Vitamin D Levels in Pre-frail Older Adults and Its Correlation with Hand Grip Strength

Noto Dwimartutie[1,2]*, Siti Setiati[1], Tirza Z. Tamin[3], Ani Retno Prijanti[4], Alida R. Harahap[2], Dyah Purnamasari[5], Kuntjoro Harimurti[1], I Dewa Putu Pramantara[6]

[1]Division of Geriatric, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia.
[2]Doctoral Program in Medical Sciences, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia.
[3]Division of Musculoskeletal Rehabilitation, Department of Physical Medicine and Rehabilitation, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia.
[4]Department of Biochemistry and Molecular Biology, Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia.
[5]Division of Endocrinology and Metabolism, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia.
[6] Division of Geriatric, Department of Internal Medicine, Faculty of Medicine, Publich Health and Nursing, Universitas Gadjah Mada, Sardjito Hospital, Yogyakarta, Indonesia.

Coresponding author:
Noto Dwimartutie, MD. Division of Geriatric, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia - Cipto Mangunkusumo Hospital. Jl. Diponegoro no. 71, Jakarta 10430, Indonesia. Email: noto.dwimartutie@ui.ac.id.

ABSTRACT

Background: *Vitamin D deficiency is frequent in older adults and associated with poor musculoskeletal function. The prevalence of pre-frailty is also high in older persons, who may proceed to a frail state. This study aimed to determine the vitamin D levels in pre-frail older adults and its correlation with hand grip strength.* ***Methods:*** *A cross-sectional study was conducted on older adults (age ≥ 60 years) with a pre-frail condition who were visiting the outpatient geriatric clinic at Cipto Mangunkusumo Hospital in Jakarta, Indonesia. Serum levels of vitamin D, measured as 25(OH)D, were determined by enzyme-linked immunosorbent assay (ELISA), and hand grip strength was measured using a Jamar hydraulic dynamometer. Correlations between vitamin D levels and hand grip strength were evaluated by Spearman's rank correlation coefficient. Multiple linear regression analysis was carried out to assess contribution of variables that influence hand grip strength.* ***Results:*** *Of 95 pre-frail older adults (mean age 70.08 ± 5.35 years), 67.4% were female, and the median vitamin D level was 17.91 (interquartile range/IQR 13.68–26.36) ng/mL. Overall, 11.6% of the participants had normal vitamin D levels, whereas 34.7% and 53.7% had insufficient and deficient levels, respectively. Females were more likely to have inadequacy of vitamin D than males. Those with vitamin D deficiency tended to have a higher body mass index (BMI) and lower vitamin D intake than normal levels. A significant correlation between serum vitamin D levels and hand grip strength was observed (r = 0.283; P = 0.006). After adjusting for age, comorbidities, nutritional status, functional status, BMI, protein intake, and sun exposure score, regression analysis between hand grip strength and vitamin D levels gave standard coefficient beta = 0.255 (P = 0.013).* ***Conclusion:*** *In this study, pre-frail older adults had a high proportion of deficient and insufficient vitamin D levels, and a significant correlation was found between serum vitamin D levels and hand grip strength.*

Keywords**:** *Hand grip strength, older adults, pre-frail, vitamin D level.*

INTRODUCTION

Vitamin D is a hormone that plays an important role in various organ systems, including the musculoskeletal system. Vitamin D affects muscle mass by stimulating muscle cell proliferation and muscle function by exerting both genomic and non-genomic effects. Vitamin D deficiency is known to cause muscle weakness.[1] In older populations, many people have been found to have vitamin D deficiency. Although Indonesia is a tropical country with abundant sunshine, the prevalence or proportion of vitamin D deficiency in older adults is quite high.[2,3]

Frailty is a geriatric syndrome characterized by a decrease in various organ functions that make individuals more vulnerable to stressors. Decreased hand grip strength and walking speed, weight loss, fatigue, and low physical activity are phenotypes of frailty.[4] Older adults with a frail condition easily fall into disability conditions, require hospital care, have low quality of life and high mortality.[5] Vitamin D deficiency is considered to be one of the causes of sarcopenia and frailty.[6,7] Studies found that pre-frail conditions are more common than frail conditions in older adults.[8] Pre-frail seniors with vitamin D deficiency are at increased risk of frailty and mortality compared with those who are not[9], which highlights the importance of maintaining good vitamin D status in pre-frail older adults to prevent deterioration into a frail condition.

However, studies on the relationship between vitamin D levels and hand grip strength have reported inconsistent results. While several studies have reported an association[10-14], others have found no relationship.[15-19] As far as the researcher is concerned, until now, there has been no research on the vitamin D level and its correlation with hand grip strength in pre-frail older adults. Therefore, this study aimed to determine vitamin D levels in older adults with a pre-frail condition and its correlation with hand grip strength.

METHODS

This cross-sectional study consecutively recruited older adults aged ≥ 60 years who were visiting the outpatient geriatric clinic at Cipto Mangunkusumo Hospital in Jakarta, Indonesia from June to August 2021. The inclusion criteria were pre-frail older adults as defined by the Cardiovascular Health Study[4], and who could understand and follow instructions. We excluded older adults who had acute medical conditions or exacerbation of previous medical conditions, who had conditions that could affect the assessment of muscle performance, such as paresis, who had cognitive impairment (abbreviated mental test score < 8), and mental status disorder/depression (Geriatric Depression Scale score > 10), or who refused to participate. All participants provided written informed consent before the study began. Ethical approval was obtained from Ethical Committee of the Faculty of Medicine Universitas Indonesia.

The comorbidity index of each participant was evaluated using the Cumulative Illness Rating Scale (CIRS)[20], nutritional status was evaluated based on the Mini Nutritional Assessment[21] which classified into normal (≥24), risk of malnutrition (17-23.5) and malnutrition (<17); functional status was evaluated based on Barthel's Activity of Daily Living (ADL) Index[22] which classified into totally dependent (0–4), severely dependent (5–8), moderately dependent (9–11), mildly dependent (12–19), and independent (20); sarcopenia was evaluated using the SARC-F[23] which classified into score ≥ 4 (at risk of sarcopenia) and score <4; nutritional intake was evaluated using a 3-day food recall (2 working days and 1 holiday), and body mass index (BMI) was evaluated based on Asia-Pacific criteria.[24] Sun exposure was evaluated using questionnaire to assess time in sun and skin exposure[25], and divided into 2 categories low (≤18) and moderate-high (19-56) exposure.[26] All data were collected from the patient's medical history and medical record.

Hand grip strength was measured three times in the dominant hand using a Jamar hydraulic dynamometer and the average was taken. Serum vitamin D levels (measured as 25(OH) D) were determined using the enzyme-linked immunosorbent assay technique with commercial 25-OH Vitamin D reagent (Euroimmun). Serum vitamin D was classified into three levels: normal (≥ 30 ng/mL), insufficient (20–<30 ng/mL), and

deficient (< 20 ng/mL).

The data were analysed using SPSS statistical package software. Descriptive data were presented in the form of text and tables. Subjects characteristics presented in number and percentages, mean and standard deviation if the distribution was normal, or median and interquartile range (IQR) if the distribution was not normal. Pearson's test was used for the correlation between vitamin D levels and hand grip strength if the distribution was normal, and the Spearman correlation test if the distribution was not normal. Multiple linear regression analysis was performed to evaluate the influence of other variables which were considered to affect hand grip strength. Values of $P < 0.05$ were considered statistically significant.

RESULTS

Of the 95 subjects who fulfilled the selection criteria, the mean age was 70.08 ± 5.35 years. Most subjects were female (67.4%). The median overall vitamin D level was 17.91 (IQR 13.68–26.36) ng/mL. Overall, 11.6% of the pre-frail older adults had a normal vitamin D level, whereas most of the others had an insufficient (34.7%) or deficient (53.7%) level. Most of the participants had normal nutritional status, independent functional status, obesity and no sarcopenia. Subjects in the vitamin D deficient group tended to have a higher BMI and lower vitamin D intake than did those in the normal groups. Hand grip strength in the subjects with normal vitamin D levels was higher than in subjects with insufficiency and deficiency. Female subjects had lower serum vitamin D level [median 17.6 ng/ml (IQR 12.66-24.83)] than male [median 23.95 ng/ml (IQR 16.63-29.59)]. Obesity had lowest vitamin D level [16.2 ng/ml (IQR 12.95-24.4)] followed by overweight [20.59 ng/ml (IQR 15.82-28.01)], normal [23.28 ng/ml (IQR 15.08-29.93)] and underweight subjects (29.59 ng/ml). General characteristics of subjects and characteristic based on vitamin D status showed in **Table 1** and **Table 2**.

A significant positive correlation was found between vitamin D levels and hand grip strength ($r = 0.283$, $P = 0.006$) (**Figure 1**).

Table 1. Characteristics of the study subjects.

Characteristics	Total (N=95)
Age, mean (SD)	70.08 (5.04)
Age group, n (%)	
- 60-69 years	40 (42.1)
- 70-79 years	50 (52.6)
- ≥ 80 years	5 (5.3)
Sex, n (%)	
- Male	31 (32.6)
- Female	64 (67.4)
Body Mass Index/ BMI (kg/m^2), mean (SD)	
- Male	24.9 (3.86)
- Female	25.8 (3.65)
BMI category, n (%)	
- Underweight	1 (1.1)
- Normal	25 (26.3)
- Overweight	20 (21.1)
- Obesity	49 (51.6)
Comorbidities, n (%)	
- Diabetes melitus	43 (45.3)
- Hypertension	76 (80)
- Dyslipidemia	61 (64.2)
- Osteoarthritis	42 (44.2)
- Coronary heart disease	20 (21.1)
- Congestive heart disease	14 (14.7)
- Chronic Obstructive Pulmonary Disease	3 (3.2)
- Osteoporosis	3 (3.2)
- Benign Prostatic Hyperplasia	18 (18.9)
- Peripheral arterial disease	3 (3.2)
CIRS score, n (%)	
- ≤ 5	24 (25.3)
- >5	71 (74.7)
Number of drugs, n (%)	
- 0-4	19 (20)
- 5-10	64 (67.4)
- >10	11 (11.6)
Vitamin D supplementation, n (%)	
- Yes	29 (30.5)
- No	66 (69.5)
Sun exposure score, median (IQR)	21 (14-28)
Sun exposure, n (%)	
- Low exposure	40 (42.1)
- Moderate - high exposure	55 (57.9)
MNA score, n (%)	
- Normal (≥24)	91 (95.8)
- Risk of malnutrition (17-23.5)	4 (4.2)

Barthel ADL score, n (%)	
- Independent	86 (90.5)
- Mild dependent	9 (9.5)
Nutritional intake, median (IQR)	
- Protein (gram)	55.6 (44.4-63.9)
- Vitamin D (mcg)	1.6 (0.6-5.8)
Handgrip strength (kg), mean (SD)	23.53 (5.04)
SARC-F Score, n (%)	
- < 4	77 (81.1)
- ≥ 4 (risk of Sarcopenia)	18 (18.9)
25(OH)D (ng/ml), median (IQR)	17.91 (13.68-26.36)

Using linear regression analysis, after adjusting for variables age, BMI, comorbidities, protein intake, nutritional status, functional status, and sun exposure score, vitamin D levels remained significantly correlated with standard coefficient beta = 0.255 (P = 0.013).

DISCUSSION

The results of this study showed that in pre-frail older adults, only 11.6% had a normal vitamin D level; most had an insufficient or deficient level. This result is in line with studies

Table 2. Subject characteristics based on vitamin D status.

Characteristics	Normal (≥ 30 ng/ml) (N=11)	Insufficiency (20-<30 ng/mL) (N=33)	Deficiency (<20 ng/mL) (N=51)
Age, mean (SD)	69.64 (5.35)	70.64 (5.49)	69.82 (4.75)
Age group, n (%)			
- 60-69 years	5 (12.5)	13 (32.5)	22 (55)
- 70-79 years	5 (10)	17(34)	28 (56)
- ≥ 80 years	1 (20)	3 (60)	1 (20)
Sex, n (%)			
- Male	7 (22.6)	13 (41.9)	11 (35.5)
- Female	4 (6.3)	20 (31.3)	40 (62.5)
BMI (kg/m2), mean (SD)			
- Male	23.04 (2.88)	24.98 (3.86)	25.99 (4.28)
- Female	23.3 (4.79)	25.34 (3.64)	26.21 (3.52)
BMI category, n (%)			
- Underweight	0	1 (100)	0
- Normal	6 (24)	9 (36)	10 (40)
- Overweight	3 (15)	8 (40)	9 (45)
- Obesity	2 (4.1)	15 (30.6)	32 (65.3)
CIRS score, n(%)			
- ≤ 5	0	9 (37.5)	15 (62.5)
- >5	11 (15.5)	24 (33.8)	36 (50.7)
Number of drugs, n (%)			
- 0-4	2 (10.5)	7 (36.8)	10 (52.6)
- 5-10	5 (7.8)	23 (35.9)	36 (56.3)
- >10	4 (36.4)	2 (18.2)	5 (45.5)
Vit D supplementation, n (%)			
- Yes	4 (13.8)	12 (41.4)	13 (44.8)
- No	7 (10.6)	21 (31.8)	38 (57.6)
Sun exposure, n (%)			
- Low exposure	5 (12.5)	15 (37.5)	20 (50)
- Moderate-high exposure	6 (10.9)	18 (32.7)	31 (56.4)
Sun exposure score, median (IQR)	21 (9-30)	20 (12-27.5)	22 (15-28)
MNA score, n (%)			
- Normal (≥24)	10 (11)	31 (34.1)	50 (54.9)
- Risk of malnutrition (17-23.5)	1 (25)	2 (50)	1 (25)

Barthel ADL score, n (%)			
- Independent	11 (12.8)	31 (36)	44 (51.2)
- Mild dependent	0	2 (22.2)	7 (77.8)
Handgrip strength (kg), mean (SD)	26.87 (4.12)	24.29 (5.44)	22.31 (4.59)
Nutritional intake, median (IQR)			
- Protein (gram)	55.7 (44.1-65.3)	57.9 (44.6-72.5)	51.1 (44.4-62.1)
- Vitamin D (mcg)	3.86 (1.2-6.5)	1.2 (0.5-9.95)	1.6 (0.6-5.1)
SARC-F score, n (%)			
- < 4	9 (11.7)	29 (37.7)	39 (50.6)
- ≥ 4 (risk of Sarcopenia)	2 (11.1)	4 (22.2)	12 (66.7)
25(OH)D (ng/ml), median(IQR)	31.33 (30.86-34.32)	25.23 (23.48-27.8)	14.04 (11.83-16.63)

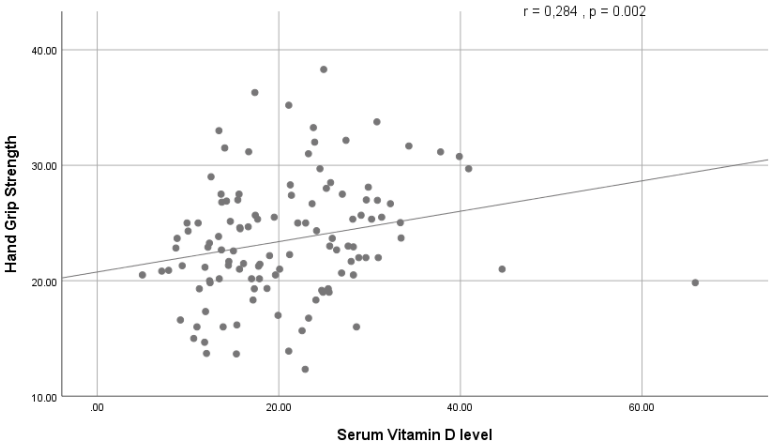

Figure 1. Correlation between serum vitamin D levels and hand grip strength

in other tropical countries such as Singapore, where 14.2% of older adults in a rehabilitation unit were found to have normal vitamin D levels.[27] In Indonesia, studies have shown that older adults are more likely to have inadequate vitamin D levels. A study of older adults in the PUSAKA Jakarta community by Sudarma et al.[28] found that the proportion of individuals with vitamin D deficiency was 80.2%, followed by insufficiency, at 15.9%; normal vitamin D levels were found in only 4%. Biben et al.[3] conducted a study in West Java and implemented a higher hypovitaminosis D cut-off value of < 36 ng/mL (compared with the laboratory reference cut-off of ≤29.9 ng/mL) as determined based on parathyroid hormone suppression, and found that this cut-off point increased the proportion of individuals with vitamin D deficiency from 90.9% to 94.3%. Our study found a higher percentage of older persons with vitamin D deficiency compared to the study by Setiati et al.[2] in nursing home, which found a 35% deficiency prevalence. This could be owing to variations in the settings, as our study was conducted in older persons at an outpatient clinic, who have various comorbidities that can be linked to low vitamin D levels.

Several factors are known to contribute to vitamin D deficiency in seniors, such as decreased vitamin D intake, increased body fat, decreased synthesis of vitamin D in the skin, a lack of outdoor activity and exposure to sunlight, and decreased kidney function1.[29,30] Based on the nutritional adequacy rate of older adults in Indonesia[31], vitamin D intake in the subjects in our study was low, even though the majority of the subjects had a good nutritional status. In our study, the majority of subjects had a low daily intake of vitamin D, in line with the findings of a systematic review on the older population in Indonesia, which showed a high prevalence of low vitamin D intake.[32] A lack of understanding

about balanced nutrition and inadequate income for consuming foods high in vitamin D may also lead to insufficient vitamin D intake.

The higher percentage of overweight and obesity found in this study may also be contributing factors to vitamin D deficiency and/or insufficiency. Previous studies have reported an association between low vitamin D levels and high BMI and body fat percentage in older adults.[33] Hypothesized mechanisms underlying the association between obesity and low vitamin D levels include differences in the lifestyle of individuals with obesity, such as eating habits, sedentary lifestyle, clothing used, the presence of vitamin D storage in adipose tissue, and impaired hydroxylation in the liver.[34,35] A meta-analysis found that the prevalence of vitamin D deficiency was 35% higher in obese than in eutrophic subjects (prevalence ratio 1.35; 95% confidence interval [CI], 1.21–1.5) and 24% higher in overweight subjects (prevalence ratio 1.24; 95% CI 1.14–1.34).[36]

According to our findings, vitamin D deficiency/insufficiency was more common in females than in males. This might be due to larger body mass index in female than male. Studies reported that females tend to have lower levels of vitamin D than males.[37,38] This sex difference occurs mainly because of the female behaviour of protecting themselves from sun exposure for reasons of beauty, the need for using sunscreen, and more closed dress style, especially in Muslim women.[38]

Although this study discovered that sun exposure scores were generally higher in subjects with vitamin D deficiency compared to those with normal vitamin D levels, the proportion of older adults who were vitamin D deficient remained higher than that of individuals with normal/insufficient vitamin D. This could be related to the lower vitamin D intake in the deficient group. Even though subjects in this study seemed to follow Indonesian Ministry of Health recommendation for older adults to keep sunbathing during the COVID-19 pandemic,[39] the possibility of ineffective vitamin D synthesis in older adults cannot be ruled out as a cause of vitamin D deficiency.[40] Sunlight promotes vitamin D synthesis in the skin and sun exposure is known to increase vitamin D levels. It is estimated that nearly 90% of the body's vitamin D comes from sunlight activation through skin synthesis.[40] After exposure to UVB sunlight (wavelength 290–315 nm), photolysis of 7-dehydrocholesterol (provitamin D3) in the skin transforms into pre-vitamin D3, which is then isomerized to vitamin D3.[41] Setiati et al.[42] reported that older adults in nursing homes who were exposed to sunlight for 25 minutes at 09:00, three times a week for 6 weeks, showed an increase in vitamin D levels from 59 to 84 nmol/L.

Based on a meta-analysis, frailty is associated with low vitamin D levels, where the lower the vitamin D level, the more severe the frailty status.[6,43] Several studies have linked vitamin D levels to a frailty component, whereas weakness, low physical activity, fatigue, and low gait speed are all associated with low vitamin D levels.[44,45] Individuals with these conditions tend to be physically inactive, which disturbs the balance of protein metabolism in the muscles. Older populations are at risk of adverse effects due to vitamin D deficiency. Inadequacy of vitamin D levels are also associated with a number of chronic diseases in addition to frailty[46], but this condition can be improved.

The results of the present study revealed a significant positive correlation between serum vitamin D levels and hand grip strength in older adults with a pre-frail condition. This is in line with studies on older women in the community by Caniago et al.[13], older outpatients by Bachry et al.[14], older males by Kocak et al.10, and patients with hip fracture by Dhanwal et al.[11] However, our results differ from a population study that included Korean men aged ≥ 50 years and postmenopausal women[16] and a Taiwanese study of participants aged ≥ 55 years[18], which reported finding no relationship between vitamin D and hand grip strength or between vitamin D and performance on the Short Physical Performance Battery (SPPB). Vitamin D is known to influence skeletal muscle through both genomic and non-genomic effects. Through genomic effects, vitamin D binds to the vitamin D receptor (VDR) in the cell nucleus, inducing gene transcription in myoblasts, thereby resulting in the proliferation and differentiation

of muscle cells. Through non-genomic effects, via regulatory pathways, the calcium messenger system affects signal transduction and affects skeletal muscle contraction.[1,47]

To the best of our knowledge, our study is the first to evaluate the vitamin D level and its relationship with hand grip strength in older adults with a pre-frail condition in Indonesia. However, because this was an observational study, no causal relationship could be investigated. Further research is needed to evaluate whether vitamin D supplementation can improve physical performance in pre-frail older adults and help prevent frailty.

CONCLUSION

In older adults with a pre-frail condition, proportion of vitamin D deficiency and insufficiency were high. There was positive correlation between serum vitamin D levels and hand grip strength in pre-frail older adults.

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CONFLICT OF INTEREST

All authors have no conflict of interest.

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