**THE RELATIONSHIP BETWEEN MINI NUTRITIONAL ASSESSMENT SCORE AND INSOMNIA SEVERITY IN OLDER ADULTS**

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**ABSTRACT**

**OBJECTIVES:** Both insomnia and malnutrition are quite common, and can cause similar negative consequences, such as falls, depression, and cognitive impairment in older adults, but there is no study investigating the relationship between the two.The aims were to investigate relationships between insomnia/insomnia severity and Mini Nutritional Assessment score, and serum nutrients levels.

**SETTING AND PARTICIPANTS:** Aged 65 years or older, 575 outpatients were included.

**METHODS:** MNA >23.5, 17-23.5, <17, were categorized as normal nutritional status, malnutrition risk, and malnutrition, respectively. Serum vitamin B12, vitamin D and folate deficiencies were also evaluated. Insomnia Severity Index (ISI) with scores of 8 and higher, indicated insomnia, which was further stratified according to ISI score as mild (8-14), moderate (15-21), or severe (22-28).

**RESULTS:** The mean age was 73.1 ± 7.7 years, with 73.2% being female. The prevalence of patients with no insomnia, mild insomnia, moderate insomnia and severe insomnia were 34.4%, 20.9%, 30.1%, and 14.6%, respectively. After adjusting for gender,education, number of drugs, Charlson comorbidity index, presence of depression, andMini-Mental State Examination scores, patients with insomnia had lower MNA scores than those without insomnia (OR=0.84, 95% CI: 0.7-0.9, p<0.001).There were significant relationships between moderate/severe insomnia and the presence of malnutrition and risk of malnutrition (OR=1.6, 95% CI: 1.0-2.5, p=0.046 / OR=1.6, 95% CI:1.0-2.7, p=0.042) and MNA scores (OR= 0.83, 95% CI:0.7-0.9, p<0.001) / OR=0.82, 95% CI:0.7-0.9, p<0.001).There was no significant difference between insomnia severity status and serum vitamin D, Vitamin B12, folate levels or classification of these nutrients (p>0.05).

**Conclusions and Implications:** There is a close relationship between MNA scores and insomnia/insomnia severity in older adults. Therefore, when evaluating an elderly patient with insomnia, malnutrition should be evaluated, or insomnia should also be questioned in an elderly patient with malnutrition. Thus, more effective management of the two can be possible.

**Keyword:** insomnia; mini nutritional assessment; micronutrient; nutrition; vitamin D; vitamin B12; folate

**INTRODUCTION**

Insomnia is defined as persistently having difficulty in initiating and sustaining sleep, or waking up too early in the mornings and not falling asleep again. (1) While the prevalence of insomnia is 12% -20% in the general population, the prevalence rate of insomnia symptoms ranges from 30% to 48% in the elderly. (2) In a study of 6,899 older adults aged 65 years and over, the incidence of annual insomnia was found to be 7%, and it has been reported that some drugs (e.g., beta blockers) and comorbidities such as chronic pain, depression, cancer, chronic obstructive pulmonary disease, cardiovascular diseases, and some other factors, such as inactivity, decreased social relationships and caregiving, are increasingly associated with insomnia. (3) On the other hand, regardless of all these and similar factors, aging-related circadian rhythm disturbances can contribute to the development of later-life insomnia, such as changes in the amplitude of the circadian oscillation of physiological parameters like melatonin or the decrease in the effectiveness of the suprachiasmatic nucleus in the hypothalamus. (4) If not treated, insomnia can lead to dementia, depression, anxiety, delirium, diminished quality of life, falls, and cardiovascular diseases such as hypertension, myocardial infarction, and stroke. (4,5) With the appropriate treatment of insomnia, the development of such complications can be prevented. However, as well as insomnia, drugs used to treat it have also a number of side effects. (6) For this reason, the number of studies investigating the reversible causes of insomnia in recent years has increased.

Both micronutrient deficiencies and malnutrition or malnutrition risk are quite common, and are risk factors for a variety of negative consequences, such as sarcopenia, frailty, falls, depression, and cognitive impairment in older adults (7–9). In only a few of these studies, a significant relationship between micronutrient abnormalities and sleep was shown following the evaluation of the effect of nutritional factors on insomnia. (10–12) One study found a relationship between low serum vitamin D levels and short sleep duration and lower sleep efficiency in older men. (11) Another identified a correlation between vitamin B12, vitamin D and folate deficiency and sleep disturbance. (8) Moreover, although malnutrition is as important as micronutrient deficiency and is common, to the best of our knowledge, there is no study investigating the relationship between malnutrition and insomnia.

Therefore, the aim of this study was to investigate the relationship between Mini Nutritional Assessment scores/nutrients and insomnia/insomnia severity in the elderly.

**Methods**

**Patients**

A total of 575 older outpatient who were admitted to a geriatric clinic were included in this study. All the patients underwent Comprehensive Geriatric Assessment (CGA). (13) The investigation conformed to the Declaration of Helsinki was approved by our local ethics committee. Informed consent was provided by each participant or a legal guardian before participating in the study.

Patients who had severe illness that may impair their general health status, such as acute cerebrovascular event, sepsis, acute renal failure, acute coronary syndrome, and acute respiratory failure; patients under 65 years of age; patients who did not agree to undergo the CGA; patients who take medication for sleep disorders or who take nutritional supplements for malnutrition or nutrient deficiencies were excluded. Patients with moderate and severe dementia were also ruled out because self-reports based on their memory might be unreliable for questions about insomnia and nutrition, but patients with mild dementia were included.

**Patients’ Characteristics:**

Patients’ age, gender, education level, and drugs were recorded. Those with hypertension, ischemic heart disease, congestive heart failure, diabetes mellitus, peripheral arterial disease, chronic obstructive pulmonary disease (COPD), cerebrovascular disease or Parkinson’s Disease were identified by their or caregivers’ self-reports. In addition, comorbidity status of the patients was evaluated using the Charlson Comorbidity Index (CCI). (14) Dementia and depression were diagnosed according to Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) criteria. (15) All the participants underwent the Mini-Mental State Examination, and Geriatric Depression Scale-15 for neurocognitive evaluation. (16,17)

**Nutritional Evaluation**

MNA (Mini Nutritional Assessment) was performed in all patients to detect nutritional status, even if their MNA-Short Form scores were ≥12. If the total score was > 23.5, 17-23.5, <17, it was accepted as well-nourished, risk of malnutrition, and malnutrition, respectively. The MNA test is composed of simple measurements and 18 brief questions that can be completed in < 10 min: anthropometric measurements (4 questions related to BMI, weight loss, brachial circumference, and calf circumference); Global assessment (6 questions related to lifestyle, medication, and mobility); Dietary questionnaire and subjective assessment (8 questions related to number of meals, food and fluid intake, and autonomy of feeding, self-perception of health and nutrition). (18) Due to the potentially multifactorial origin of nutritional risk in the older adults, the MNA specifically designed and validated for the olders. Given the multi-dimensional approach, the MNA properly addresses this requirement and the prevalence of nutritional conditions provided by the MNA appears in the measure able to reflect the nutritional features. (19) To calculate body mass index (BMI), height was measured to the nearest centimeter (cm) and weight was measured to the nearest half-kilogram (kg) with the same stadiometer.

**Assessment of Insomnia**

Insomnia Severity Index (ISI) consists of 7 questionnaire items that capture self-reported symptoms and daytime consequences of insomnia, according to criteria from the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. ISI scores range from 0 to 28, with higher scores indicating more severe insomnia. ISI scores of 8 or higher indicated insomnia, with severity further stratified according to ISI score as subthreshold (herein termed mild) (8–14), moderate (15–21), and severe (22–28). (20,21)

**Vitamin B12, folate and vitamin D assessment**

To evaluate the biochemical evidence of insufficient intake and the metabolic condition, blood samples were collected in the morning after at least 8 h of fasting. Serum vitamin B12 level was considered to be deficient and low serum vitamin B12 level when it was below 200 pg/ml and below 400 pg/ml, respectively. (22) Vitamin B12 was also evaluated according to cut-off 150 pg/ml.(23) Folate deficiency and low folate level were evaluated according to both < 3 ng/ml and 6 ng/ml, respectively. (7) After blood collection the gel tubes were centrifuged within one hour and the sera stored at 200C for serum vitamin D analysis. 25(OH) D was measured by radioimmunoassay method. Patients with 25(OH) D < 10 ng/ml were considered to have vitamin D deficiency, and 25(OH) D=10-20 ng/ml was accepted as insufficiency. (24)

**Laboratory Findings**

Laboratory tests were performed to assess biochemical, metabolic, and nutritional status of the patients included measurements of complete blood count, kidney and liver functions, cholesterol levels, thyroid stimulating hormone, and HbA1c. All these biochemical tests were performed using the Diagnostic Modular Systems auto analyser (Roche E170 and P-800).

**Statistical Analyses**

Data were analysed using SPSS, version 22. Descriptive statistics are shown as mean±standard deviation for variables with normal distribution, median (minimum to maximum) for non-normal distributions, and number of cases and percentage for nominal variables. When the group number was 2, the significance of differences between the groups in terms of averages was investigated by t test, and if in median values, was investigated by Mann-Whitney test. When the number of groups was more than 2, the significance was investigated by analysis of variance and the Kruskal-Wallis test for averages and medians, respectively. Nominal variables were assessed by the Pearson chi-square or Fisher exact test. Variances in more than 2 groups were assessed by post hoc Tukey tests. We used linear regression and logistic regression to analyse associations between sleep status and nutritional status and MNA scores, adjusted for all covariates including gender, education, number of drugs, CCI, presence of depression, and MMSE scores. For p <0.05, results were considered statistically significant.

**RESULTS**

The mean age of 575 patients was 73.1 ±7.7, 73.2% of them was female and mean education level was 3.2 ± 1.9. The prevalence of patients without insomnia was (ISI < 8) 34.4%. The prevalence of patients with mild insomnia, moderate insomnia and severe insomnia were 20.9%, 30.1%, and 14.6%, respectively. There is no difference between the groups in terms of laboratory findings including kidney and liver functions, cholesterol levels, thyroid stimulating hormone (p>0.05). Table 1 shows demographic and clinical characteristics. There was a significant difference between groups in terms of gender, education, number of drugs, CCI, presence of depression, and MMSE scores (p<0.05). The four insomnia severity groups were compared with respect to nutritional parameters, and lower MNA scores and higher rates of malnutrition and malnutrition risk were detected in patients with moderate and severe insomnia compared to the patients with mild insomnia or without insomnia (p<0.001). When groups were adjusted for all covariates, the significant differences between nutritional status and insomnia severity status persisted (p<0.05). There were no significant differences between insomnia severity status and serum vitamin D, Vitamin B12, folate levels or classification of these nutrients (p>0.05).

The relations between nutritional status and insomnia groups were investigated usinglogistic regression analysis adjusting for all the covariates. Results showed that there was a statistically significant relationship between insomnia status and MNA and nutritional status (p<0.05). Their odd ratios were shown in Table 2. Relationships between insomnia status and MNA and nutritional status were investigated using multiple linear regression models and are shown in Table 2. There were significant positive correlations between malnutrition/risk of malnutrition and insomnia/moderate and insomnia/severe insomnia, whereas insomnia status and MNA scores showed a significant negative correlation (p<0.05).

Figure 1 shows the comparison ofprevalence of insomnia according to nutritional status (p<0.05).

**Discussion**

In this study, the relationship between insomnia and insomnia severity and nutritional status was investigated in the elderly, and MNA scores were found to be lower in patients with moderate and severe insomnia. Insomnia or moderate to severe insomnia have been shown to be significantly correlated with nutritional status and associated with low MNA scores. However, for mild insomnia, this relationship was not detected.

Insomnia is common in older adults, but the prevalence of both insomnia and moderate and severe insomnia in our study was more frequent than previous studies. (25) In a meta-analysis, the prevalence of sleep problems was found to be high in low- and middle-income countries and was associated with depression, low education and low socioeconomic status; which may explain the high insomnia prevalence in our study. (26) In addition to this high incidence of insomnia, it may be associated with difficulty in maintaining daily activities, falling, fractures, stroke, physical disability, dementia, respiratory symptoms and cardiac diseases. (3) Moreover, considering that the drugs used for the treatment of insomnia in the elderly have numerous side effects, the importance of revealing the causes of reversible insomnia, which may lead to insomnia, will be better understood. (6)

Malnutrition/the risk of malnutrition, such as insomnia, is one of the most important geriatric syndromes that may cause complications similar to that of insomnia with increasing age; however, there is no study investigating how insomnia is affected by nutritional status of patients. In our study, it was found that MNA scores and normal nutritional status were lower in patients with insomnia, particularly in patients with moderate and severe insomnia. Possible mechanisms that explain this may include: Firstly, malnutrition may cause neurodegeneration and white matter damage, which may impair the regulation of brain functions. (27–29) For example, in previous studies, dialysis patients with anorexia nervosa and severe weight loss had a higher risk of the brain atrophy and low fat mass was associated with more white matter hyperintensities (WMHs). (28) In a study by Marian et al., it was claimed in the elderly that malnutrition may cause WMHs rather than brain atrophy, which may be explained by malnutrition alone that impairs cardiovascular homeostasis independently of other cardiovascular risk factors, as in our study. (29,30) Additionally, malnutrition-related inflammation is another cause of WMHs. (31) In recent years, these WMHs have been found to cause insomnia by disrupting the integrity between left thalamus and pars triangularis tracts. (32) In another study, the dysfunctions of white matter structural network connectivity in healthy adults were found to be associated with insomnia symptoms. (33) On the other hand, experimental studies have shown that in rats with malnutrition, the size of the suprachiasmatic nucleus, which is the most powerful pacemaker for circadian rhythm, has a key role in sleep physiology, and that sleep deprivation is decreased by energy and nutritional supplementation. (34,35) Secondly, dietary factors can affect melatonin release. (36) Melatonin is a circulating neurohormone, which is mainly secreted at night and is produced from tryptophan, an essential amino acid. (35) It is important to detect the daily light and dark cycle, so that the circadian rhythm can be regulated and help us fall asleep and stay asleep. (36) There are many studies showing the effect of diet on the synthesis or concentration of melatonin. For example, it has been shown in human studies that energy restriction decreases the release of melatonin at night. (36-38) In short-term (2 days) fasting healthy men, melatonin secretion was decreased compared to the control group, and normalization of melatonin levels were found after glucose supplementation. (38) Similar studies have been made in obese and the same results have been obtained. (40) Thirdly, in patients with malnutrition, Orexin, a neuropeptide released from the hypothalamus to increase nutrition, also increases alertness. (41) Accordingly, a large number of studies have shown that sleep is adversely affected in patients with anorexia and bulimia nervosa compared to those without; therefore, sleep is thought to be a clinical marker for eating disorders. (42) Orexin neurons “fire” with circadian rhythm; thus, orexin levels increase during periods of wakefulness, whereas serum rates of Orexin decrease during sleep. A recent study demonstrated that plasma orexin levels were higher in patients with insomnia than those without insomnia. (43) Orexin receptor antagonists also were shown to improve sleep, and might be potential pharmacologic agents for treatment of disordered eating in humans. (44,45) However, further research is necessary to address this issue. Lastly, insomnia itself may also affect dietary behaviors and intake. (46) For example, decreased appetite for heart failure patients was associated with insomnia. (47) On the other hand, decreased sleep time may also help to explain the cause of worsening nutrient status by increasing insomnia severity. (48) However, future studies utilizing a longitudinal or experimental design are needed to establish the accuracy of all these hypotheses.

Our study is the first to investigate insomnia severity and nutritional status in the elderly. So far, correlation between malnutrition and insomnia was vaguely mentioned in studies investigating geriatric syndromes associated with malnutrition in the elderly, but this correlation could not elaborately be evaluated because they were not aimed for this purpose. (49,50) Although some studies have shown that vitamin B12, folate and especially vitamin D may cause insomnia (10,11), it is unclear whether this relationship is due to malnutrition or indeed nutrient deficiency, since none of these studies concurrently have nutritional status assessed.

The strengths of our study are: the number of adequate samples; grading not only the presence of insomnia, but also the severity of insomnia; MNA-long form applied to all patients; simultaneous evaluation of both nutritional and vitamin B12, folate and vitamin D. However, our study is not without limitation. First, the present study was cross-sectional in design and the direction of the association is not known. That is, it is not known whether insomnia leads to poor nutritional parameters or whether poor nutritional parameters lead to insomnia. It is possible that the relationship is bidirectional. Future research of an experimental prospective design is now needed. Second, only the insomnia severity index scale was used for insomnia, future studies should consider using objective measures of sleep to diagnose insomnia, such as actigraphy. Third, the correlations between MNA items associated with food intake or weight/weight loss variables and insomnia were not evaluated. Last, the number of patients with folate deficiency was so low that it was not able to be analysed.

**Conclusions and Implications**

In conclusion, there is a close relationship between insomnia and insomnia severity and nutritional status in the elderly. Especially in patients with moderate and severe insomnia, MNA scores are lower. Therefore, when evaluating an elderly patient with insomnia in geriatric practice, malnutrition should be evaluated or insomnia should be questioned in an elderly patient with malnutrition. Thus, more effective management of the two will be possible.

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**References**

1. Yaremchuk K. Sleep Disorders in the Elderly. Clinics in Geriatric Medicine. 2018; 34(2):205-216.

2. Patel D, Steinberg J, Patel P. Insomnia in the elderly: A review. Journal of Clinical Sleep Medicine. 2018; 15;14(6):1017-1024.

3. Foley DJ, Monjan A, Simonsick EM, Wallace RB, Blazer DG. Incidence and remission of insomnia among elderly adults: An epidemiologic study of 6,800 persons over three years. J Sleep Res Sleep Med. 1999; 1;22 Suppl 2:S366-72.

4. Gulia KK, Kumar VM. Sleep disorders in the elderly: a growing challenge. Psychogeriatrics. 2018; 18(3):155-165.

5. Kamel NS, Gammack JK. Insomnia in the Elderly: Cause, Approach, and Treatment. American Journal of Medicine. 2006; 119(6):463-9.

6. Kalan U, Soysal P, Isik AT. Delirium associated with only one dose of zopiclone in an older adult. Psychogeriatrics. 2018; 18(4):321-323

7. Soysal P, Smith L, Capar E, Kalan U, Arik F, Isik AT. Vitamin B12 and folate deficiencies are not associated with nutritional or weight status in older adults. Exp Gerontol. England; 2018;116:1–6.

8. Soysal P, Turan Isik A. Vitamin B<inf>12</inf>deficiency can be a cause of acute reversible parkinsonism and cognitive impairment in older adults. Geriatr Gerontol Int. 2018;18(4).

9. Ates Bulut E, Soysal P, Aydin AE, Dokuzlar O, Kocyigit SE, Isik AT. Vitamin B12 deficiency might be related to sarcopenia in older adults. Exp Gerontol. 2017; 95:136-140

10. Beydoun MA, Gamaldo AA, Canas JA, Beydoun HA, Shah MT, McNeely JM, et al. Serum nutritional biomarkers and their associations with sleep among US adults in recent national surveys. PLoS One. 2014; 19;9(8):e103490

11. Massa J, Stone KL, Wei EK, Harrison SL, Barrett-Connor E, Lane NE, et al. Vitamin D and Actigraphic Sleep Outcomes in Older Community-Dwelling Men: The MrOS Sleep Study. Sleep. 2015;38(2):251-7.

12. Grandner MA, Jackson N, Gerstner JR, Knutson KL. Sleep symptoms associated with intake of specific dietary nutrients. J Sleep Res. 2014; 23(1):22-34.

13. Unutmaz GD, Soysal P, Tuven B, Isik AT. Costs of medication in older patients: Before and after comprehensive geriatric assessment. Clin Interv Aging. 2018; 9;13:607-613.

14. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. J Chronic Dis. 1987; 40(5):373-83

15. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders DMS V. Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. 2013.

16. Dokuzlar O, Soysal P, Usarel C, Isik AT. The evaluation and design of a short depression screening tool in Turkish older adults. Int Psychogeriatrics. 2018; 30(10):1541-1548.

17. Güngen C, Ertan T, Eker E, Yaşar R, Engin F. Reliability and validity of the standardized Mini Mental State Examination in the diagnosis of mild dementia in Turkish population. Türk Psikiyatr Derg. 2002; 13(4):273-81.

18. Vellas B, Guigoz Y, Garry PJ, Nourhashemi F, Bennahum D, Lauque S, et al. The mini nutritional assessment (MNA) and its use in grading the nutritional state of elderly patients. Nutrition. 1999; 15(2):116-22.

19. [Cereda E](https://www.ncbi.nlm.nih.gov/pubmed/?term=Cereda%20E%5BAuthor%5D&cauthor=true&cauthor_uid=22037014). Mini nutritional assessment. [Curr Opin Clin Nutr Metab Care.](https://www.ncbi.nlm.nih.gov/pubmed/22037014) 2012 Jan;15(1):29-41.

20. Bastien CH, Vallières A, Morin CM. Validation of the insomnia severity index as an outcome measure for insomnia research. Sleep Med. 2001; 2(4):297-307.

21. Morin CM, Belleville G, Bélanger L, Ivers H. The insomnia severity index: Psychometric indicators to detect insomnia cases and evaluate treatment response. Sleep. 2011; 1;34(5):601-8.

22. Bozoglu E, Isik AT, Doruk H, Kilic S. The effects of early vitamin B12 replacement therapy on the cognitive and functional status of elderly subjects. Klin Psikofarmakol Bul. 2010; 20:120-124.

23. Abeywickrama HM, Koyama Y, Uchiyama M, Shimizu U, Iwasa Y, Yamada E, et al. Micronutrient Status in Sri Lanka: A Review. Nutrients. Switzerland; 2018;10(11).

24. Thacher TD, Clarke BL. Vitamin D insufficiency. Mayo Clinic Proceedings. 2011; 86(1):50-60

25. Dragioti E, Bernfort L, Larsson B, Gerdle B, Levin LA. Association of insomnia severity with well-being, quality of life and health care costs: A cross-sectional study in older adults with chronic pain (PainS65+). Eur J Pain. England; 2018 Feb;22(2):414–25.

26. Mazzotti DR, Guindalini C, Sosa AL, Ferri CP, Tufik S. Prevalence and correlates for sleep complaints in older adults in low and middle income countries: A 10/66 Dementia Research Group study. Sleep Med. 2012; 13(6):697-702.

27. Masanori Mukai, Kazumitsu Mukai, Hiroo Ichikawa, Mikio Wakasa, Daisuke Sanada, Takanori Shibata, Mitsuru Kawamura TA. Malnutrition and cerebral white matter lesions in dialysis patients. Nippon Toseki Igakkai Zasshi. 2008;41(7):421–8.

28. Fleta Zaragozano J, Jiménez Vidal A, Velilla Picazo M, González Castro G, Pina Leita I, Olivares López JL. [Anorexia nervosa and cerebral atrophy in adolescents]. Med Clin (Barc). 2005; 124(15):571-2.

29. de van der Schueren MAE, Lonterman-Monasch S, van der Flier WM, Kramer MH, Maier AB, Muller M. Malnutrition and Risk of Structural Brain Changes Seen on Magnetic Resonance Imaging in Older Adults. J Am Geriatr Soc. 2016; 64(12):2457-2463.

30. Handler P BF. Influence of dietary factors on hypertension induced by choline deficiency. Am J Physiol. 1950;162:189.

31. Zheng K, Wang H, Hou B, You H, Yuan J, Luo K, et al. Malnutrition-inflammation is a risk factor for cerebral small vessel diseases and cognitive decline in peritoneal dialysis patients: A cross-sectional observational study. BMC Nephrol. 2017; 20;18(1):366.

32. Kang JM, Joo SW, Son Y-D, Kim H, Ko K-P, Lee JS, et al. Low white-matter integrity between the left thalamus and inferior frontal gyrus in patients with insomnia disorder. J Psychiatry Neurosci. Canada; 2018 Nov;43(6):366–74.

33. Lu F-M, Dai J, Couto TA, Liu C-H, Chen H, Lu S-L, et al. Diffusion Tensor Imaging Tractography Reveals Disrupted White Matter Structural Connectivity Network in Healthy Adults with Insomnia Symptoms. Front Hum Neurosci. 2017; 30;11:583.

34. Cintra L, Galvan A, Diaz-Cintra S, Escobar C. Protein malnutrition on suprachiasmatic nucleus cells in rats of three ages. Boletin de estudios medicos y biologicos. 1994; 42(1-4):11-9.

35. Everson CA. Functional consequences of sustained sleep deprivation in the rat. Behav Brain Res. 1995; 69(1-2):43-54.

36. Peuhkuri K, Sihvola N, Korpela R. Dietary factors and fluctuating levels of melatonin. Food Nutr Res. 2012; 56.

37. Michalsen A, Schlegel F, Rodenbeck A, Lüdtke R, Huether G, Teschler H, et al. Effects of short-term modified fasting on sleep patterns and daytime vigilance in non-obese subjects: Results of a pilot study. Ann Nutr Metab. 2003; 47(5):194-200.

38. Röjdmark S, Rössner S, Wetterberg L. Effect of short-term fasting on nocturnal melatonin secretion in obesity. Metabolism. 1992; 41(10):1106-9.

39. Rojdmark S, Wetterberg L. Short-term fasting inhibits the nocturnal melatonin secretion in healthy man. Clin Endocrinol (Oxf). England; 1989 Apr;30(4):451–7.

40. Mossavar-Rahmani Y, Jung M, Patel SR, Sotres-Alvarez D, Arens R, Ramos A, et al. Eating behavior by sleep duration in the Hispanic Community Health Study/Study of Latinos. Appetite. England; 2015 Dec;95:275–84.

41. Allison KC, Spaeth A, Hopkins CM. Sleep and Eating Disorders. Current Psychiatry Reports. 2016; 18(10):92.

42. Asaad Abdou T, Esawy HI, Abdel Razek Mohamed G, Hussein Ahmed H, Elhabiby MM, Khalil SA, et al. Sleep profile in anorexia and bulimia nervosa female patients. Sleep Med. 2018; 48:113-116.

43. Tang S, Huang W, Lu S, Lu L, Li G, Chen X, et al. Increased plasma orexin-A levels in patients with insomnia disorder are not associated with prepro-orexin or orexin receptor gene polymorphisms. Peptides. 2017; ;88:55-61.

44. Sun H, Kennedy WP, Wilbraham D, Lewis N, Calder N, Li X, et al. Effects of suvorexant, an orexin receptor antagonist, on sleep parameters as measured by polysomnography in healthy men. Sleep. 2013; 36(2):259-67.

45. Cole S, Mayer HS, Petrovich GD. Orexin/Hypocretin-1 Receptor Antagonism Selectively Reduces Cue-Induced Feeding in Sated Rats and Recruits Medial Prefrontal Cortex and Thalamus. Sci Rep. England; 2015 Nov;5:16143.

46. Kim S, Deroo LA, Sandler DP. Eating patterns and nutritional characteristics associated with sleep duration. Public Health Nutr. 2011; 14(5):889-95.

47. Andreae C, Strömberg A, Årestedt K. Prevalence and associated factors for decreased appetite among patients with stable heart failure. J Clin Nurs. 2016; 25(11-12):1703-12.

48. Jung CM, Melanson EL, Frydendall EJ, Perreault L, Eckel RH, Wright KP. Energy expenditure during sleep, sleep deprivation and sleep following sleep deprivation in adult humans. J Physiol. 2011; 589(Pt 1):235-44.

49. El-Desouky R, Abed H. Screening of malnutrition and its correlates among a sample of rural elderly in Qalyobeya Governorate, Egypt. J Egypt Public Health Assoc. England; 2017 Sep;92(3):156–66.

50. Saka B, Kaya O, Ozturk GB, Erten N, Karan MA. Malnutrition in the elderly and its relationship with other geriatric syndromes. Clin Nutr. 2010; 29(6):745-8.

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| **Table 1. Demographic and Clinical Characteristics Insomnia Status** | | | | | |
|  | **Insomnia Severity Index (No=575)** | | | | |
| **Characteristic** | **No insomnia**  **(198)** | **Mild insomnia**  **(120)** | **Moderate**  **Insomnia**  **(173)** | **Severe insomnia**  **(84)** | **p value** |
| Age (years) | 72.9±7.8 | 72.1±7.2 | 74.2±8.0 | 72.8±7.8 | 0.151 |
| \*Gender (Female, %) | 60.6 | 78.3 | 80.9 | 79.8 | **<0.001** |
| \*Education (years) | 4.5±3.9 | 3.3±2.9 | 2.5±3.4 | 2.6±3.2 | **<0.001** |
| \*CCI | 0.8 ±1.1 | 0.8±0.7 | 2.2±9.3 | 1.1±1.6 | **<0.05** |
| \*Number of Drugs | 3.7±2.6 | 4.4±2.6 | 4.3±2.6 | 5.1±3.3 | **0.005** |
| Obesity (%) | 59.1 | 65.0 | 57.8 | 57.1 | 0.338 |
| **COMORBIDITIES (%)** |  |  |  |  |  |
| Cerebrovascular Events | 6.1 | 1.7 | 6,9 | 7.1 | 0.170 |
| Diabetes Mellitus | 31.8 | 39.2 | 37.0 | 32.1 | 0.493 |
| Ischemic Heart Disease | 12.2 | 15.8 | 15.0 | 16.7 | 0.709 |
| Congestive heart failure | 4.5 | 4.2 | 7.0 | 9.5 | 0.304 |
| Hypertension | 67.2 | 69.2 | 69.4 | 64.3 | 0.848 |
| COPD | 9.6 | 10.0 | 12.7 | 19.0 | 0.134 |
| Osteoarthritis | 22.2 | 26.7 | 30.6 | 25.0 | 0.326 |
| Parkinson's disease | 3.5 | 5.0 | 6.4 | 7.14 | 0.078 |
| Dementia | 5.1 | 3.3 | 5.2 | 7.1 | 0.903 |
| \*Depression | 38.6 | 35.6 | 59.2 | 62.3 | **<0.001** |
| \***MMSE** | 25.6±3.2 | 24.6±4.4 | 22.9±5.4 | 23.8±3.8 | **<0.001** |
| **Nutritional Determinants** |  |  |  |  |  |
| **\*Nutritional Status** | | | | | |
| * Malnutrition | 1.5 | 5.8 | 10.4 | 7.1 | **<0.001\*\*** |
| * Risk of Malnutrition | 22.7 | 30.0 | 43.4 | 52.3 |
| * Well-nourished | 78.8 | 64.2 | 46.2 | 40.6 |
| MNA scores | 25.4±3.0 | 24.4±3.4 | 22.7±4.0 | 22.6±3.3 | **<0.001\*\*** |
| **Classification of Vitamin D (%)** | | | | | |
| * ≤ 10 ng/ml | 34.3 | 49.2 | 42.8 | 38.1 | 0.266 |
| * 10-20 ng/ml | 24.2 | 18.3 | 22.0 | 32.1 |
| * >20 ng/ml | 41.5 | 32.5 | 35.2 | 29.8 |
| Serum Vitamin D levels | 20.7±16.7 | 18.0±11.7 | 17.0±11.7 | 18.1±12.9 | 0.709 |
| **Classification of Vitamin B12 (%)** | | | | | |
| * <200 pg/ml | 14.1 | 13.3 | 15.0 | 12.2 | 0.934 |
| * 200-400 pg/ml | 48.0 | 42.5 | 46.8 | 50.0 |
| * >400 pg/ml | 37.9 | 44.2 | 38.2 | 37.8 |
| * < 150 pg/mL | 21.2 | 18.3 | 17.3 | 16.7 | 0.793 |
| * ≥ 150 pg/mL | 78.8 | 81.7 | 82.7 | 83.3 |
| Serum Vitamin B12 levels | 267.3±157.2 | 229.4±119.3 | 277.1±158.0 | 267.4±166.5 | 0.098 |
| **Serum Folate Levels** | 8.7±3.6 | 9.0±3.2 | 8.9±3.2 | 9.6±4.1 | 0.518 |
| **Classification of Folate (%)** | | | | | |
| * **Folate < 3 ng/ml** | 3.2 | 1.7 | 1.9 | 2.5 | NA |

**CCI:** Charlson Comorbidity Index; MMSE: Mini Mental State Examination; NA: Not Applicable

**\***The parameters were significantly different between patients with insomnia (≥ 8 ISI score) and control group (< 8 ISI score)

\*\* After adjustment for gender, education, number of drugs, CCI, presence of depression, and MMSE scores, p value was still found significant (p< 0.05)

NA: Because the number of patients with folate deficiency was so low that it was not able to be analyzed

**Table 2. Associations Between Nutritional Status and Insomnia Severity Status**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Insomnia** | | **Mild Insomnia** | | **Moderate Insomnia** | | **Severe Insomnia** | |
|  | **Logistic Regression** | | | | | | | |
|  | **OR (%95 CI)** | **p** | **OR (%95 CI)** | **p** | **OR (%95 CI)** | **p** | **OR (%95 CI)** | **p** |
| **Malnutrition and**  **Risk of Malnutrition** | 1.6 (0.9-2.7) | 0.070 | 1.8 (0.8-4.1) | 0.124 | 1.6 (1.0-2.5) | 0.046 | 1.6 (1.0-2.7) | 0.042 |
| **MNA scores** | 0.84 (0.7-0.9) | <0.001 | 0.9 (0.8-1.0) | 0.051 | 0.83 (0.7-0.9) | 0.000 | 0.82 (0.7-0.9) | 0.001 |
|  | **Linear Regression** | | | | | | | |
|  | **Beta** | **p** | **Beta** | **p** | **Beta** | **p** | **Beta** | **p** |
| **Malnutrition** | 0.348 | <0.001 | 0.135 | 0.39 | 0.508 | <0.001 | 0.440 | 0.02 |
| **Risk of Malnutrition** | 0.213 | <0.001 | 0.097 | 0.12 | 0.261 | <0.001 | 0.304 | 0.04 |
| **MNA scores** | -0.285 | <0.001 | -0.022 | 0.09 | -0.358 | <0.001 | -0.383 | <0.001 |

