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Sex differences in insomnia symptoms: A population-based study

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Sex differences in insomnia symptom: A population-based study

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ABSTRACT

Sex differences in insomnia symptom: A population-based study

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Introduction

Insomnia is the most common sleep disorder with significant psychiatric/physical comorbidities in the general population. Sex, age, mood, lifestyle factors and medical conditions are known predictors of insomnia. The aim of this study is to investigate whether socioeconomic and demographic factors are associated with sex differences in insomnia and insomnia subtypes in South Korea.

Method

The present study used data from the nationwide, cross-sectional study with a structured questionnaire on headache and sleep among all Koreans aged 19 to 69 years conducted by trained interviewers. The Insomnia Severity Index (ISI) was used to diagnose and classify insomnia and its subtypes (cutoff value: 9.5). Other questionnaires included the Pittsburgh Sleep Quality Index (PSQI), Goldberg Anxiety Scale (GAS) and Patient Health Questionnaire-9 (PHQ-9) to measure sleep quality, anxiety and depression.

Results

A total of 2695 participants completed the survey (50.1% women; 49.9% man). 715 (26.5%) of the participants were classified as suffering from poor sleep quality. The overall prevalence of insomnia symptom was 10.7%, including difficulty in initiating sleep (DIS) (6.8%), difficulty in maintaining sleep (DMS) (6.5%), early morning awakening (EMA) (6.5%), and non-restorative sleep (NRS) (8.2%), and these symptoms were more prevalent in women than in men. Multivariate analysis showed that female sex, shorter sleep time and psychiatric complications

such as anxiety and depression were found to be independent predictors for insomnia symptoms and subtypes. Lower education level and older age were associated with higher risk of EMA. After adjusting for covariates among these factors, female sex remained a significant risk factor for insomnia symptom and its subtypes.

Conclusion

Approximately one-tenth of the sample from the Korean general population had insomnia symptom. The prevalence of insomnia symptom was higher in women than in men. Among the subtypes of insomnia symptom, DIS, DMS, EMA and NRS were more prevalent in women than men. Sex is an independent factor for insomnia symptom.

Key words: Insomnia, Sex, Gender, Sex difference, Epidemiology

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I. INTRODUCTION

Insomnia is the most common sleep disorder in the general population. It is associated with impaired social performance and daytime functioning, along with other psychological/physical conditions.[1-3] Insomnia affects 6 – 18% of the general population.[4-7] Therefore, insomnia imposes a significant personal and social burden.[8] Insomnia prevalence varies according to the definition of insomnia or insomnia symptoms.[9]

Different insomnia symptoms have been defined as subtypes of insomnia. These subtypes include difficulty in initiating sleep (DIS), difficulty in maintaining sleep (DMS) and early morning awakening (EMA).[9] There are differences in the prevalence, association with excessive daytime sleepiness and psychiatric comorbidities among these subtypes.[10]

Sex, age, socioeconomic status and psychiatric comorbidities are known to be significant factors for insomnia prevalence.[9] The elderly population has an increased insomnia prevalence compared to the young or middle age population in almost all epidemiological studies.[11-13] Insomnia prevalence is stable from 15 to 44 years of age and increases over 45 years.[9] Insomnia prevalence is typically higher among individuals with lower incomes and lower education levels.[14] However, some studies have reported contradictory results.[15,16] The association between insomnia and psychiatric disorders has been repeatedly demonstrated. Approximately 90% and 80% of individuals with anxiety and depression had insomnia symptoms in cross-sectional studies, respectively.[17,18] Longitudinal studies confirmed the close association of anxiety and depression with insomnia.[16,19]

Short sleep time and poor sleep quality are significant factors for insomnia symptoms. A survey in six European countries showed that a significant proportion of individuals with insomnia had short sleep times either voluntarily or non-voluntarily.[20] The authors classified sleep deprivation as a subtype of insomnia. Poor sleep quality is also common among individuals with insomnia.[21] Female sex has been recognized as a significant factor for insomnia symptoms. Epidemiological studies have consistently shown a higher prevalence of insomnia symptoms among women compared to men.[22-24] The difference in insomnia symptom prevalence between women and men increases with age.[9] In addition to insomnia or insomnia symptoms, women report more frequent dissatisfaction with sleep and the daytime consequences of insomnia.[4, 22, 24]

Nevertheless, information regarding sex differences in insomnia subtypes is currently limited. In addition, sex differences in insomnia symptoms adjusting for significant covariates has rarely been reported.

The Korean Headache-Sleep Study (KHSS) is a nation-wide population-based survey regarding sleep and headache. Its data provides an opportunity to investigate sex differences in insomnia symptoms and its subtypes regarding covariates in a population-based setting. The aim of this study is to investigate sex differences in insomnia symptoms and its subtypes regarding covariates using data from the KHSS.

II. MATERIALS AND METHODS

1. Study population and survey process

The present study used data from the Korean Headache-Sleep Study (KHSS). The study design and process have been previously described.[25] Briefly, the KHSS is a nationwide, cross-sectional study on headache and sleep among all Koreans aged 19 to 69 years. The KHSS used a 2-stage clustered random sampling method proportional to the population distribution for all Korean territories except Jeju-do. Trained interviewers conducted structured interviews using a questionnaire to assess sleep time, sleepiness, anxiety and depression using a face-to-face interview. The interview included questions on headache symptoms and sleep status. To

minimize potential interest bias, we informed candidates that the topic of the survey was social health issues rather than headache and sleep issues. All interviewers were employed by Gallup Korea and had previous social survey interviewing experience.

2. Assessment for sleep time

We asked all participants to report their usual sleep time in terms of hours and minutes, separately for workdays and free days, during the past month. The average sleep time was a weighted mean of the sleep time on workdays and free days, calculated as [(workday sleep time x 5) + (free day sleep time x 2)]/7. Short sleep time was defined as an average sleep time of <6 h.[26]

3. Assessment for insomnia symptoms and poor sleep quality

The Insomnia Severity Index (ISI) was used to diagnose and classify insomnia symptoms. The ISI is a self-reporting, brief screening measure of insomnia that contains questions corresponding in part to the diagnostic criteria of insomnia.[27] The ISI comprises seven items concerning the severity of sleep-onset difficulty, sleep-maintaining difficulty, early awakening and satisfaction with sleep patterns. Each item was rated on a 0-4 scale.[28] The ISI was previously validated with good sensitivity and specificity and showed a 9.5 cut-off score for discriminating patients with insomnia in the population-based sample.[29] Among those who satisfy this definition (ISI score ≥10), we further classified the subtypes of insomnia symptoms as difficulty in initiating sleep (DIS), difficulty in maintaining sleep (DMS), early morning awakening (EMA) and non-restorative sleep (NRS) if a participant responded with ≥ 2 on the scale (intermediate or higher) for those items.[20]

The Pittsburgh Sleep Quality Index (PSQI) was used to measure sleep quality. If a participant's PSQI score was 6 or higher, she/he was classified as having poor sleep quality.[30]

4. Anxiety and depression assessment

We used the Goldberg Anxiety Scale (GAS) to diagnose anxiety among participants. The GAS questionnaire was composed of nine items: four screening items and five supplementary items. Anxiety was diagnosed when there were positive answers to two or more screening items and five or more of all scale items.[31] The Korean version of the scale has a sensitivity of 82.0% and specificity of 94.4% for diagnosing anxiety.[32]

The Patient Health Questionnaire-9 (PHQ-9) was used to diagnose depression.[33] It is composed of nine items each scored 0 to 3. Participants who scored 10 or higher on this measure were considered to have depression. The Korean PHQ-9 has a sensitivity of 81.8% and specificity of 89.9%.[34]

5. Statistical analysis

The Kolmogorov–Smirnov test was used to confirm the normality of the distribution. The Student's t-test was used to compare continuous variables after the normality of the sample was confirmed. Post hoc analyses were performed using Tukey's method. Categorical variables were compared using the Chi-square test. The significance level was set at $p < 0.05$ for all analyses.

We calculated the odds ratios (ORs) with 95% confidence intervals (CIs) for the occurrence of insomnia and its subtypes through univariable and multivariable logistic regression analyses. In univariable analyses, we modelled the ORs for insomnia symptoms without adjusting for covariates. In multivariable analyses, we used four models. In Model 1, adjustment was conducted for sociodemographic variables (age, sex, size of residential area and educational level) and short sleep time. Model 2 incorporated anxiety (GAS score) with Model 1. Model 3 included depression (PHQ-9 score ≥ 10) with Model 1. The final model, Model 4, incorporated poor sleep quality (PSQI score ≥ 6), anxiety and depression with Model 1. Statistical analyses were performed using the Statistical Package for Social Sciences 23.0 (IBM, Armonk, NY, USA).

III. RESULTS

1. Survey

The interviewers approached 7430 individuals and 3114 of them agreed to take the survey. After 352 individuals suspended the interview, 2695 participants completed the survey (cooperation rate of 36.2%; Fig. 1).

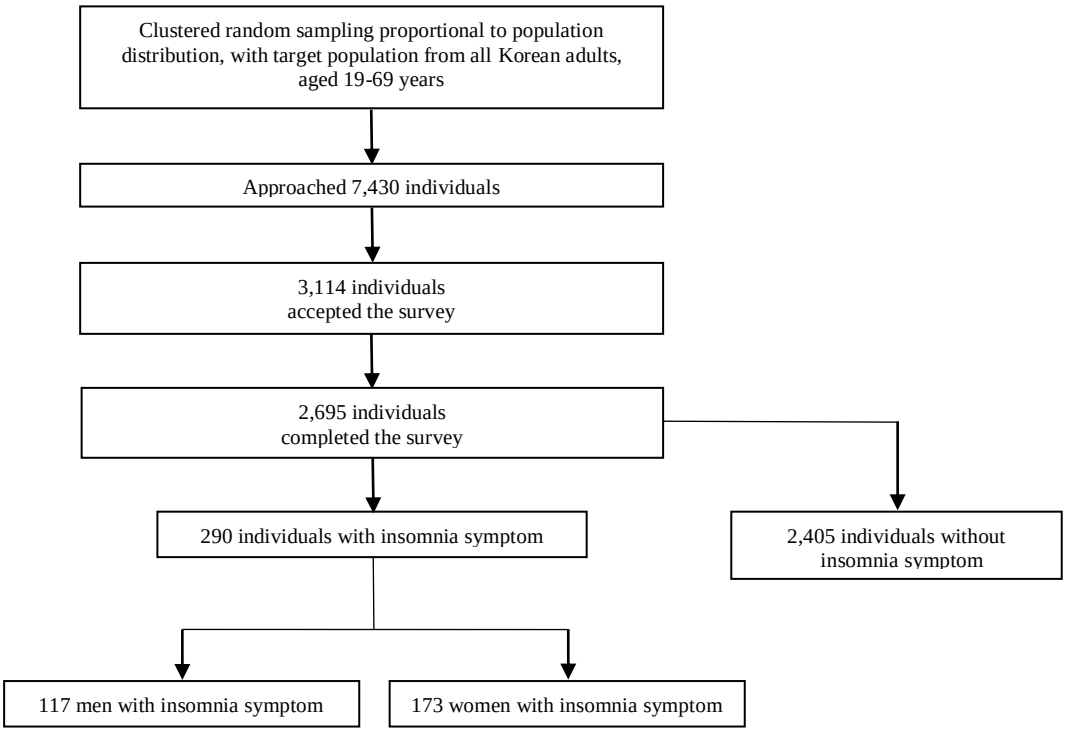


Figure 1. Flow chart depicting the participation of subjects in the Korean Headache-Sleep Study

The distributions of age, sex, size of residential area and educational level were not significantly different from those of the general population of Korea (Table 1).

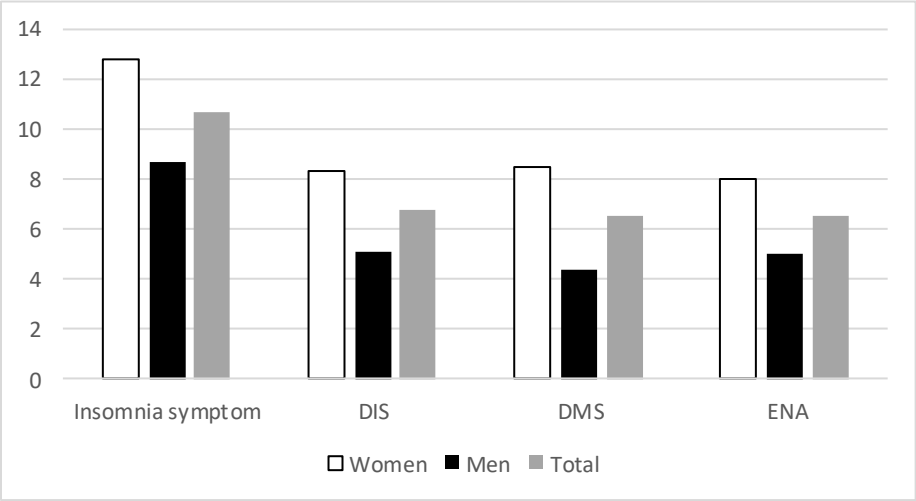
Table 1. Sociodemographic characteristics of survey participants; the total Korean population; and cases identified as having migraine, probable migraine, anxiety, and depression

	Survey participants N (%)	Total population N (%)	P	Poor sleep quality N , % (95% CI)	p	Insomnia N, % (95% CI)	p	Short sleep time	p	Average sleep time (hours + SD)	P
Sex											
Men	1,345 (49.3)	17,584,365 (50.6)	0.854 a	334, 24.8 (22.5-27.1)	0.046	117, 8.7 (7.2-10.2)	0.001	141, 10.5 (8.8-12.1)	0.727	7.3 + 1.2	0.109
Women	1,350 (50.7)	17,198,350 (49.4)		381, 28.2 (25.8-30.6)		173, 12.8 (11.0-14.6)		136, 10.1 (8.5-11.7)		7.3 + 1.2	
Age											
19–29	542 (20.5)	7,717,947 (22.2)	0.917 a	153, 28.3 (24.4-32.0)	0.028	59, 10.9 (9.2-12.6)	0.426	45, 8.3 (6.0-10.6)	0.002	7.6 + 1.3	<0.001
30–39	604 (21.9)	8,349,487 (24.0)		136, 22.5 (19.2-25.9)		53, 8.8 (7.3-10.3)		42, 7.0 (4.9-9.0)		7.5 + 1.1	
40–49	611 (23.1)	8,613,110 (24.8)		167, 27.3 (23.8-30.1)		66, 10.8 (9.1-12.5)		73, 11.9 (9.4-14.5)		7.1 + 1.2	
50–59	529 (18.9)	6,167,505 (17.7)		160, 30.2 (26.3-34.2)		63, 11.9 (10.2-13.6)		70, 13.2 (10.3-16.1)		7.1 + 1.3	
60–69	409 (15.6)	3,934,666 (11.3)		99, 24.2 (20.0-28.4)		49, 12.0 (10.2-13.7)		47, 11.5 (8.4-14.6)		7.1 + 1.2	
Size of residential area											
Large city	1,248 (46.3)	16,776,771 (48.2)	0.921 a	338, 27.1 (24.6-30.0)	0.541	136, 10.9 (9.2-12.6)	0.945	131, 10.5 (8.8-12.2)	0.670	7.3 + 1.2	0.471
Medium-to-small city	1186 (44.0)	15,164,345 (43.6)		303, 25.5 (23.1-28.0)		125, 10.5 (8.9-12.2)		116, 9.8 (8.1-11.5)		7.3 + 1.2	
Rural area	261 (9.7)	2,841,599 (8.2)		74, 28.4 (22.8-33.9)		29, 11.1 (9.4-12.8)		30, 11.5 (7.6-15.4)		7.3 + 1.3	
Education											
Middle school or Less	393 (14.9)	6,608,716 (19.0)	0.752 a	110, 28.0 (23.5-32.4)	0.917	62, 15.8 (13.8-17.7)	0.006	47, 12.0 (8.7-15.2)	0.514	7.2 + 1.3	0.012
High school	1,208 (44.5)	15,234,829 (43.8)		317, 26.2 (24.0-28.7)		116, 9.6 (8.0-11.2)		127, 10.5 (8.8-12.3)		7.4 + 1.3	
College or more	1,068 (39.6)	12,939,170 (37.2)		281, 26.3 (23.7-29.0)		109, 10.2 (8.6-11.8)		100, 9.4 (7.6-11.1)		7.4 +1.2	
Not responded	26 (9.6)			7, 26.9 (8.7-45.2)		3, 1.0 (0.9-1.3)		3, 11.5 (0.0-24.7)		7.4 + 1.3	
Total	2695 (100.0)	34,782,715 (100.0)		715, 26.5 (24.8-28.2)		290, 10.7 (9.1-12.4)		277, 10.3 (9.1-11.4)		7.4 + 1.3	7.2 + 1.3

aComparison of gender, age group, size of residential area, and educational level distributions between the sample in the present study and the total population of Korea
Abbreviations: CI = confidential interval

2. Prevalence of insomnia and poor sleep quality

Of the 2695 participants, 290 (10.7%) were classified as having insomnia symptoms according to the ISI score. Seven-hundred and fifteen (26.5%) participants who reported PSQI scores higher than 5 were classified as having poor sleep quality. 182 (6.8%) were accompanied by DIS, 175 (6.5%) with DMS, 176 (6.5%) with EMA and 221 (8.2%) with NRS. (Fig. 2).



p was calculated by χ2 test.
Abbreviations:
DIS = Difficulty in Initiating Sleep, DMS = Difficulty in Maintaining Sleep,
EMA = Early Morning Awakening

Figure 2. Prevalence of insomnia symptom in men and women

3. Demographic characteristics, psychiatric comorbidities and short sleep time according to the presence of insomnia symptoms

The mean age of participants with insomnia symptom did not significantly differ from participants without insomnia symptom (43.8 ± 14.2 vs. 42.9 ± 13.7, p = 0.823). The proportion of women was higher among participants with insomnia symptom than those without insomnia symptom (59.6% vs. 49.1%, p < 0.001). The prevalence of anxiety and depression was significantly higher among participants with insomnia symptom than in those without (40.3% vs. 6.3%, p < 0.001 for anxiety and 25.9% vs. 1.7%, *p* < 0.001 for depression). The average sleep time of all participants was 7.4 ± 1.3 h.

Two-hundred and seventy-seven (10.3%) participants were classified as having short sleep time.

The average sleep time of participants with insomnia symptom was significantly shorter than that of participants without insomnia symptom (6.7 ± 1.5 h vs. 7.4 ± 1.2 h, $p < 0.001$). The prevalence of short sleep time (< 6 hours of average sleep time) was higher among participants with insomnia symptom (35.5% vs. 15.2%, $p < 0.001$; Table 2).

Table 2. Distribution of demographic, social and life style factors according to the presence of insomnia symptom

	Subjects with insomnia (N=290)	Subjects without insomnia (N=2405)	P-value
Demographics			
Mean age ± SD (years)	43.76±14.20	42.88±13.70	0.366
Women, N (%)	173 (59.6)	1182 (49.1)	0.001
Education level			
Middle school or less	62	331	0.006
High school	116	1092	
College or more	109	959	
Not responded	3	23	
Residential area			
Large city	136	1112	0.943
Medium-to-small city	125	1061	
Rural area	29	232	
Smoking, N (%)	78 (26.9)	666 (27.7)	0.486
Alcohol, N (%)	185 (63.8)	1597 (66.4)	0.313
ISI score, ± SD	14.37±4.39	2.47±2.50	
Anxiety, N (%)	117 (40.3)	151 (6.3)	<0.001
Depression, N (%)	75 (25.9)	41 (1.7)	<0.001
BMI, ± SD (kg/cm^2)	23.09± 3.30	22.94± 2.97	0.031
Average sleep duration, ± SD, N (short sleep duration)	6.68± 1.54 (103)	7.36± 1.17 (366)	<0.001
Poor sleep quality, N (%)	221 (76)	494 (20.5)	<0.001

p was calculated by $\chi 2$ test or student's t test.

4. Prevalence of insomnia symptoms in women and men

A higher percentage of women reported insomnia symptom compared to men (12.8% vs. 8.7%, p = 0.001). The mean ISI score was significantly higher in women compared to men (4.2 ± 4.9 vs. 3.3 ± 4.2, $p < 0.001$). All subtypes of insomnia symptoms including DIS (8.3% vs. 5.1%, $p < 0.001$), DMS (8.5% vs. 4.4%, $p < 0.001$), EMA (8.0% vs. 5.0%, $p = 0.001$) and NRS (10.2% vs. 6.2%, p<0.001) were more prevalent in women than men (Fig. 2).

5. Insomnia severity of women and men among participants with insomnia

Among 290 participants with insomnia, the total ISI score was not significantly different between women and men (14.6 ± 4.4 vs. 14.0 ± 4.3, p = 0.199). The prevalence of DIS (37.6% vs. 33.3%, p = 0.460), DMS (40.5% vs. 32.5%, p = 0.168), EMA (36.4% vs. 29.9%, p = 0.251) and NRS (39.9% vs. 31.6%, p = 0.152) did not significantly differ between women and men.

6. Factors associated with insomnia symptoms in women and men

When comparing participants with insomnia to participants without insomnia, age, size of residential area and education level did not significantly affect the prevalence of insomnia. In contrast, female sex (OR = 1.3, 95% CI = 1.0 - 1.78), short sleep time (OR = 2.6, 95% CI = 1.9 - 3.5), anxiety (OR = 6.0, 95% CI = 4.3 - 8.3) and depression (OR = 9.6, 95% CI = 6.0 - 15.3) were found to be independent predictors of insomnia symptoms in multiple regression analysis (Table 3).

Table 3. Univariable and multivariable regression analysis for insomnia symptom

	Univariable ORs		**Multivariable analysis ORs**							
			Model 1		Model 2		Model 3		Model4	
	OR (95%Ci)	p-value	OR (95%Ci)	p-value	OR (95%Ci)	p-value	OR (95%Ci)	p-value	OR (95%Ci)	p-value
Sex (Women)	1.543 (1.204-1.977)	0.001	1.513 (1.172-1.953)	0.001	1.401 (1.068-1.839)	0.015	1.388 (1.057-1.824)	0.018	1.327 (1.000-1.760)	0.05
Age (40 years or older)	1.199 (0.934-1.539)	0.155	0.928 (0.702-1.226)	0.599	0.938 (0.698-1.261)	0.673	1.028 (0.762-1.387)	0.856	0.999 (0.734-1.361)	0.997
Size of residential area (Large city)	1.027 (0.804-1.311)	0.831	1.037 (0.807-1.332)	0.779	1.004 (0.768-1.312)	0.977	1.010 (0.771-1.321)	0.944	0.990 (0.749-1.308)	0.943
Education (Middle school or less)	1.707 (1.260-2.314)	0.001	1.552 (1.105-2.180)	0.011	1.427 (0.993-2.051)	0.055	1.556 (1.083-2.235)	0.017	1.473 (1.009-2.150)	0.045
Sleep duration (6 hours or shorter)	3.069 (2.354-4.000)	<0.001	3.081 (2.348-4.042)	<0.001	2.738 (2.039-3.675)	<0.001	2.780 (2.069-3.736)	<0.001	2.604 (1.913-3.544)	<0.001
Anxiety	10.095 (7.579-13.447)	<0.001			9.284 (6.910-12.473)	<0.001			6.014 (4.344-8.325)	<0.001

Depression	20.113 (13.409-30.170)	<0.001	18.626 (12.243-28.336)	<0.001	9.588 (6.026-15.257)	<0.001

Subject with missing data was excluded from the analysis.
p was calculated by the univariable / multiple logistic regression analysis.
Abbreviations: OR = odds ratio, CI = confidential interval.

For DIS, female sex (OR = 1.4, 95% CI = 1.0 - 2.0), short sleep time (OR = 3.1, 95% CI = 2.1 - 4.4), anxiety (OR = 5.0, 95% CI = 3.4 - 7.3) and depression (OR = 9.6, 95% CI = 6.0 - 15.5) were found to be independent predictors (Supplementary table 1).

In univariable analysis, age was a significant predictor of DIS (1.5, 95% CI = 1.1 - 2.1) and DMS (OR = 1.5, 95% CI = 1.1 - 2.0). However, age lost significance for DIS (p = 0.235) and DMS (*p* = 0.219) in multiple regression analysis. Female sex (OR = 1.8, 95% CI = 1.2 - 2.6), short sleep time (OR = 2.5, 95% CI = 1.7 - 3.7), anxiety (OR = 5.2, 95% CI =3.6 - 7.7) and depression (OR = 8.6, 95% CI = 5.3 - 13.9) were significant predictors of DMS in multiple regression analysis (Supplementary table 2).

In multiple regression analysis for EMA, female sex (OR = 1.4, 95% CI = 1.0 - 2.0), age (OR = 1.8, 95% CI = 1.2 - 2.6), educational level (OR = 1.6, 95% CI = 1.1 - 2.5), short sleep time (OR = 3.7, 95% CI = 2.6 - 5.3), anxiety (OR = 5.1, 95% CI = 3.4 - 7.6) and depression (OR = 5.7, 95% CI = 3.4 - 9.4) were independent predictors (Supplementary table 3).

In multiple regression analysis for NRS, female sex (OR = 1.5, 95% CI = 1.1 - 2.1), short sleep time (OR = 3.0, 95% CI = 2.1 - 4.2), anxiety (OR = 6.2, 95% CI = 4.3 - 8.8) and depression (OR = 10.1, 95% CI = 6.3 – 16.2) were significant predictors (Supplementary table 4).

IV. DISCUSSION

The main findings of the present study were as follows: 1) The prevalence of insomnia symptoms in a Korean general population-based sample was 10.7% and 2) The prevalence of insomnia symptoms was significantly higher in women than men. Among the subtypes of insomnia symptoms, there was a higher prevalence of DIS, DMA, EMA and NRS in women than in men and 3) female sex was a significant factor for insomnia symptoms even after

adjusting for covariates including sociodemographic variables, short sleep time, anxiety and depression.

Sex differences in insomnia or insomnia symptoms has been demonstrated in epidemiological studies. A meta-analysis combining data from 29 studies reported that women were at a 41% greater risk for having insomnia than men in adult populations.[22] Our results are in agreement with the previous findings that women had more insomnia symptoms than men. This similarity in the preponderance of insomnia symptom prevalence in women between the present study and previous reports suggests that the present study properly investigated insomnia symptoms in women and men.

What are possible mechanisms for higher insomnia prevalence in women? One possible explanation is roles of sex steroids. The major gonadal sex steroids are estrogen and progesterone in women and testosterone in men.[35] Sleep complaints typically co-occur in women. with the fluctuation of ovarian steroids such as puberty, pregnancy, the menstrual cycle and the menopausal period.[36-38] Estrogen replacement therapy improves sleep disturbances in menopausal women.[37] In men, androgen deprivation therapy worsen insomnia in prostate cancer patients.[39] On the contrary, high-dose testosterone replacement was associated with a reduction of sleep efficacy and total sleep time.[40] In summary, low or fluctuating levels of estrogen was consistently associated with increase occurrence of sleep disturbances including insomnia in women. Nevertheless, role of testosterone level on sleep is currently uncertain owing to inconsistent results.

Another possible explanation is role of biological sex. Androgen and estrogen affect differently on sleep between women and men. Gonadectomized female and male rats showed no significant difference in NREM and REM sleep amount. However, estradiol replacement significantly reduces NREM and REM sleep time in dark phase in female rats. In contrast, NREM and REM sleep architecture did not change by estradiol treatment in male rats.[41] Therefore, sex difference may be owing to biological sex rather than sex steroids.

The higher prevalence of mood symptoms in women could be a reason for sex difference. Both

anxiety and depression are closely associated with sleep disturbances, including insomnia. Epidemiological studies have consistently reported a close association of insomnia with anxiety and depression. A meta-analysis including 21 longitudinal epidemiological studies showed an odds ratio for insomnia to predict depression of 2.60 (confidence interval: 1.98-3.42).[42] Women preponderance of anxiety and depression has been persistently noted.[43, 44] Therefore, a higher prevalence of anxiety and depression in women may account for the higher prevalence of insomnia in women than men. Nevertheless, insomnia prevalence was significantly higher in women than men even after adjusting for anxiety and depression in the present study (Table 3). Therefore, the higher prevalence of insomnia in women could not be solely explained by the higher prevalence of anxiety and depression in women.

The present study showed that all subtypes of insomnia symptom including DIS, DMS, EMA and NRS were more common in women than men. The significant differences in prevalence between women and men persisted even after adjusting for covariates including sociodemographic variables, short sleep time, anxiety and depression. Sex differences in the subtypes of insomnia have been demonstrated in epidemiological studies. Janson et al. reported that female sex was positively related to DMS in a European study.[45] An interview-based study showed a clear correlation between female sex and insomnia symptom as well as the DMS-IV inclusion criteria[23]. Another study showed that 11.9% (14.0% of women vs. 9.3% of men) of the Hong Kong Chinese adult population complained of insomnia in the preceding month. Insomnia and insomnia symptom, including DIS, DMS and EMA, more prominently appeared in women than in men. Sex (as women) was a specific risk factor despite common risk factors for insomnia in both sexes.[24]

The prevalence of EMA only showed significance in older individuals after including anxiety and depression in the adjustment (Supplementary table 3). Still, we found a tendency that prevalence of insomnia symptom increased with age. In this study, inclusion criteria for participants maximally limited to 69 years, and the size of the sample was small. These are possible explanations for the absence of statistical significance. (Table 1). Sex differences in

insomnia prevalence were apparent in the elderly in epidemiological studies. In elderly populations, the risk of insomnia in women was almost doubled compared to that of men. Elderly (>65 years) women had a 73% greater risk of insomnia compared to elderly men.[22] In contrast, the predisposition for insomnia in women did not appear before puberty. These findings suggest a possible role of hormonal changes in the differences in insomnia between women and men.[46, 47] Additionally, we failed to report lower education levels as independent risk factor for insomnia and all subtypes in multiple regression analysis.[9]

Despite of the low response rate (36.3%), we can speculate the general status of the Korean population through our data: 1) there were no significant differences in the distribution of age, sex, size of residential area, and educational level between survey participants and the Korean general population. 2) the prevalence of insomnia, anxiety, depression, and short sleep duration in the KHSS were similar to that of previous studies.[4, 25]

The present study has some limitations. First, this study did not use any objective measurement of sleep or sleep disorders such as polysomnography or actigraphy. Nevertheless, we evaluated insomnia symptom, sleep habits and sleep quality using validated questionnaires via face-to-face interviews. Second, we did not evaluate the use of antidepressants, anxiolytics, hypnotics or caffeine. Antidepressants, anxiolytics or hypnotics may have a positive effect on sleep time and caffeine may negatively affect sleep time. Also, we could not measure sleep-relevant-treatments such as sleep-education, relaxation training or cognitive behavioral therapy for insomnia (CBTI). Third, although the present study was a large population-based study, some subgroup analyses might not have statistical significance due to the limited sample size and low response rate. In other words, the lack of significant findings in subgroup analyses could be due to the small subgroup sample size. Lastly, much of the data in this study were collected 6 years ago.

The present study has several strengths. First, the present study included a large sample size across the Korean general population. The distribution of age, sex, size of residential area and educational level of our sample was similar to the Korean population. Second, the present study

assessed potential covariates of insomnia such as sociodemographic variables, poor sleep quality, short sleep time, anxiety and depression, which are related to insomnia symptom. Third, we investigated sex differences in the subtypes of insomnia symptom including DIS, DMS, EMA and NRS in addition to overall insomnia symptoms. Further, we analyzed the factors affecting insomnia subtypes.

V. CONCLUSION

Approximately one-tenth of the Korean general population sample had insomnia symptoms. The prevalence of insomnia symptoms was higher in women than men. Among the subtypes of insomnia symptoms, DIS, DMS, EMA and NRS were more prevalent in women than in men. The predisposition of insomnia symptoms in women was prominent even after adjusting for covariates including anxiety and depression.

REFERENCES

1. Thase ME. Correlates and consequences of chronic insomnia. General hospital psychiatry 2005;27:100-12.
2. Benca RM. Diagnosis and treatment of chronic insomnia: a review. Psychiatric services 2005;56:332-43.
3. Léger D, Guilleminault C, Bader G, Lévy E, Paillard M. Medical and socio-professional impact of insomnia. Sleep 2002;25:621-5.
4. Cao X-L, Wang S-B, Zhong B-L, et al. The prevalence of insomnia in the general population in China: A meta-analysis. PloS one 2017;12:e0170772.
5. Yeo B, Perera I, Kok L, Tsoi W. Insomnia in the community. Singapore Med J 1996;37:282-4.
6. Kim K, Uchiyama M, Okawa M, Liu X, Ogihara R. An epidemiological study of insomnia among the Japanese general population. Sleep 2000;23:41-7.
7. Ohayon MM, Hong S-C. Prevalence of insomnia and associated factors in South Korea. Journal of Psychosomatic Research 2002;53:593-600.
8. Daley M, Morin CM, LeBlanc M, Grégoire J-P, Savard J. The economic burden of insomnia: direct and indirect costs for individuals with insomnia syndrome, insomnia symptoms, and good sleepers. Sleep 2009;32:55-64.
9. Ohayon MM. Epidemiology of insomnia: what we know and what we still need to learn. Sleep medicine reviews 2002;6:97-111.
10. Hara C, Stewart R, Lima-Costa MF, et al. Insomnia subtypes and their relationship to excessive daytime sleepiness in Brazilian community-dwelling older adults. Sleep 2011;34:1111-7.
11. Henderson S, Jorm AF, Scott LR, Mackinnon AJ, Christensen H, Korten AE. Insomnia in the elderly: its prevalence and correlates in the general population. The Medical Journal of Australia 1995;162:22-4.
12. Foley DJ, Monjan AA, Brown SL, Simonsick EM, Wallace RB, Blazer DG. Sleep complaints among elderly persons: an epidemiologic study of three communities. Sleep 1995;18:425-32.
13. Chiu HF, Leung T, Lam LC, et al. Sleep problems in Chinese elderly in Hong Kong. Sleep 1999;22:717-26.
14. Bixler EO, Kales A, Soldatos CR, Kales JD, Healey S. Prevalence of sleep disorders in the Los Angeles metropolitan area. The American Journal of Psychiatry 1979.
15. Ancoli-Israel S, Roth T. Characteristics of insomnia in the United States: results of the 1991 National Sleep Foundation Survey. I. Sleep 1999;22:S347-53.
16. Breslau N, Roth T, Rosenthal L, Andreski P. Sleep disturbance and psychiatric disorders: a longitudinal epidemiological study of young adults. Biological psychiatry 1996;39:411-8.
17. Ohayon MM, Shapiro CM, Kennedy SH. Differentiating DSM-IV anxiety and depressive disorders in the general population: comorbidity and treatment consequences. The Canadian Journal of Psychiatry 2000;45:166-72.
18. Weissman MM, Bland RC, Canino GJ, et al. Cross-national epidemiology of major depression and bipolar disorder. Jama 1996;276:293-9.
19. Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric disorders: an opportunity for prevention? Jama 1989;262:1479-84.
20. Ohayon MM, Roth T. What are the contributing factors for insomnia in the general population? Journal of psychosomatic research 2001;51:745-55.
21. Tsai P-S, Wang S-Y, Wang M-Y, et al. Psychometric evaluation of the Chinese version of the Pittsburgh Sleep Quality Index (CPSQI) in primary insomnia and control subjects. Quality of Life Research 2005;14:1943-52.
22. Zhang B, Wing Y-K. Sex differences in insomnia: a meta-analysis. Sleep 2006;29:85-93.
23. Pallesen S, Nordhus IH, Nielsen GH, et al. Prevalence of insomnia in the adult Norwegian population. Sleep 2001;24:771-9.
24. Li R, Wing Y, Ho S, Fong S. Gender differences in insomnia—a study in the Hong Kong Chinese population. Journal of psychosomatic research 2002;53:601-9.
25. Cho S-J, Chung YK, Kim J-M, Chu MK. Migraine and restless legs syndrome are associated in adults under age fifty but not in adults over fifty: a population-based study. The journal of headache and pain 2015;16:75.
26. Itani O, Jike M, Watanabe N, Kaneita Y. Short sleep duration and health outcomes: a systematic review, meta-analysis, and meta-regression. Sleep medicine 2017;32:246-56.
27. Association AP. Diagnostic and statistical manual of mental disorders (DSM-5®): American Psychiatric Pub, 2013.

28. Bastien CH, Vallières A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. Sleep medicine 2001;2:297-307.
29. Morin CM, Belleville G, Bélanger L, Ivers H. The Insomnia Severity Index: psychometric indicators to detect insomnia cases and evaluate treatment response. Sleep 2011;34:601-8.
30. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry research 1989;28:193-213.
31. Goldberg D, Bridges K, Duncan-Jones P, Grayson D. Detecting anxiety and depression in general medical settings. Bmj 1988;297:897-9.
32. Kim JS, Kim YS, Lee GY, et al. The standardization of Korean-translated Goldberg's shart screening scale for Anxiety and Depression. Journal of the Korean Academy of Family Medicine 1997;18:1452-60.
33. Pignone MP, Gaynes BN, Rushton JL, et al. Screening for depression in adults: a summary of the evidence for the US Preventive Services Task Force. Annals of internal medicine 2002;136:765-76.
34. Choi HS, Choi JH, Park KH, et al. Standardization of the Korean version of Patient Health Questionnaire-9 as a screening instrument for major depressive disorder. Journal of the Korean Academy of Family Medicine 2007;28:114-9.
35. Mong JA, Cusmano DM. Sex differences in sleep: impact of biological sex and sex steroids. Phil. Trans. R. Soc. B 2016;371:20150110.
36. Zhang J, Chan NY, Lam SP, et al. Emergence of sex differences in insomnia symptoms in adolescents: a large-scale school-based study. Sleep 2016;39:1563-70.
37. Polo-Kantola P, Erkkola R, Helenius H, Irjala K, Polo O. When does estrogen replacement therapy improve sleep quality? American Journal of Obstetrics & Gynecology 1998;178:1002-9.
38. Moline ML, Broch L, Zak R. Sleep in women across the life cycle from adulthood through menopause. Medical Clinics of North America 2004;88:705-36.
39. Savard J, Hervouet S, Ivers H. Prostate cancer treatments and their side effects are associated with increased insomnia. Psycho-Oncology 2013;22:1381-8.
40. Liu PY, Yee B, Wishart SM, et al. The short-term effects of high-dose testosterone on sleep, breathing, and function in older men. The Journal of Clinical Endocrinology & Metabolism 2003;88:3605-13.
41. Cusmano DM, Hadjimarkou MM, Mong JA. Gonadal steroid modulation of sleep and wakefulness in male and female rats is sexually differentiated and neonatally organized by steroid exposure. Endocrinology 2014;155:204-14.
42. Baglioni C, Battagliese G, Feige B, et al. Insomnia as a predictor of depression: a meta-analytic evaluation of longitudinal epidemiological studies. Journal of affective disorders 2011;135:10-9.
43. Kendler KS, Prescott CA, Myers J, Neale MC. The structure of genetic and environmental risk factors for common psychiatric and substance use disorders in men and women. Archives of general psychiatry 2003;60:929-37.
44. Gallo EAG, Munhoz TN, de Mola CL, Murray J. Gender differences in the effects of childhood maltreatment on adult depression and anxiety: a systematic review and meta-analysis. Child abuse & neglect 2018;79:107-14.
45. Janson C, Gislason T, Backer WD, et al. Prevalence of sleep disturbances among young adults in three European countries. Sleep 1995;18:589-97.
46. Johnson EO, Roth T, Schultz L, Breslau N. Epidemiology of DSM-IV insomnia in adolescence: lifetime prevalence, chronicity, and an emergent gender difference. Pediatrics 2006;117:e247-e56.
47. Calhoun SL, Fernandez-Mendoza J, Vgontzas AN, Liao D, Bixler EO. Prevalence of insomnia symptoms in a general population sample of young children and preadolescents: gender effects. Sleep medicine 2014;15:91-5.

APPENDICES

Supplementary table 1. Univariable and multivariable regression analysis for difficult initiating asleep (DIS)

	Univariable ORs		**Multivariable analysis ORs**							
			Model 1		Model 2		Model 3		Model4	
	OR (95%Ci)	p-value	OR (95%Ci)	p-value	OR (95%Ci)	p-value	OR (95%Ci)	p-value	OR (95%Ci)	p-value
Sex (Women)	1.689 (1.240-2.302)	0.001	1.628 (1.183-2.240)	0.003	1.523 (1.089-2.131)	0.014	1.472 (1.045-2.074)	0.027	1.425 (1.002-2.027)	0.049
Age (40 years or older)	1.507 (1.097-2.071)	0.011	1.105 (0.777-1.571)	0.580	1.144 (0.792-1.652)	0.474	1.300 (0.888-1.903)	0.177	1.266 (0.858-1.868)	0.235
Size of residential area (Large city)	1.017 (0.752-1.375)	0.912	1.022 (0.750-1.393)	0.891	0.981 (0.707-1.360)	0.907	0.976 (0.698-1.365)	0.887	0.947 (0.671-1.337)	0.757
Education (Middle school or less)	1.918 (1.337-2.751)	<0.001	1.565 (1.047-2.340)	0.029	1.430 (0.937-2.182)	0.097	1.565 (1.016-2.410)	0.042	1.468 (0.940-2.293)	0.092
Sleep duration (6 hours or shorter)	3.868 (2.826-5.293)	<0.001	3.755 (2.722-5.178)	<0.001	3.267 (2.317-4.606)	<0.001	3.301 (2.320-4.698)	<0.001	3.088 (2.148-4.441)	<0.001
Anxiety	9.975 (7.185-13.849)	<0.001			8.875 (6.317-12.470)	<0.001			4.983 (3.384-7.339)	<0.001
Depression	20.668 (13.764-31.036)	<0.001					19.412 (12.612-29.877)	<0.001	9.614 (5.950-15.532)	<0.001

Subject with missing data was excluded from the analysis.
p was calculated by the univariable / multiple logistic regression analysis.
Abbreviations: OR = odds ratio, CI = confidential interval.

Supplementary table 2. Univariable and multivariable regression analysis for difficult maintaining asleep (DMS)

	Univariable ORs		**Multivariable analysis ORs**							
			Model 1		Model 2		Model 3		Model4	
	OR (95%Ci)	p-value	OR (95%Ci)	p-value	OR (95%Ci)	p-value	OR (95%Ci)	p-value	OR (95%Ci)	p-value
Sex (Women)	1.994 (1.446-2.751)	<0.001	1.965 (1.410-2.736)	<0.001	1.866 (1.318-2.643)	<0.001	1.828 (1.284-2.603)	0.001	1.787 (1.242-2.569)	0.002
Age (40 years or older)	1.452 (1.052-2.003)	0.023	1.112 (0.777-1.592)	0.562	1.158 (0.796-1.683)	0.444	1.310 (0.891-1.928)	0.170	1.281 (0.863-1.899)	0.219
Size of residential area (Large city)	0.928 (0.682-1.263)	0.634	0.936 (0.682-1.284)	0.681	0.884 (0.633-1.235)	0.470	0.878 (0.624-1.235)	0.455	0.843 (0.593-1.198)	0.340
Education (Middle school or less)	1.907 (1.319-2.757)	0.001	1.513 (1.005-2.279)	0.047	1.386 (0.902-2.129)	0.136	1.507 (0.974-2.331)	0.065	1.404 (0.894-2.205)	0.140
Sleep duration (6 hours or shorter)	3.269 (2.367-4.514)	<0.001	3.214 (2.305-4.482)	<0.001	2.730 (1.913-3.896)	<0.001	2.712 (1.885-3.902)	<0.001	2.507 (1.722-3.650)	<0.001
Anxiety	10.149 (7.278-14.154)	<0.001			9.158 (6.494-12.915)	<0.001			5.247 (3.554-7.746)	<0.001
Depression	19.294 (12.830-29.015)	<0.001					17.947 (11.679-27.578)	<0.001	8.575 (5.301-13.871)	<0.001

Subject with missing data was excluded from the analysis.
p was calculated by the univariable / multiple logistic regression analysis.
Abbreviations: OR = odds ratio, CI = confidential interval.

Supplementary table 3. Univariable and multivariable regression analysis for early morning awakening (EMA)

	Univariable ORs		**Multivariable analysis ORs**							
			Model 1		Model 2		Model 3		Model4	
	OR (95%Ci)	p-value	OR (95%Ci)	p-value	OR (95%Ci)	p-value	OR (95%Ci)	p-value	OR (95%Ci)	p-value
Sex (Women)	1.633 (1.194-2.234)	0.002	1.581 (1.139-2.194)	0.006	1.509 (1.071-2.128)	0.019	1.461 (1.037-2.059)	0.030	1.435 (1.009-2.043)	0.045
Age (40 years or older)	2.124 (1.507-2.994)	<0.001	1.515 (1.037-2.214)	0.032	1.606 (1.084-2.379)	0.018	1.771 (1.187-2.641)	0.005	1.755 (1.168-2.637)	0.007
Size of residential area (Large city)	0.873 (0.642-1.189)	0.390	0.892 (0.647-1.229)	0.485	0.845 (0.603-1.184)	0.328	0.844 (0.602-1.183)	0.325	0.813 (0.574-1.151)	0.243
Education (Middle school or less)	2.394 (1.684-3.403)	<0.001	1.726 (1.167-2.554)	0.006	1.615 (1.072-2.432)	0.022	1.730 (1.149-2.605)	0.009	1.643 (1.078-2.505)	0.021
Sleep duration (6 hours or shorter)	4.683 (3.416-6.420)	<0.001	4.413 (3.191-6.104)	<0.001	3.915 (2.778-5.519)	<0.001	3.922 (2.782-5.530)	<0.001	3.719 (2.612-5.296)	<0.001
Anxiety	8.949 (6.415-12.484)	<0.001			8.090 (5.691-11.499)	<0.001			5.105 (3.446-7.563)	<0.001
Depression	12.937 (8.579-19.509)	<0.001					12.508 (7.984-19.596)	<0.001	5.684 (3.430-9.420)	<0.001

Subject with missing data was excluded from the analysis.
p was calculated by the univariable / multiple logistic regression analysis.
Abbreviations: OR = odds ratio, CI = confidential interval.

Supplementary table 4. Univariable and multivariable regression analysis for non-restorative sleep (NRS)

	Univariable ORs		**Multivariable analysis ORs**							
			Model 1		Model 2		Model 3		Model4	
	OR (95%Ci)	p-value	OR (95%Ci)	p-value	OR (95%Ci)	p-value	OR (95%Ci)	p-value	OR (95%Ci)	p-value
Sex (Women)	1.633 (1.194-2.234)	0.002	1.581 (1.139-2.194)	0.006	1.509 (1.071-2.128)	0.019	1.461 (1.037-2.059)	0.030	1.435 (1.009-2.043)	0.045
Age (40 years or older)	2.124 (1.507-2.994)	<0.001	1.515 (1.037-2.214)	0.032	1.606 (1.084-2.379)	0.018	1.771 (1.187-2.641)	0.005	1.755 (1.168-2.637)	0.007
Size of residential area (Large city)	0.873 (0.642-1.189)	0.390	0.892 (0.647-1.229)	0.485	0.845 (0.603-1.184)	0.328	0.844 (0.602-1.183)	0.325	0.813 (0.574-1.151)	0.243
Education (Middle school or less)	2.394 (1.684-3.403)	<0.001	1.726 (1.167-2.554)	0.006	1.615 (1.072-2.432)	0.022	1.730 (1.149-2.605)	0.009	1.643 (1.078-2.505)	0.021
Sleep duration (6 hours or shorter)	4.683 (3.416-6.420)	<0.001	4.413 (3.191-6.104)	<0.001	3.915 (2.778-5.519)	<0.001	3.922 (2.782-5.530)	<0.001	3.719 (2.612-5.296)	<0.001
Anxiety	8.949 (6.415-12.484)	<0.001			8.090 (5.691-11.499)	<0.001			5.105 (3.446-7.563)	<0.001
Depression	12.937 (8.579-19.509)	<0.001					12.508 (7.984-19.596)	<0.001	5.684 (3.430-9.420)	<0.001

Subject with missing data was excluded from the analysis.
p was calculated by the univariable / multiple logistic regression analysis.
Abbreviations: OR = odds ratio, CI = confidential interval.

ABSTRACT(IN KOREAN)

인구 조사를 통한 불면증의 성별 차이

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서론

불면증은 일반 인구에서 중요한 정신/신체 합병증을 가진 가장 흔한 수면 장애이다. 성별, 나이, 정서, 생활 습관 및 건강 상태는 불면증의 예측 인자로 알려져 있다. 본 연구의 목적은 한국 사회 내의 불면증의 실태와 불면증에 대해서 사회 경제적 요인과 인구 통계적 요인이 성별 차이와 관련이 있는지를 조사하고자 하였다.

재료 및 방법

본 연구에서는 19 세에서 69 세까지의 모든 한국인의 두통 및 수면에 대해서 훈련된 면접관이 구조화된 설문지를 사용하여 시행한 두통 수면 연구 (KHSS) 데이터를 사용했다. 불면증 및 그 하위 유형을 진단하고 분류하기 위해 ISI (Insomnia Severity Index)를 사용하였다. 또한 수면의 질, 불안 및 우울 정도를 측정하기 위해 피츠버그 수면 품질 지수 (PSQI), 골드버그 불안 척도 (GAS) 및 환자 건강 설문지 -9 (PHQ-9)를 사용하였다.

결과

총 2695 명 (50.1 % 여성, 49.9 % 남성)이 설문조사에 참여하였다. 참가자 중 715 명 (26.5 %)은 수면의 질이 좋지 않은 것으로 분류되었다. 불면증 증상의 전체 유병률은 10.7%였고 그 하위 유형으로 입면 장애 (DIS) (6.8 %), 수면 유지 장애 (DMS) (6.5 %) , 조조 각성 (EMA) (6.5 %) 및 비회복성 수면 (NRS) (8.2%)을 보였으며 이러한 증상은 남성보다 여성에서 높게 관찰되었다. 다변량 분석 결과, 여성의 성별, 수면 시간의 단축, 불안 및 우울증과 같은 정신병 합병증이 불면증 증상 및 아형에 대한 독립적인 예측 인자로 나타났다. 낮은 교육 수준과 노년층은 EMA의 위험도와 관련이 있었다. 이러한 요인들을 종합하여 공변량 분석을 시행한 후에도 여성이라는 성별이 불면증 증상과 그 하위 유형에 대해 유의미한 인자로 관찰되었다.

결론

한국인을 대상으로 한 표본의 약 1/10이 불면증 증상을 보였다. 불면증 증상의 유병율은 남성보다 여성에서 높았다. 불면증 증상의 아형 중 DIS, DMS, EMA 및 NRS가 남성보다 여성에서 더 많았다. 성별은 불면증 증상의 독립적인 요소로 사료된다.

핵심되는 말: 불면증, 성, 성별 차이, 역학