

ORIGINAL ARTICLE

Association Between Serum 25-Hydroxyvitamin D Levels and Severity of Pain Due to Knee Osteoarthritis in Elderly Patients at KPKM FK UIN Syarif Hidayatullah Jakarta

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ABSTRACT

Introduction: The term “pain” refers to an unpleasant sensory and emotional experience that is linked to real or potential tissue damage. Patients with osteoarthritis complain of joint pain to a more severe degree. The pain can be felt continuously, causing impaired mobility. Vitamin D deficiency is a worldwide symptom that plays an important role in the progression of knee OA. This condition can also be related to chronic pain disorders in patients. **Methods:** This is a cross-sectional analytic study with 150 subjects that was collected by the original researcher in Mei 2017. The data was analyzed by the Kruskal-Wallis test. **Results:** The results showed that 53.3% of subjects had insufficient serum vitamin D levels, 34% had sufficient levels, and 12.7% were deficient. Based on the data analyzed, there was no significant relationship ($p = 0,862$) between serum vitamin D levels and the severity of pain due to knee osteoarthritis. **Conclusion:** There was no median value difference for serum vitamin D concentration and WOMAC pain score based on the elderly category. The insufficient and deficient groups had higher maximum WOMAC pain scores than the sufficiency group. Female subjects had a lower median vitamin D serum and a higher WOMAC maximum score than males. However, there was no statistically significant relationship between serum vitamin D concentrations and pain due to knee OA.

Keywords: Serum vitamin D levels, Knee osteoarthritis, Elderly patients

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INTRODUCTION

Pain is defined by the International Association For The Study Of Pain (IASP) as an unpleasant sensory and emotional experience linked to existing or potential tissue damage.⁽¹⁾ Based on the time after occurrence, pain is divided into chronic and acute pain. Chronic pain persists after the tissue healing period and continues beyond the normal healing period (more than 6 months)^(2,3). Research conducted by Wu Zhenqiang et al. found that 1732 of the 5049 subjects (34%) had arthritis and 871 of them (17%) reported chronic pain⁽²⁾.

As a form of arthritis that is most commonly found in the community and is one of the degenerative diseases, osteoarthritis is characterized by complaints of joint pain, tenderness, limitation of motion, crepitus, effusion, and chronic local inflammation^(4,5). Patients with OA complain about joint pain which at a more severe degree

can be felt continuously causing mobility impairment in patients⁽⁵⁾. Increasing age causes physiological functions to decrease, so that non-communicable diseases appear more in the elderly⁽⁶⁾. The Central Statistics Agency (BPS) found that the total elderly population in Indonesia in 2020 was 9.8%⁽⁷⁾. As the second most common disease suffered by the elderly, with a prevalence of 45% in the age group 55-64 years, 51.9% in the age group 65-74 years and 54.8% in the age group ≥ 75 years, the high prevalence of OA and its nature chronic-progressive causes a large socio-economic impact, both in developed and developing countries^(5,6).

Global Religious Future 2020 states that the total Muslim population in Indonesia is 229 million people, and with its majority of the Muslim population, it is feared that OA will be able to disrupt the Indonesian Muslim worship⁽⁸⁾. Mahamed Ateef et al found that knee OA patients will find it difficult to kneel and bend their knees during prayer, so it is not impossible that knee OA can disrupt the implementation of Muslim worship. The conflicting results in proving the association of vitamin D and pain have made the relationship between serum

25-hydroxyvitamin D concentrations and pain are unclear (9–14).

MATERIALS AND METHODS

This research is an observational analytic study with a cross-sectional method that analyzes secondary data conducted at the Community Health Service Clinic (KPKM) FK UIN Syarif Hidayatullah in Reni Jaya in Pamulang Village, Pamulang District, South Tangerang City, Banten in January 2017. Subjects were 150 people aged 60 to 80 who had knee pain due to OA and met clinical and radiological criteria according to KL for at least the previous month, had not done strenuous physical activity / strenuous exercise for at least the previous month, had not been diagnosed with Rheumatoid or Psoriasis Arthritis, did not experience knee trauma including ligament or meniscus injury before the study, and did not undergo intra-articular therapy including the consumption of pain-reducing drugs in the 3 months before the study because of its feared effect on the quality of reported pain. The data was further classified by gender (female and male), elderly (60 – 69 years and 70 – 79 years), and serum vitamin D concentrations (sufficient, insufficient, and deficient). Data was analyzed by looking at the frequency and proportion of each variable using the Kruskal-Wallis test. The approval and ethical clearance from the Faculty of Medicine UIN Syarif Hidayatullah Jakarta were attained upon commencement of the study [Reference No: B-029/F12/KEPK/TL.00/9/2020].

RESULTS

As table I shows, demographically present, there were 150 subjects aged 60 years, 111 (74%) subjects were classified as young elderly (60–69 years; $p = 0.200$) and 39 (26%) were middle elderly (70–79 years; $p = 0.073$). The majority of subjects were female (73.3%) with a total of 110 people ($p = 0.047$) and 26.7% about of the 40 subjects were male ($p = 0.933$). In this study, 80 subjects (53.3%) had insufficient serum vitamin D concentrations (25–50 nmol/l; $p = 0.200$), 51 subjects (34%) were classified as deficient (>50-125 nmol/l; $p = 0.002$), and 19 subjects (12.7%) were noted to have a serum vitamin D concentration of <25 nmol/l, which was classified as deficient ($p = 0.084$).

Table II shows the relationship between serum vitamin D concentrations and pain due to knee osteoarthritis. Based on the bivariate analysis in Table II, it was found that there was no statistically significant relationship ($p = 0.862$) between serum vitamin D concentrations and pain due to knee osteoarthritis. Table III shows the relationship between serum vitamin D concentrations by age and gender category on WOMAC pain. Serum vitamin D levels in the 60-69 age group were sufficient in 30 people (27%), insufficient in 64 people (58%), and deficient in 17 people (15%).. Meanwhile, the

Table I: Characteristics of Subjects

Variabe	Count (n) = 150 (%)	P value of Normality Test
Age		
• 60 – 69 years	111 (74)	0,200
• 70 – 79 years	39 (26)	0,073
Sex		
• Male	40 (26,7)	0.933
• Female	110 (73,3)	0,047
25(OH)D Serum Concentration		
• Sufficient (> 50 - 125 nmol/l)	51 (34)	0,002
• Insufficient (25 - 50 nmol/l)	80 (53,3)	0,200
• Defficient (<25 nmol/l)	19 (12,7)	0,084
WOMAC Score		
	7,9 ^a 7,5 ^b (5 – 15) ^c	0,000
25(OH)D Serum Concentration		
	43,74 ^a 41,95 ^b (15 – 92) ^c	0,039

*a : Mean ; *b : Median ; *c : Min – Max

Table II: Serum Vitamin D Concentration Against WOMAC Pain

	25(OH)D Serum Concentration	Median (Min - Max)	p Value*
WOMAC Pain	Sufficient (> 50 - 125 nmol/L)	8 (5 - 14) 63 (50,7 – 91,6) nmol/L	0,862
	Insufficient (25 - 50 nmol/L)	7 (5 - 15) 37 (25,2 – 50) nmol/L	
	Defficient (<25 nmol/L)	7 (5 - 15) 20,3 (15 – 25) nmol/L	

*Kruskall – Wallis Test

serum concentration of vitamin D in the 70–79 year old in the sufficient category was 21 people (54%), in the insufficient group it was 16 people (41%) and 2 people deficient (0.5%). This study shows no significant relationship between serum vitamin D concentrations based on the elderly category, both in the 60 – 69 years group ($p = 0.849$) and the 70 – 79 years group ($p = 0.847$) with pain due to knee osteoarthritis.

The examination of the association between serum vitamin D concentrations by gender with pain related to knee osteoarthritis can also be found in Table III. Table III shows that the female subject group had a serum vitamin D concentration of 22 people (20%), insufficiency was 69 people (62%), and 19 people were deficient (17%). Meanwhile, in the male subject group, the sufficient category has 29 people (72%), insufficiency has 11 people (28%), with no one classified as deficiency. There is no significant relationship between serum vitamin D concentrations and pain related to knee osteoarthritis in both female ($p = 0.839$) and male ($p = 1,000$) categories.

DISCUSSION

The responsiveness of chondrocytes to growth factor stimulation deteriorates with age, resulting in a breakdown of cartilage homeostasis, which leads

Table III: Association Between Serum 25-Hydroxyvitamin D levels by Age and Severity of Pain due to Knee Osteoarthritis in Elderly Patients

		25(OH)D Serum Concentration	Median (Min - Maks)	<i>p Value*</i>
WOMAC Pain	60 – 69 years	Sufficient	7,5 (5 - 14) 62,2 (50,7 – 87,1) nmol/L	0,849
		Insufficient	7 (5 - 15) 38 (25,2 – 50) nmol/L	
		Defficient	7 (5 - 15) 19,6 (15 – 25) nmol/L	
	70 – 79 years	Sufficient	8 (5 - 12) 59,7 (52,2 – 91,6) nmol/L	0,847
		Insufficient	7,5 (5 - 11) 33,8 (25,7 – 44) nmol/L	
		Defficient	8 (7 – 9) 23,9 (23,8 – 24,1) nmol/L	
	Female	Sufficient	8 (5 - 14) 57,65 (50,7 – 82,4) nmol/L	0,839
		Insufficient	7 (5 - 15) 35,7 (25,2 – 50) nmol/L	
		Defficient	7 (5 - 15) 20,3 (15 – 25) nmol/L	
	Male	Sufficient	8 (5 - 12) 62 (52,7 – 91,6) nmol/L	1,000
		Insufficient	7 (5 - 10) 41,4 (25,2 – 49,7) nmol/L	

*Kruskall Wallis Test

to osteoarthritis.(15) The Indonesian Rheumatology Association reported that 74.48% of all cases (1297) of rheumatism at the rheumatology clinic of Hasan Sadikin Hospital, Bandung in 2007 and 2010 were OA cases.69% of them were women, and the majority were knee OA cases with a percentage of 87%.(4) Much research has been carried out in Indonesia regarding vitamin D deficiency.(16,17) Toding et al.'s study of elderly patients who visited the Family Benefit Center (PUSAKA) in two different locations in Jakarta in 2011 also found a very high prevalence of vitamin D deficiency, rate: 92.5% (17).

Low levels of vitamin D were associated with levels of pro-inflammatory cytokines such as TNF-α. It was also discovered that 1,25(OH)2D3 can boost macrophage chemotaxis, phagocytosis, and antimicrobial peptide production while inhibiting IL-12, TNF-α, IL-6, and IP-10 production in monocytes and macrophages (18). Vitamin D inhibits pain pathways through several pathways by suppressing TNF-α, which is involved in peripheral and central sensitivity levels and suppressing macrophage colony-stimulating factor (M-CSF).(19) By inhibiting the release of pro-inflammatory cytokines (particularly TNF-α); the lower the vitamin D level, the higher the levels of pro-inflammatory cytokines and the

more severe the disease activity, the degree of pain, as well as limitations in carrying out daily activities (20).

The relationship between serum vitamin D concentrations and pain is still up for dispute. A cross-sectional study conducted by Muraki et al. with 787 subjects found that serum concentrations of 25-hydroxyvitamin D < 35.5 nmol/L tended to have a significant relationship (p = 0.031) with knee OA pain compared with serum vitamin D concentrations >35.5 nmol/L. However, the population used in this study is a specific population with a genetic abnormality in the Vitamin D Receptor (VDR) that might affect the results obtained. This is evidenced by the finding of a significant relationship between the Fok1 gene polymorphism and the Cdx2 gene in VDR with knee pain in osteoarthritis patients.(21) Meanwhile, Cakar Murat et al. with their research in Turkey found that there was no significant relationship (p = 0.506) between serum vitamin D concentrations (mean = 11.5±9; median (min-max) = 9.3 (2.4-63) nmol/L) with knee pain (mean = 7.5±1.9; median (min-max) = 8 (1–10)) in osteoarthritis patients. Wu Zhenqiang, et al. in their study involving 5049 subjects aged 50-84 years, also found that there was no significant relationship (p = 0.65) between serum 25-hydroxyvitamin D and chronic pain (2,10).

A retrospective analytical study in the period January–June 2018, found that there was an increase in the incidence of knee osteoarthritis along with age.(22) The production and status of vitamin D deficiency are known to be linked to the decline of physiological function that occurs with aging. Vitamin D levels that are adequate can also help to slow down the aging process.(23,24) Jansen and Haddad in their study on 139 patients with an age range of 48-88 years found that vitamin D deficiency was also detected in a high percentage of older individuals with knee osteoarthritis who were scheduled for arthroplasty (25).

he increasing incidence of knee osteoarthritis in the elderly is related to the aging process in the joint cartilage, including joint surface fibrillation, reduced size and aggregation of aggrecan proteoglycan molecules, and loss of matrix stiffness and tensile strength. These changes are a result of the aging process in chondrocyte function, which reduces the ability of cells to maintain tissue. It has an effect on the increasing incidence of knee osteoarthritis in the elderly (26,27). WHO said that at the age of under 45 years, men suffer from OA more than women, but after 55 years, women suffer from OA more than men. Approximately 45% of women over the age of 65 will experience symptoms associated with OA, and 70% of women over the age of 65 will have radiological evidence of OA. Osteoarthritis of the knee is a common cause of mobility loss, particularly in women. According to the World Health Report 2002's Global Burden of Disease 2000, OA is the fourth greatest cause of Years Lost to Disability (YLD) globally,

accounting for 3% of all YLD.(28) A large study found that there was a significant relationship between serum 25(OH)D and increased pain levels in 3495 women but not in 3365 men with knee osteoarthritis.(29) Because at the age of more than 50 years, women's estrogen is being reduced significantly as an effect of menopause.

Estrogen receptors are located on chondrocytes, synoviocytes, subchondral bone cells, ligament fibroblasts and myoblasts. Through the presence of these receptors, estrogen can directly contribute to the process of cartilage mineralization and maturation by increasing the synthesis of proteoglycans.(30) If estrogen decreases, the synthesis of proteoglycans will also decrease. This will have an impact on cartilage elasticity and its ability to absorb shock.(31) In contrast to the theory, this study found no significant relationship between serum vitamin D concentrations and pain related to knee osteoarthritis in both female and male categories.

CONCLUSION

A total of 53.3% of subjects were classified as having vitamin D insufficiency (25-50 nmol/L), 34% as having insufficiency (> 50-125 nmol/L), and 12.7% as deficient (25 nmol/L). The insufficient and deficient groups had a higher WOMAC maximum pain score than the inefficient group of subjects. Female subjects had a lower median vitamin D serum concentration and a higher WOMAC maximum pain score than males. There was no difference in the median value of serum vitamin D concentration and WOMAC pain scores based on the elderly category. The relationship between serum vitamin D concentration and the degree of pain due to knee osteoarthritis was also not statistically significant ($p = 0.862$). In addition, there was also no significant relationship between serum vitamin D concentrations based on age category in both the 60–69 years group ($p = 0.849$) and the 70–79 years group ($p = 0.847$), and based on gender category in both the female ($p = 0.839$) and male group ($p = 1000$) with the degree of pain due to knee osteoarthritis.

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