The Association Between Vitamin D Deficiency and Type 2 Diabetes Mellitus in Elderly Patients

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ABSTRACT

Aim: *to identify the association between vitamin D deficiency and type-2 diabetes mellitus in elderly population.*

Methods: *a study was conducted at the geriatric clinic of Cipto Mangunkusumo Hospital in November 2007, with a cross-sectional design. The accessible population of our study were patients with type-2 diabetes mellitus and non-diabetes mellitus patients who visited the clinic for treatment. The subject criteria were: patients >60 years old with operational definition of type-2 diabetes mellitus, and willing to participate in the study.*

Data collected included characteristics, such as age, sex, education level, history of family illness, frequency of outdoor activity, duration of direct sun exposure in their outdoor activities, history of using sun protector; and the laboratory data such as 25(OH)D_3 serum level, calcium and albumin serum level. Data analysis was done by Chi-Square test and multivariate analysis was performed by logistic regression technique to control some identified confounding factors. All data processing and statistical analyses were done with SPSS 11.5 for windows.

Results: *we found a total number of 78 subjects. Of them, 40 subjects were with DM, and 38 subjects without DM. Most subjects were female (66.7%), and obese (44.9%). Direct sun exposure of most subjects was indicated by the frequency of outdoor activity of more than 3 times a week (74.4%). Duration of exposure in most subjects was less than 15 minutes (43.6%), with application of sun protector agent (56.4%). The prevalence of vitamin D deficiency was 78.2%, with a cut-off of <50 nmol/L.*

Conclusion: *sex, BMI and the use of sun protectors proven as variables are associated with vitamin D deficiency. The association between vitamin D deficiency and type-2 diabetes mellitus cannot be proven statistically in our study (p=0.482; OR=0.8; CI=0.5-1.3).*

Key words: *vitamin D deficiency, type-2 diabetes mellitus, elderly.*

INTRODUCTION

Vitamin D is an essential nutrition component, which has a unique metabolism and physiological effects compared to other vitamins; in fact, it is more suitable to be classified as a hormone.[1-5] In humans, vitamin D is acquired from two sources, namely exogenous and endogenous sources. The endogenous source is the main source of vitamin D_3 which is synthesized in the skin with the help of ultraviolet lights.[1,6,7] Vitamin D deficiency may occur in all population groups with its various risk-factors. The elderly population is the more susceptible population to suffer vitamin D deficiency, especially the elderly who live in nursing homes and who are hospitalized.[3,8-10] Hollick found that >84% African males and females >65 years old in Boston experienced vitamin D deficiency.[2,11] Meanwhile, Setiati found 35.1% prevalence in the female population aged 60-90 years old who lived in the nursing home.[12-19]

The facts about the role of vitamin D on insulin secretion and sensitivity has led to hypotheses about vitamin D role in treatment of type-2 diabetes mellitus; however, for confirmed conclusion, further longitudinal-prospective studies are necessary.[20-30] Correlated to such role of vitamin D, VDR polymorphism has also been known, which may be varied among populations.[31-34] According to epidemiological studies, the prevalence of diabetes mellitus increases every year along with the increase in life expectancy and lifestyle change (diet and physical activities).[35-37] A similar thing also occurs in Indonesia, for example in Jakarta, in which the prevalence of DM was 1.7% in 1982, subsequently increased to 12.8% in 2001.[36]

Associated with the elderly population, the fact indicates that there is a tendency in increased prevalence of type-2 diabetes mellitus in elderly

patients along with increased life expectancy.[35,38-41] Various epidemiological data demonstrate that the prevalence of type-2 diabetes mellitus in population aged >65 years old is 10-20%.[35,40-44] However, data in Indonesia, as described in the WHO *Global InfoBase Online* data, there are approximately 27.9% diabetes mellitus patients of the group aged more than 56 years old.[45] In the elderly groups, the pathophysiology of type-2 diabetes mellitus is dominated by a defect in insulin secretion more than by insulin resistance.[34,38,46-47] The condition of vitamin D deficiency obviously affecting both mechanisms, i.e. insulin resistance and defect in insulin secretion of pancreatic beta-cells, although the latter mechanism is more likely to occur and it has been successfully proven in various studies. [4,16,21,29]

Considering the increased number of the elderly in Indonesia, and both abovementioned problems, namely the increased prevalence of diabetes mellitus and the high occurrence of vitamin D deficiency, it is interesting for us to study their correlation. Therefore, if vitamin D is then found to have a great role in developing type-2 diabetes mellitus of elderly patients, then the management of vitamin D deficiency will also become an integral part of type-2 diabetes mellitus treatment in Indonesia, especially for the elderly.[3,8-10,45]

The aim of our study is to find the prevalence of vitamin D deficiency in an elderly population and to identify its affecting factors, as well as the association between vitamin D deficiency and type-2 diabetes mellitus in elderly population.

METHODS

It was a cross-sectional study, conducted at the outpatient Geriatric Clinic, Department of Internal Medicine, Faculty of Medicine, University of Indonesia, Cipto Mangunkusumo Hospital in November 2007 until the sample size has been achieved.

The accessible population of our study were patients with type-2 diabetes mellitus and non-diabetes mellitus. The subject criteria were: patients >60 years old with operational definition of type-2 diabetes mellitus, willing to participate in the study. Moreover, the patients should not have acute diabetes mellitus complications, malignancy and/or cytostatics and steroids treatment, severe deterioration of liver function, kidney function disorder (CCT<30ml/minute), and hypocalcemia (Ca serum level <8.4 mg/dL). The sample size of 84 subjects was determined. The subjects were recruited with consecutive sampling.

Data collected included characteristics, such as age, sex, education level, history of family illness, frequency of outdoor activity, duration of direct sun exposure in their outdoor activities, history of using sun protector; and the laboratory data such as 25(OH)D_3 serum level, calcium and albumin serum level. Data analysis was done by Chi-Square test and multivariate analysis was performed by logistic regression technique to control some identified confounding factors. All data processing and statistical analyses were done with SPSS 11.5 for windows. Ethical clearance from the ethical committee for Medical Research in the Faculty of Medicine, University of Indonesia was obtained prior to the study, and all subjects signed informed consent.

RESULTS

Our study has recruited a total of 78 subjects to be analyzed including 40 subjects in the DM group, and 38 subjects in the non-DM group. Distribution of subject characteristics is demonstrated on **Table 1 and 2**.

Most subjects were females (66.7%), with the mean age of 71.21 years (SD ±6.0). The majority of

Table 1. Subject Characteristics

Characteristics	N	%
Sex		
- Female	52	66.7
- Male	26	33.3
Age		
- 60-75 (years)	59	75.6
- ≥ 75 (years)	19	24.4
Education		
- Elementary School	6	7.7
- Junior High School	14	17.9
- Senior High School	32	41.1
- College/University	26	33.3
BMI		
- Under weight (<18.5 kg/m2)	7	9.0
- Normal (18.5-22.9 kg/m2)	20	25.6
- Over weight (23-24.9 kg/m2)	16	20.5
- Obese (≥25 kg/m^2)	35	44.9
Sun protector applied		
- No protector	34	43.6
- Hijab	38	48.7
- Sunscreen cream	5	6.4
- Hat	1	1.3
Frequency of outdoor activities		
- 1-3x/week	20	25.6
- >3x/week	58	74.4
Duration of sun exposure		
- ≤15 minutes	34	43.6
- 30 minutes	23	29.5
- ≥60 minutes	21	26.9
Vitamin D supplements		
- Yes	2	2.6
- No	51	65.9
- Unknown	25	32.1
Vitamin D deficiency		
- Yes	61	78.2
- No	17	21.8

Table 2. Distribution of Subject Characteristics based on Mean, Standard Deviation, and Minimal-Maximum Range Value

Characteristics	Mean	Standard Deviation (SD)	Range Value	
			Min	Max
Age	71.21	6.00	60.0	87.0
BMI	25.38	5.44	13.4	43.0
Vitamin D level	38.94	16.28	12.5	90.7

subjects were Javanese/Sundanese (49.7%) and Sumatrans (44.9%), the education level of most subjects were high school and college/university graduates (74.4%). The subjects mostly were obese (44.9%) with the mean of BMI 25.38 kg/m^2 (SD ± 5.44). Direct sun exposure in the majority of subjects was indicated by their frequency of having outdoor activity >3 times in a week (74.4%) and with the longest duration of less than 15 minutes (43.6%). Most of them applied sun protectors such as the "hijab", hats, and sunscreen cream when they went outdoors (56.4%) and only two subjects (2.6%) consumed vitamin D supplements. With the cut-off level of <50 nmol/L to define the deficiency, we found the total prevalence of vitamin D deficiency of 78.2%.

Bivariate analysis was performed to identify factors affecting the development of vitamin D deficiency by using chi-square methods on variables of sex, age, BMI, the frequency of outdoor activities, sun protectors applied, and vitamin D supplementation (**Table 3**). Results of such analysis suggested evidences that variables of sex, BMI, and sun protectors had significantly affected the occurence of vitamin D deficiency.

The prevalence of vitamin D deficiency was higher in females (56%) than in males (19%) and the difference was significant (p=0.012; OR=1.4; CI=1.1-1.9). Moreover, based on the BMI category, there were 89% of the obese group (BMI 25 kg/m^2) who had vitamin D deficiency (p=0.045; OR=1.3; CI=1.1-1.6). In the group who applied sun protectors (hat, veil, and sunscreen cream), 64% subjects experienced vitamin D deficiency (p=0.011; OR=1.4; CI=1.1-1.8). Other analysis performed to evaluate the correlation between sex and applied sun protector (**Table 3**), showed a significant difference in applied sun protector used in male and female groups (p=0.000).

Bivariates analysis was also performed in DM and non-DM groups to identify factors affecting the development of type-2 diabetes mellitus (**Table 5**). Among the analyzed-variables, only the sex variable showed statistically significant result (p=0.025); while the variable of vitamin D deficiency was not statistically proven to be correlated to type-2 diabetes mellitus (p=0.482). Moreover, multivariate analysis with logistic regression (**Table 6**) was also performed for variables which had been estimated as strongly affecting the development of type-2 diabetes mellitus, although it was not significant statistically in bivariate analysis. In addition, similar result was found, i.e. there was no significant correlation between vitamin D deficiency and type-2 diabetes mellitus (p=0.456). Furthermore, there was a significant correlation in the group applying sun protector (p=0.016).

Table 3. Factors affecting the development of vitamin D deficiency (bivariate analysis)

Variables	Def.	Non-def	OR	CI	p
Sex					
- Female	45	7	1.4	1.1-1.9	0.012
- Male	16	10			
Age group					
- 60-75 years	46	13	0.9	0.7-1.3	0.928
- >75 years	15	4			
BMI group					
- Obese	31	4	1.3	1.1-1.6	0.045
- Non-obese	30	13			
Freq. of outdoor activities					
- 1-3x/week	15	5	0.9	0.7-1.3	0.687
- >3x/week	46	12			
Sun protectors applied					
- Yes	39	5	1.4	1.1-1.8	0.011
- No	22	12			
Vitamin D supplementation					
- Yes	1	1	0.7	0.2-2.6	0.393
- No	39	12			

Def. = Group with vitamin D deficiency; Non-def. = Group without vitamin D deficiency

Table 4. Proportion of respondents based on group applying the sun protector and the sex group

Sex Group	Group of Applying Sun Protection				Total	
	Yes		No		n	%
	n	%	n	%		
Female	41	78.9	11	21.2	52	100
Male	3	11.5	23	88.5	26	100

x^2=31.935; p=0.000

DISCUSSION

Subject Characteristics

In this study, we tried to carry on a study in subjects with more characteristics compared with previous studies that had been conducted in Indonesia. The study conducted by Setiati was implemented on elderly females who lived in a nursing home; while Sumariyono and Oemardi obtained the data from

Table 5. Factors affecting the development of DM (bivariate analysis)

Variables	DM	Non-DM	OR	CI	p
Vitamin D deficiency					
- Deficiency	30	31	0.8	0.5-1.3	0.482
- Non-deficiency	10	7			
Sex					
- Female	22	30	0.6	0.4-0.9	0.025
- Male	18	8			
Age group					
- 60-75 years	32	27	1.2	0.7-2.3	0.357
- >75 years	8	11			
BMI group					
- Obese	20	15	1.2	0.8-1.9	0.350
- Non-obese	20	23			
Family history of DM					
- Yes	16	13	1.1	0.7-1.7	0.597
- No	24	25			
Group applying sun protector					
- Yes	24	20	1.2	0.7-1.8	0.512
- No	16	18			

Table 6. Multivariate analysis to evaluate the correlation between vitamin D deficiency and type-2 DM

Variables	DM	Non-DM	OR	CI	p
Vitamin D deficiency					
- Deficiency	30	31	0.6	0.2-2.3	0.456
- Non-deficiency	10	7			
Sex					
- Female	22	30	0.1	0.0-0.4	0.004
- Male	18	8			
BMI group					
- Obese	20	15	2.2	0.8-6.1	0.147
- Non-obese	20	23			
Group applying sun protector					
- Yes	24	20	14.2	1.6-122	0.016
- No	16	18			

DM = Group with type-2 diabetes mellitus; Non-DM = Group without type-2 diabetes mellitus

post-menopausal female groups.[12,48,49] In contrast, our study was carried on elderly male and female subjects of the general population who were having treatment for DM at the Outpatient Geriatric Clinic of Cipto Mangunkusumo Hospital. (**Table 7**)

Most subjects in our study had BMI>25 kg/m^2 and categorized as obese. Different from the Setiati study, most subjects had normal BMI, and it is assumed that it may also have affected the prevalence of vitamin D deficiency.[12] The quite interesting fact that high obesity rate in geriatric patient groups will definitely become a risk factor in most of the metabolic or degenerative disease. On the other hand, we found that the high malnutrition rate as previously assumed in the elderly population had not been obviously proven in our population group. It could be explained when we consider their social background lived in the big city who mostly had education level at least to high school and middle to high class economic background.

Table 7. Various studies on the prevalence of vitamin D deficiency in elderly

Studies	Results	Subject Characteristics
Baynes, et.al[22]	39.0%	Elderly male, in Netherlands
Hollick, et.al[2,11]	84.0%	Elderly African population, USA
Setiati[12]	35.1%	Elderly female in nursing home, Indonesia
Sumariyono,et.al[49]	61.9%	Post-menopausal female, having treatment in hospital, Indonesia
Our study	**78.2%**	**Elderly male and female, having treatment in hospital, Indonesia**

In most subjects, it was obvious that they had less sunlight exposure despite the fact that they live in a tropical country with rich of sunlight almost all over the year. Most subjects had their outdoor activities only for 15 minutes with sun protector including sun screen cream, hijab or hat in spite of their quite frequent outdoor activities (> 3x/week). Vitamin D supplementation was also slightly consumed by the subjects (2.5%).

Vitamin D Deficiency and The Affecting Factors

In the present study, we used the cut-off level less than 50 nmol/L in order to define vitamin D deficiency and we found a 78.2% prevalence. When compared with previous studies in elderly populations, especially in Indonesia, our study obtained higher prevalence rate (**Table 7**). It is due to the different subjects characteristics, which was not limited only to the elderly female group as the previous studies. Our study involved elderly, male and female subjects of general population and not only on limited population such as subjects who lived in nursing home.[2,11,12,22,49] There was an exception for the study conducted by Hollick, which found 84% prevalence in African elderly population in the USA; however, the climate and skin color or melanin level were extremely prominent.[2,11]

Some factors estimated as affecting factors on the development of vitamin D deficiency were analyzed (**Table 3**) and we found evidence that sex, BMI and sun protectors were statistically significant. The sex variable seemed to be the most affecting factor in the development of vitamin D deciency, which was higher in female (56%) compared to male (19%). Other analysis has found significant different proportion in the group applying sun protector between male and female group (**Table 4**). Female subjects often used sun protectors (hat, hijab, and sunscreen cream), which consequently reduced the direct sun light exposure. Other possibilities include difference in their activities, i.e. male subjects generally had more frequent and

longer duration in doing outdoor activities; therefore most of them had more exposure to direct sun light. However, the statistical analysis did not successfully provide evidences for such possibility.

BMI was also found to be a statistically significant variable in the development of vitamin D deficiency. The greater BMI is, the higher occurence of vitamin D deficiency; especially in the obese group (BMI>25 kg/m^2). Theoretically, it could be explained as the result of vitamin D deposition in body lipid and reduced bioavailability of vitamin D_3 from skin.[50]

Based on previous studies, it is known that sun light exposure greatly affects the vitamin D_3 level, which could be seen by observing the frequency of outdoor activities, the duration, and applied sun protectors/ sun screen cream. In general, although it was not statistically significant, our study subjects had lesser sun light exposure, especially the duration of outdoor activities, which only ≤15 minutes. In contrast, analysis on the variable of sun protector-applied, which was also affected by sex, showed a significant effect on the development of vitamin D deficiency. The study conducted by Setiati suggests that Indonesian people should have sun light exposure for 25 minutes at 09.00, or 15 minutes at 09.00-10.00 to have vitamin D concentration of 2700 IU in blood for each exposure, and minimally 3x/week to prevent the development of vitamin D deficiency.[12]

Our study is different from other studies in some western countries which have concluded that subjects who live in nursing home have more possible risk of having vitamin D deficiency. Our study concludes the contrary results.[3,8-10] Our study and a study conducted by Sumariyono, carried out in a general population, show higher prevalence (78.2% and 61.9%, respectively),[49] compared to a study by Setiati (35.1%) in elderly female population who lived in the nursing homes.[12] It may be explained since the subjects who lived in the nursing home probably had a more regular program and schedule to be given adequate sunlight exposure compared to subjects outside the nursing home.

The variable of age has become the most dominant factor in causing vitamin D deficiency, as seen in our study. It correlates with less outdoor activities and therefore less sunlight exposure.[3,8,32,51] In addition, there is also an alteration on skin organ, i.e. reduced capacity of *7-dehydroxycholesterol*, which is a precursor of vitamin D3; thus the longer exposure duration or greater supplementation of vitamin D is necessary to maintain the constant level of vitamin D in serum for the elderly than for the younger aged subjects.[2,51] The less sunlight exposure, especially in elderly, is more aggravated by the fact that there was less exogenous vitamin D supplementation. Not to mention, that in our country, vitamin D fortification in foods or drinks is not usual and it has not been routinely applied.

The Association Between Vitamin D and Type-2 Diabetes Mellitus

The association between vitamin D and type-2 diabetes mellitus had been proven by a lot of studies in some countries. A study conducted by Baynes *et.al* found that 25(OH)D_3 concentration has inverse correlation to blood glucose concentration in one hour period after 75 grams glucose loading.[22] Another study by *New Zealand Workforce Survey* has identified that in patients with type-2 diabetes mellitus and glucose tolerance disorder, there was a lower level of vitamin D compared with control group.[28] Some other studies also conclude similar results (**Table 2**).[20-24,26-29,52,53-55] However, our study suggests different results, that no statistic evidence has been provided on the correlation between vitamin D deficiency and type-2 diabetes mellitus, either by bivariate analysis (*chi-square*) or multivariate analysis (logistic regression).

There are issues that may affect and explain why the results of our study different from most of similar studies in various countries. The first issue is the high prevalence of vitamin D deficiency in our study. The sample size calculation in our study was performed by using prevalence data of previous studies (35.1%);[12] therefore, we would need a minimal number of 84 subjects in each group. In contrast, the prevalence of vitamin D deficiency in our study was 78.2%; therefore, we needed greater sample based on the statistics calculation, i.e. at least 168 subjects in both groups.

The second issue includes the absence of studies and consensus on the cut off level to define vitamin D deficiency, especially in Indonesian population, through evaluation and consideration of the PTH and calcium level. The cut-off level of 50 nmol/L was used in our study and by other similar studies in Indonesia, which is adopted from various study results in the western countries.[9,56,57] Geographic condition with a lot of sunlight exposure or low calcium consumption, which usually occurs in Indonesia, will certainly affect the cut off level for the development of vitamin D deficiency. The third issue includes the possibility of difference or VDR polymorphism between Indonesian population and other population, including the Caucasian. Therefore, in this case, further studies are

necessary to evaluate the VDR polymorphism factors by using better methods. [27,32-34,58,59]

It is interesting that a multivariate analysis found a significant correlation between applying sun protectors and type-2 diabetes mellitus. We assume that it is associated with a significant risk of vitamin D deficiency in the population group applying sun protector (**Table 3**), as has been described in our previous report.

Our study was a cross-sectional study; therefore, it could not evaluate the causal association directly among the studied variables as observed in longitudinal or interventional study. Another limitation in our study includes the limited sample size. The high prevalence of vitamin D deficiency in our study consequently will call for greater sample size. Parathyroid level should also be studied as an indicator of vitamin D deficiency. Furthermore, we also need to examine the variables which were specifically necessary to evaluate the effect of vitamin D on type-2 diabetes mellitus, such as insulin secretion factor and insulin resistance. Those variables also have not been evaluated in our study.

CONCLUSION

The prevalence of vitamin D deficiency in elderly group is quite high, i.e. 78.2%. The prevalence of vitamin D deficiency in the female elderly group is higher than in the male elderly group. Lesser sunlight exposure seems to be etiologic factor of the high prevalence of vitamin D deficiency, especially due to the infrequent use of sun protectors and vitamin D supplementation. Our study has not found significant association between vitamin D deficiency and type-2 diabetes mellitus.

We need to disseminate the benefits of optimal sunlight exposure and/or adequate supplementation of vitamin D, in order to prevent vitamin D deficiency. Further studies are necessary to evaluate the correlation between vitamin D deficiency and type-2 diabetes mellitus by better methods, especially by using the prospective method and by considering the VDR polymorphism factor.

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