RESEARCH

ASSOCIATION BETWEEN VITAMIN D LEVEL AND TOTAL COMORBIDITY STATUS IN GERIATRIC PATIENTS

Abstract

Introduction: Vitamin D is known as an anti-inflammatory, antitumor, and immune-modulating hormone, which plays an important role in common diseases in the geriatric population, such as hypertension and cerebrovascular disorders. Vitamin D deficiency has been linked to various diseases in the literature. However, the association between vitamin D and multiple comorbidities remains unclear due to limited published data. The aim of the present study was to evaluate the association between vitamin D levels and multiple comorbidities in elderly patients.

Materials and Method: The study design was cross-sectional. Geriatric patients (aged ≥65 years) who underwent serum 25(OH)D evaluation to determine the vitamin D status during the last 3 months were assessed for eligibility. Demographic data and 25(OH)D levels of patients were obtained from the electronic database of the hospital and a telephonic interview. In addition, a comorbidity questionnaire was completed via telephonic interviews. The correlation between comorbidity scores, demographic data, and vitamin D levels in elderly patients was analyzed.

Results: Data on 25(OH)D levels in 685 geriatric patients was obtained. Among these patients, 211 (169 female, 42 male) who were contacted over telephone were enrolled. The mean values for age, vitamin D level, and comorbidity scores were 70.4±5.0 years, 16.8±9.2 ng/ml, and 11.3±4.7, respectively. A moderate-good negative correlation was found between 25(OH)D levels and comorbidity scores (r=−0.503).

Conclusion: Low vitamin D levels were associated with total comorbidity status in geriatric patients. This result suggests that vitamin D deficiency may be a risk factor for comorbidities in geriatric patients.

Keywords: Comorbidity; Geriatrics; Vitamin D

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ARAŞTIRMA

GERİATRİ YAŞ GRUBUNDAKİ HASTALARDA D VİTAMİNİ DÜZEYİ İLE TOTAL KOMORBİDİTE DURUMU ARASINDAKİ İLİŞKİ

Öz

Giriş: Vitamin D, anti-inflamatuvar, anti-tümör ve immünmodulatuvar etkileri nedeniyle; hipertansiyon ve serebrovasküler hastalıklar gibi, geriatrik popülasyonda sık görülen bazı sağlık problemlerinde önemli role sahiptir. Literatürde farklı hastalıklarda vitamin D eksikliğinin rolü gösterilmiştir. Ancak, birden fazla sağlık probleminin olduğu ileri yaş grubunda, vitamin D seviyesi ile komorbidite arasındaki ilişki net değildir. Bu çalışmada, yaşlı hastalarda, vitamin D seviyesi ile komorbidite arasındaki ilişkinin saptanması amaçlanmıştır.

Gereç ve Yöntem: Çalışma dizaynı kesitseldir. Son 3 ay içinde 25(OH)D seviyeleri bakılmış olan geriatrik hastalar (≥65 yaş) uygunluk açısından değerlendirildi. Hastane veri tabanından ve telefon görüşmesi ile, hastaların demografik verileri ve 25(OH)D seviyeleri kaydedildi. Ayrıca, telefon görüşmesi ile hastaların komorbidite anketi dolduruldu. Geriatrik hastaların, komorbidite skoru, demografik özellikleri ve serum 25(OH)D düzeyi arasındaki korelasyon değerlendirildi.

Bulgular: Veri tabanında 65 yaş ve üzeri toplam 685 hastanın 25(OH)D seviyeleri mevcuttu. Bu hastalardan telefon aracılığıyla ulaşılabilen 211 hasta (169 kadın, 42 erkek) çalışmaya dahil edildi. Hastaların yaş, 25(OH)D düzeyi ve komorbidite skoru için ortalama değerleri sırasıyla; 70.4±5.0 yıl, 16.8±9.2 ng/ml ve 11.3±4.7 idi. Yapılan korelasyon analizinde, serum 25(OH) D seviyesinin, komorbidite skoru ile orta-iyi derecede negatif korele olduğu tespit edildi (r=−0.503).

Sonuç: Geriatrik hastalarda düşük vitamin D düzeyleri total komorbidite durumu ile ilişkili bulunmuştur. Bu nedenle, vitamin D eksikliği yaşlı hastalarda komorbidite için bir risk faktörü olarak düşünülebilir.

Anahtar sözcükler: Komorbidite; Geriatri; Vitamin D

INTRODUCTION

Comorbidity is described as the occurrence of additional disorders in a patient who has an index disease at a given time point (1). An index disease is defined as a single disease of interest. Additional disorders are classified according to comorbidity as causality, complication, and coincidence. Causality is an abnormality linked with the pathophysiology of the index disease; complications are impairments due to the treatment of the index disease; and coincidence is the coexistence of any disease that is not related to the index disease (1). Multimorbidity is defined as the coexistence of two or more chronic diseases of equal importance in the same patient (1,2). In the literature, the impact of comorbidities on patients' health has been investigated and associated with poor outcomes, impaired mental functioning, increased percentages of disability and frailty, prolonged hospital stays, risk of adverse drug reactions related to polypharmacy, and higher mortality (1,3-5). The number of comorbidities increases with age, disease duration, and/or disease activity (1,6); thus, there is an increased prevalence of comorbidity in the geriatric population (6). This association has encouraged physicians to investigate contributors or exacerbators of comorbid conditions (3). The association between comorbidity and factors, including genes, environment, diet, and exercise, has been stated in the literature (7-9). Particularly, vitamin D is one of the most prominent factors accounting for disorders and impairments that contribute to comorbidity.

Vitamin D is a fat-soluble vitamin and hormone that affects not only the musculoskeletal system but also almost all the tissues with vitamin D receptors (10). Several studies have investigated the association between vitamin D and specific diseases. According to the literature, low vitamin D levels are suggested to be a fundamental risk factor for various disorders, including hypertension, cardiovascular disease, cerebrovascular disease, chronic musculoskeletal pain, decreased physical performance, increased fall risk, and some types of malignancies which are common in the geriatric population (3,11-13). However, studies showing an association between decreased vitamin D levels and comorbidity are very limited in the literature (3).

We hypothesized that low levels of vitamin D may contribute to comorbidities and hence evaluated the association between vitamin D levels and total comorbidity rather than one specific disease in geriatric patients.

MATERIALS AND METHOD

Study population

Geriatric patients (aged ≥65 years) who underwent serum 25(OH)D evaluation during the last 3 months were assessed for eligibility. Of these patients, those who agreed to participate in the study and who met none of the exclusion criteria were included. Exclusion criteria were deafness, cognitive impairment, and unavailability due to other reasons.

The Local Ethics Committee of the University approved the study protocol. All the patients included in the study gave verbal consent.

Vitamin D evaluation

For each patient, serum 25(OH)D levels were tested by high performance liquid chromatography and categorized as sufficient (≥30 ng/ml), insufficient (21–29 ng/ml), and deficient (<20 ng/ml) according to the guidelines of the Endocrine Society (14).

Comorbidity evaluation

Total comorbidity status was assessed using a self-administered comorbidity questionnaire (15), with 12 defined medical comorbidities and 3 optional conditions. The questionnaire was completed via a telephonic interview with each participant during a 6-week period. Each interview lasted approximately 10 min. The medical

conditions defined in the questionnaire included heart disease, high blood pressure, lung disease, diabetes, ulcer or stomach disease, kidney disease, liver disease, anemia or other blood disease, cancer, depression, osteoarthritis and rheumatoid arthritis, back pain, and other diseases (with 3 open-ended questions). The questionnaire asked not only about the presence of any comorbidity but also whether the patient sought any treatment for the present comorbidity and whether the comorbidity had any impact on the individual's physical function. Each separate comorbidity was scored as 1=present and 0=absent. If a comorbid condition required treatment, an additional point was added. If this comorbidity limited the activity of the patient, another point was added. Thus, each comorbidity could score between 0 and 3 points; the total score ranged between 0 and 36, without the optional conditions, and the maximum score was calculated as 45 points when the open-ended items were also included (15).

Statistical analysis

SPSS statistical software version 20.0 was used for analysis. The normality of variables was checked using normality tests. Nonparametric tests (Mann–Whitney U and Kruskal–Wallis tests) were performed to analyze non-normally distributed continuous variables between the groups.

Demographic variables and comorbidity scores were analyzed according to vitamin D subgroups. The difference between the groups was examined using a *post-hoc* comparison test.

The results were expressed as the mean±standard deviation (SD). P values <0.05 were considered statistically significant. Correlations were tested with the Spearman correlation coefficient. The strength of the correlation was classified as none, very weak, weak–moderate, moderate–strong, and very strong when the correlation coefficient (r_s) values were 0–0.24, 0.25–0.49, 0.50–0.74, and 0.75–1.00, respectively.

RESULTS

A total 211 patients (169 female, 42 male) were included in the study. The mean values for age, body mass index (BMI), and comorbidity scores were 70.5±5.0 years, 28.5±5.7 kg/m^2, and 11.3±4.7 points, respectively.

The mean 25(OH)D levels in our study group were 16.8±9.2 ng/ml. These levels were <20 ng/ml (vitamin D deficiency) in 139 (65.9%) patients and 20–29 ng/ml (vitamin D insufficiency) in 50 (23.7%). Vitamin D levels were sufficient in only 22 (10.4%) patients.

Approximately 3.8% (n=8), 31.3% (n=66), and 37.4% (n=79) of the patients were morbidly obese (BMI ≥40 kg/m^2), obese (BMI ≥30 kg/m^2), and overweight (BMI=25–29.9 kg/m^2), respectively. The descriptive data and 25(OH)D levels of the study population are shown in 1.

When the results were analyzed according to vitamin D subgroups (deficient, insufficient, and sufficient), comorbidity scores and BMI were statistically significant among the groups (p< 0.001, p=0.04, respectively) (Table 2; Figure 1).

The *post-hoc* analysis revealed that patients with vitamin D deficiency had higher comorbidity scores than those with insufficiency and sufficiency (p=0.001). The study population was analyzed according to BMI groups (morbidly obese, obese, overweight, normal weight, and underweight), and no significant difference was found in terms of comorbidity scores and vitamin D levels.

A moderate-good negative correlation was found between serum 25(OH)D levels and comorbidity scores (r=−0.503). No correlation was found among the other parameters (Table 3).

We hypothesized that the comorbidity score would increase as vitamin D levels decreased. Based on the findings of this study, a moderate-good correlation between comorbidity score and vitamin D level was found, which confirmed our hypothesis.

Table 1. Demographic variables and 25(OH)D level of study population.

Characteristics	Mean±sd Median (min-max) Total (n=211)
Age (year)	70.5±5.0 69 (65-89)
BMI (kg/m²)	28.5±5.7 27.5 (15.6-49.6)
Comorbidity score	11.3±4.7 11 (2-25)
25-(OH)D (ng/ml)	16.8±9.2 15.2 (2.6-39.4)

BMI: Body mass index; Values are given as mean±standard deviation and median (minimum-maximum).

Table 2. Comparison of comorbidity scores and body mass index according to vitamin D levels.

Characteristics	Group 1 (n=139)	Group 2 (n=50)	Group 3 (n=22)	p	Comparison group	Post hoc p
F/M	110/29	39/11	20/2			
Age (year)	70.5±5.0	70.0±4.5	70.8±6.4	0.93		
BMI (kg/m²)	29.2±5.9	27.4±4.7	26.5±5.4	**0.04***	1 Vs 2	0.166
					1 Vs 3	0.141
					2 Vs 3	1.000
Comorbidity score	12.6±4.6	8.9±4.1	8.7±3.6	**<0.001¶**	1 Vs 2	**<0.001§**
					1 Vs 3	**0.001§**
					2 Vs 3	1.000

Group 1: <20 ng/ml; Group 2: 21-29 ng/ml; Group 3: ≥30 ng/ml; F/M: Female/Male; BMI: Body mass index; Values are given as mean±standard deviation. The results were derived from the Kruskal-Wallis test (* p<0.05, ¶ p<0.01) and Post hoc p values were analyzed (§ p<0.0167).

Table 3. Correlation between vitamin D level and clinical variables.

Characteristics	Age	BMI	Comorbidity Score	25-(OH)D
Age (year)	1	-0.116	0.172*	0.009
BMI (kg/m²)		1	0.000	-0.091
Comorbidity score			1	**-0.503**§
25-(OH)D (ng/ml)				1

Values represent the Spearman's correlation coefficient (r_s). BMI: Body Mass Index, p*<0.05, ¶p<0.01, §p<0.001

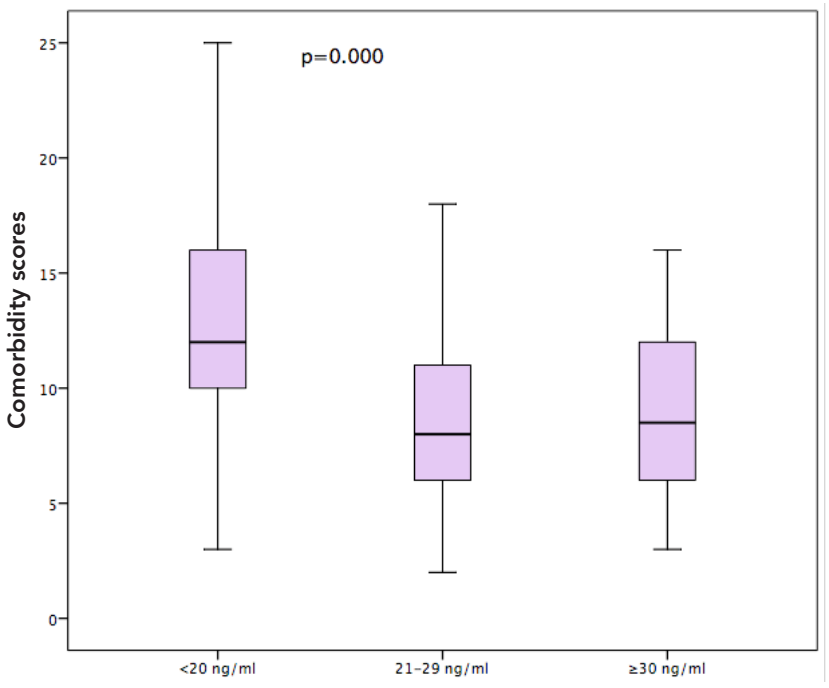

Figure 1. Comorbidity scores in the three groups of vitamin D level.

DISCUSSION

In the present study, we assessed patients' comorbidities using a self-administered comorbidity questionnaire that not only evaluated the comorbid conditions and drugs administered for these conditions but also investigated the ongoing impact of disorders on patients' functionality. The goal of our study was to determine the association of vitamin D levels with multiple comorbidities rather than a single disease or comorbidity.

A negative correlation was found between 25(OH)D levels and comorbidity scores in geriatric patients. In other words, we established the fact that low vitamin D levels are associated with increased comorbid conditions. Vitamin D affects many tissues in the body via several molecular mechanisms. It may also affect the expression of various genes, including those involved in pathophysiological pathways of cell proliferation, differentiation, apoptosis, and angiogenesis, as well as inflammation via these molecular mechanisms. However, it is unclear whether vitamin D modulates the expression of a particular gene in a particular organ under a particular condition (16,17). Studies investigating its effects on genes have shown that low levels of vitamin D may be associated with a cause and/or exacerbation of the illnesses. Consequently, decreased vitamin D levels have been linked with several diseases, especially age-related disorders (3,11-13,16-19). Nevertheless, the role of vitamin D in diseases could be viewed as a "chicken or egg" issue; i.e., low vitamin D levels may be a cause of certain disorders or a consequence of disorders and aging (3,10). Autier et al. showed an inverse relationship between vitamin D levels and certain diseases, but the efficiency of vitamin D supplementation in diseases was not determined. They suggested that decreased vitamin D level is a marker for ill health rather than a cause or risk factor for certain diseases (3,20). Similarly, Meems et al. demonstrated that low levels of vitamin D were associated with a high prevalence of multimorbidity and proposed vitamin D deficiency as a marker for health status (3).

In the current study, we also evaluated the association between comorbidity and demographic variables, such as age and BMI. Comorbidity scores in our study group were not correlated with BMI and were very weakly correlated with age. In a cross-sectional study investigating obesity prevalence and health consequences, Eggers et al. showed a positive correlation between BMI and age. In addition, they found that the incidence of certain comorbidities, such as asthma, diabetes, and hypertension, increases with increasing BMI (21).

According to the literature, the proportion of individuals aged ≥60 years has steadily increased from 8.1% in 1960 to 12% in 2015. This percentage is expected to further increase in the next 30-year period (22,23). Comorbid health conditions, such as heart disease, pulmonary disease, diabetes, hypertension, and arthritis, are common in these geriatric patients (24). Therefore, chronic diseases related to aging have replaced infectious diseases as the main reason for seeking healthcare (22). Numerous studies have investigated the factors that contribute to disorders in the elderly population, and one of the most important factors believed to impact these diseases is the vitamin D level (11,16,25). However, most studies have only assessed a specific illness and its association with vitamin D levels. Therefore, in the current study, we specifically aimed to evaluate the impact of vitamin D level on patients with multiple comorbidities.

The limitations of the present study are as follows: (i) retrospective nature of our search to predict the target population; and (ii) lack of vitamin D supplementation assessment. The strength of the current study is the confirmation of an inverse association between vitamin D levels and total comorbidity status in geriatric patients. Also, our results provide attention into this association for physicians dealing with geriatric population.

In conclusion, a decreased vitamin D level is associated with increased comorbidity in geriatric patients. Our results suggested that vitamin D deficiency may be a risk factor for comorbidities, particularly in geriatric patients. However, the actual cause of this association remains unclear. Longitudinal studies are warranted to determine whether diseases trigger vitamin D deficiency or low levels of vitamin D cause or exacerbate these diseases.

Conflicts of interest

The authors declare that they have no conflicts of interest.

REFERENCES

1. Alkan S, Sarsan A, Alkan H, Yıldız N, Topuz O, Ardıç F. Relationship between balance, physical performance and quality of life with vitamin D levels in the elderly. Turkish Journal of Geriatrics 2012;15(2):156-63.
2. Autier P, Boniol M, Pizot C, Mullie P. Vitamin D status and ill health: a systematic review. Lancet Diabetes Endocrinol 2014;2(1):76-89. (PMID:24622671).
3. Boeckxstaens P, Vaes B, Legrand D, Dalleur O, De Sutter A, Degryse JM. The relationship of multimorbidity with disability and frailty in the oldest patients: a cross-sectional analysis of three measures of multimorbidity in the BELFRAIL cohort. Eur J Gen Pract 2015;21(1):39-44. (PMID:24980394).
4. Chen LY, Liu LK, Hwang AC, et al. Impact of malnutrition on physical, cognitive function and mortality among older men living in veteran homes by minimum data set: A Prospective Cohort Study in Taiwan. J Nutr Health Aging 2016 Jan;20(1):41-7. (PMID:26728932).
5. de Borst MH, de Boer RA, Stolk RP, Slaets JP, Wolffenbuttel BH, Navis G. Vitamin D deficiency: universal risk factor for multifactorial diseases? Curr Drug Targets 2011;12(1):97-106. (PMID:20795934).
6. Dekker J, de Rooij M, van der Leeden M. Exercise and comorbidity: the i3-S strategy for developing comorbidity-related adaptations to exercise therapy. Disabil Rehabil 2016;38(9):905-9. (PMID:26176170).
7. Eggers S, Remington PL, Ryan K, Nieto J, Peppard P, Malecki K. Obesity prevalence and health consequences: Findings From the Survey of the Health of Wisconsin, 2008-2013. WMJ 2016;115(5):238-44. (PMID:29095585).
8. Güler H, Turhanoğlu A, Özer C. The effect of vitamin D supplementation on balance and quality of life in older women. Turkish Journal of Geriatrics 2008;11(2):57-61.
9. Gündüz E, Eskin F, Gündüz M, et al. Effects of sleep quality, income level and comorbid conditions on quality of life in a Turkish Elderly population: A multicenter study. Turkish Journal of Geriatrics 2015;18(2):136-42.
10. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2011;96(7):1911-30. (PMID:21646368).
11. Karlamangla A, Tinetti M, Guralnik J, Studenski S, Wetle T, Reuben D. Comorbidity in older adults: nosology of impairment, diseases, and conditions. J Gerontol A Biol Sci Med Sci 2007;62(3):296-300. (PMID:17389727).
12. Klimek P, Aichberger S, Thurner S. Disentangling genetic and environmental risk factors for individual diseases from multiplex comorbidity networks. Sci Rep 2016 Dec 23;6:39658. (PMID:28008973).
13. Liu GL, Pi HC, Hao L, Li DD, Wu YG, Dong J. Vitamin D status is an independent risk factor for global cognitive impairment in peritoneal dialysis patients. PLoS One 2015;10(12):e0143782. (PMID:26630385).
14. Marengoni A, Angleman S, Melis R, et al. Aging with multimorbidity: a systematic review of the literature. Ageing Res Rev 2011 Sep;10(4):430-9. (PMID:21402176).
15. Meems LM, de Borst MH, Postma DS, et al. Low levels of vitamin D are associated with multimorbidity: results from the LifeLines Cohort Study. Ann Med 2015;47(6):474-81. (PMID:26340085).
16. Muschitz C, Kocijan R, Stütz V, et al. Vitamin D levels and comorbidities in ambulatory and hospitalized patients in Austria. Wien Klin Wochenschr 2015;127(17-18):675-84. (PMID:26184408).
17. Piccirillo JF, Vlahiotis A, Barrett LB, Flood KL, Spitznagel EL, Steyerberg EW. The changing prevalence of comorbidity across the age spectrum. Crit Rev Oncol Hematol 2008;67(2):124-32. (PMID:18375141).
18. Radner H, Yoshida K, Smolen JS, Solomon DH. Multimorbidity and rheumatic conditions enhancing the concept of comorbidity. Nat Rev Rheumatol 2014;10(4):252-6. (PMID:24418765).
19. Rodríguez-Pérez A, Alfaro-Lara ER, Albiñana-Perez S, et al. Novel tool for deprescribing in chronic patients with multimorbidity: List of Evidence-Based Deprescribing for Chronic Patients criteria. Geriatr Gerontol Int 2017;17(11):2200-07. (PMID:28544188).
20. Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The self-administered comorbidity questionnaire: a new method to assess comorbidity for clinical and health services research. Arthritis and Rheumatism 2003;49(2):156-63. (PMID:12687505).

21. Sogomonian R, Alkhawam H, Jolly J, et al. Serum vitamin D levels correlate to coronary artery disease severity: a retrospective chart analysis. Expert Rev Cardiovasc Ther 2016;14(8):977-82. (PMID:27187061).

22. Timpini A, Pini L, Tantucci C, Cossi S, Grassi V. Vitamin D and health status in elderly. Intern Emerg Med 2011;6(1):11-21. (PMID:20517656).

23. Toscano Guzmán MD, Galván Banqueri M, Otero MJ, Alfaro Lara ER, Casajus Lagranja P, Santos Ramos B. Development of a trigger tool to identify adverse drug events in elderly patients with multimorbidity. J Patient Saf 2017 Jun 14. (PMID:28617720).

24. United Nations. World Population Aging: The 2015 Report: 27. [Internet] Available from: http://www.un.org/en/development/desa/population/publications/pdf/ageing/WPA2015_Report.pdf. Accessed: 01.12.2017

25. Vimaleswaran KS, Cavadino A, Berry DJ, et al. Association of vitamin D status with arterial blood pressure and hypertension risk: a mendelian randomisation study. Lancet Diabetes Endocrinol 2014;2(9):719-29. (PMID:24974252).