:** Maral Kargin, İlknur Dolu; **Literature Review:** Maral Kargin, İlknur Dolu, Evrim Çelebi; **Writing the Article:** Maral Kargin, İlknur Dolu, Evrim Çelebi; **Critical Review:** Maral Kargin, İlknur Dolu; **References and Fundings:** Maral Kargin, İlknur Dolu, Evrim Çelebi; **Materials:** Maral Kargin, İlknur Dolu, Evrim Çelebi.

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