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Vitamin D levels of obesity and non-obesity health workers: a cross-sectional study in Dr. Sardjito General Hospital/Faculty of Medicine, Public Health, and Nursing Universitas Gadjah Mada, Yogyakarta

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ABSTRACT

Obesity is one of the causes of chronic diseases, such as diabetes, hypertension, stroke, cancer, dyslipidemia, and heart disease. It is considered a financial burden on national health insurance since it drains the largest health fund. The study aimed to determine the difference in vitamin D levels in obese and non-obese health workers and analyze the factors that influence it. This was a cross-sectional study of the obese and non-obese health workers at Dr. Sardjito General Hospital, Yogyakarta. A total of 50 subjects, including 25 obese and 25 non-obese subjects were involved. Serum vitamin D levels was determined by ELISA. There was no significant difference between the obese and non-obese groups on vitamin D status (p<0.365). Vitamin D deficiency was found in 10% of subjects, whereas insufficient vitamin D levels were found in 46 and 44% of subjects, respectively. Vitamin D deficiency was more common in the obese (12%) than non-obese (8%) group. Contrarily, vitamin D insufficiency was more common in the non-obese (56%) than obese (36%) group. The serum vitamin D levels in the obese [30.08 (14.67-101.71) ng/mL] was not significantly different compare to those non-obese [28.54 (14.38-54.41) ng/mL] (p = 0.691). The multivariate analysis significantly showed that outdoor activities <30 min had a 7.061 times greater risk of having vitamin D deficiency/insufficiency compared to outdoor activities >30 min (OR 7.061; 95% CI: 1.064-46.872; p=0.043). In conclusion, there is no significant difference in vitamin D levels between the obese and non-obese groups. Vitamin D deficiency/insufficiency is more common in non-obese subjects than in obese subjects. Outdoor activity <30 min is a risk factor for vitamin D insufficiency/deficiency despite living in a tropical country with abundant sunlight throughout the year.

ABSTRAK

Obesitas merupakan salah satu penyebab penyakit kronis, seperti diabetes, hipertensi, stroke, kanker, dislipidemia, dan penyakit jantung. Obesitas dikhawatirkan menjadi beban jaminan kesehatan nasional karena menyedot dana kesehatan terbesar. Penelitian ini bertujuan untuk mengetahui perbedaan kadar vitamin D pada tenaga kesehatan dengan obesitas dan non obesitas serta menganalisis faktor-faktor yang mempengaruhinya. Penelitian potong lintang yang dilakukan pada tenaga kesehatan dengan obesitas dan non obesitas di RSUP Dr. Sardjito Yogyakarta. Total sampel penelitian ini adalah 50 subjek, meliputi 25 subjek obesitas dan 25 subjek non-obesitas. Kadar vitamin D serum diukur dengan metode ELISA. Tidak ada perbedaan nyata kadar vitamin D pada kelompok obesitas dan non obesitas (p<0,365). Defisiensi vitamin D ditemukan pada 10% subjek, sedangkan insufisiensi dan kecukupan vitamin D ditemukan pada 46% dan 44% subjek. Defisiensi vitamin D lebih

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sering terjadi pada obesitas (12%) daripada non-obesitas (8%). Sebaliknya, insufisiensi vitamin D lebih sering terjadi pada kelompok non-obesitas (56%) daripada obesitas (36%). Rerata kadar vitamin D pada kelompok obesitas [30,08 (14,67-101,71) ng/mL] tidak berbeda nyata denga kelompok non-obesitas [28,54 (14,38-54,41) ng/mL] (p=0,691). Analisis multivariat menunjukkan bahwa aktivitas di luar ruangan <30 min secara nyata memiliki risiko 7.061 kali lebih besar mengalami kekurangan vitamin D dibandingkan dengan aktivitas di luar ruangan >30 min (OR 7,061; 95% CI:1,064-46,872; p=0,043). Kesimpulan, tidak ada perbedaan nyata kadar vitamin D pada kelompok obesitas dan non obesitas (p<0,365). Defisiensi/insufisiensi vitamin D lebih sering terjadi pada subjek non-obesitas daripada subjek obesitas. Berbagai faktor mempengaruhi perbedaan kadar vitamin D pada kedua kelompok. Aktivitas luar ruangan <30 min terbukti nyata sebagai faktor risiko defisiensi/insufisiensi vitamin D meskipun tinggal di negara tropis dengan sinar matahari yang melimpah hampir sepanjang tahun.

INTRODUCTION

Obesity is one of the contributing causes of chronic diseases, such as diabetes, hypertension, stroke, cancer, dyslipidemia, and heart disease. Obesity is considered a financial burden on national health insurance since it is the largest drain on the health fund. Accordingly, as a risk factor for various diseases, obesity needs to be addressed and treated properly. The global prevalence of obesity in 2017-2018 was 42.4%.[1,2] Data in Indonesia showed as many as 13.5% of adults aged 18 years and over are overweight, while 28.7% are obese with a body mass index (BMI) 25. In 2016, the National Health Indicators Survey (*Survei Indikator Kesehatan Nasional*/SIRKERNAS) reported that the obesity rate of BMI 27 rises to 20.7%, while obesity with BMI 25 became 33.5% (P2PTM, 2018).[3]

Obesity can be multifactorial caused included genetic, environmental (diet, and physical activity), chemical (steroids), and hormonal (leptin, ghrelin, thyroid, insulin, and estrogen) factors.[4] People have been advised to do activities at home and limit activities outside the home during the COVID-19 pandemic, increasing the community's sedentary lifestyle, and thereby increasing the risk of obesity and vitamin D deficiency due to lack of sun exposure.[5] Obesity is a systemic disease with excessive and abnormal body fat accumulation. Obesity will negatively impact individual health. Obesity is associated with higher comorbidity such as type 2 diabetes mellitus, dyslipidemia, hypertension, obstructive sleep apnea, certain types of cancer, steatohepatitis, obesity-related glomerulopathy, chronic kidney disease, gastroesophageal reflux, arthritis, polycystic ovarian syndrome, and also infertility. The severely obese patient also has a limitation in daily activities such as walking, climbing stairs, and bathing, which can lead to mental distress. Inheritable factors also account for a 70% difference in BMI in adult life.[6]

A bidirectional genetic study showed that the higher the BMI, the lower the 25(OH)D level. The basis for low vitamin D concentrations in obesity is still under debate.[7,8] Several causes of vitamin D deficiency include lack of vitamin supplementation, poor dietary habits, low sun exposure, and changes in activity and expression of enzymatic pathways in vitamin D metabolism. Indoor activity and the use of sunscreen will cause a decrease in the formation of endogenous vitamin D in the body.[8,9]

Vitamin D deficiency often occurs not only in countries with four seasons with limited sun exposure, but currently, vitamin D deficiency is also reported to occur in tropical countries with excellent, year-round sun exposure, including Indonesia.[10-12] Based on the literature search, no study has examined the comparison of vitamin D levels in obese and non-obese subjects in Indonesia's population of health workers. Vitamin D deficiency in health workers increases the risk of being infected with COVID-19, so they need special attention. This study compared serum vitamin D levels in obese and non-obese participants to evaluate the factors influencing the obese and non-obese health workers' vitamin D levels.

MATERIAL AND METHODS

Research subjects

This cross-sectional study used purposive sampling until the total number of samples reached 25 obese and 25 non-obese subjects. The research subjects were health workers over 18 years old at Dr. Sardjito General Hospital and the Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta. The study was conducted in the dry season between August and September 2021 to ensure abundant sunlight during sampling.

Exclusion criteria were patients with endocrine disorders other than diabetes mellitus (including thyroid disorders, and hypopituitary gland disorders), uncontrolled hypertension, chronic inflammatory diseases, kidney disorders, liver disorders, angina pectoris, myocardial infarction, heart failure, genetic heart disease, stroke, psychiatric disorders, underwent intestinal and gastric surgery, pregnancy, vitamin D and omega-3 supplementation in the last three months. Subjects who met the inclusion and exclusion criteria were followed to participate in the study and receive a consent letter. The protocol of the study was approved by the Medical and Health Research Ethics Committee of the Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada/Dr. Sardjito General Hospital, Yogyakarta, Indonesia (reference number KE/FK/0586/EC/2021).

Anthropometric data

Anthropometric data collection included measurements of height (m), weight (kg), and waist circumference (cm). The BMI criteria used were based on the World Health Organization (WHO) western pacific region (2000) for the Asia Pacific population.[13] The subjects were grouped into two categories: the obese group (BMI >25) and the non-obese group (BMI 18.5 - 22.9). Central obesity criteria were based on the WHO (2008) for South Asian ethnicity, Chinese, Malay and Asian-Indian populations. Metabolic syndrome criteria were based on the International Diabetes Federation (IDF) criteria in 2005 and the National Cholesterol Education Program Third Adult Treatment Panel (NCEP ATP III) criteria in 2005.

Assessment of sun exposure, physical activity, and nutritional intake

The risk factors for sun exposure were assessed using a sun exposure questionnaire that had previously been tested for validity and reliability. Validity test with product-moment correlation obtained r count of 0.521 - 0.683, which means it is valid as a measuring tool. A reliability test with a Cronbach alpha value of 0.750 (>0.70) indicates good reliability.

Physical activity assessment was analyzed using the International Physical Activity Questionnaire-Short Form (IPAQ short form) questionnaire with validity and reliability that has been used internationally. Physical activity was categorized into three levels, namely category 1 (low physical activity) with <600 MET-minutes/week, category 2 (moderate physical activity) with 600-<3,000 MET-minutes/week, and category 3 (high physical activity) with ≥3,000 MET-minutes/week.

Food intake data were obtained through interviewing subjects using a diet intake recall form of vitamin D with the Semi-Quantitative Food Frequency Questionnaire (SQ-FFQ). The amount of vitamin D intake was determined based on the converted household size into grams (g), then analyzed using a nutrition software program and compared with the 2013 Recommended Dietary Allowances (RDA), then categorized into the inadequate intake (<15 g/d) or adequate (≥15 g/d). In addition to dietary intake of vitamin D, dietary intake of calcium (mg), magnesium (mg), and phosphorus (mg) were also assessed.

Laboratory analysis

Laboratory examinations included 25(OH)D levels, fasting blood sugar, lipid profile (triglycerides, and high-density lipoprotein (HDL) cholesterol), urea, creatinine uric acid, and routine blood. Examination of serum 25(OH)D levels was conducted with the enzyme-linked immunoassay (ELISA) method using the vitamin D kit (Calbiotech, A Life Science Co., USA; Catalog No. VD220B). Plasma glucose levels were measured by the glucose oxidase method, while cholesterol (triglycerides, and HDL) by the automatic colorimetric method. Vitamin D levels in this study used the following criteria for deficiency (<20 ng/mL), insufficiency (21-29 ng/ml), sufficiency (>30 ng/mL), toxicity (>50 ng/mL), according to the cut-off value recommended by the United States Endocrine Society.[14]

Statistical analysis

The sample characteristic data are displayed as a mean with a standard deviation (SD) or a median (minimum-maximum) if not normally distributed. Independent t-tests (t) were used for continuous variables or Mann-Whitney tests if not normally distributed. Data were analyzed with bivariate statistical tests using chi-square test or Fisher's exact test, while logistic regression was used for the multivariate test. A p value <0.05 was considered to be statistically significant. Statistical analysis used the Statistical Package for Social Sciences (SPSS) version 22.0 application (SPSS Inc., College Station, TX).

RESULTS

Baseline characteristics of obese and non-obese groups

TABLE 1 shows some parameters had significant differences (p<0.05) between the obese and non-obese groups. The working duration of more than 8 h in the obese group was significantly more (56%) than in the non-obese group. Systolic and diastolic blood pressure were significantly higher in the obese group, following the criteria for hypertension, which was higher in the obese group than in the non-obese group (p<0.05). The mean weight of the obese group (73.93±9.39 kg) was significantly higher than that of the non-obese group (51.82±5.24 kg) (p = 0.001). The mean BMI in the obese group was 28.68 (25.19-37.20), while the BMI in the non-obese group was 20.83 (18.51-23) (p=0.001). Laboratory parameters such as fasting blood glucose (FBG), hemoglobin (Hb), and platelets were significantly higher in the obese group than in the non-obese group (p<0.05).

Metabolic syndrome, according to NCEP ATP III (48%) and IDF (44%), was significantly more prevalent in the obese group than in the non-obese group (p<0.05). The components of the metabolic syndrome parameters also had a statistically significant value (p<0.05). Subjects with hypertension (40%) and central obesity (96%) were more common in the obese group than in the non-obese group. The mean abdominal circumference in the obese group (94.98±9.24 cm) was higher than the non-obese group (75.56±6.53 cm) (p =

0.001). In obesity, FBG levels were higher than in the non-obese group, 95 (69-185) mg/dL in obese and 87 (58-103) mg/dL in non-obese. Meanwhile, triglyceride levels in the obese group were 92 (63-289) mg/dL, which were higher than the non-obese group with 79 (59-135) mg/dL.

Dietary intake of foods containing vitamin D in the obese group was slightly higher than in the non-obese group. The mean dietary vitamin D intake levels in the obese and non-obese groups were 6.80 (1.5-28.9) μg and 5.40 (2.70-28.30) μg (TABLE 1). The dietary needs target of vitamin D based on the RDA is 15 μg.[24] Based on this targeted recommendation, the percentages of vitamin D intake in the obese and non-obese groups were only 45.33% and 36%, respectively. Dietary intakes of calcium-containing foods in the obese and non-obese groups were 359.6 (124-791) mg and 289 (99.7-1375.3) mg from the target based on the RDA of 1,000 mg. Dietary intake of magnesium in the obese and non-obese groups was 139.4 (46.9-431.7) mg and 144.4 (52.2-453.9) mg, respectively, far from the target of 340-360 mg. Meanwhile, the average dietary intake of phosphorus-containing foods in the obese and non-obese groups was 658.3 (246.5-1433) mg and 607.5 (289.3-1930.1) mg, still lower than the target of 700 mg.

The average total physical activity in the obese group was higher than in the non-obese group (p=0.497). The proportion of strenuous activity (>3,000 met-min/wk) was found to be the same in the obese and non-obese groups. Most of the obese group (36%) did a strenuous activity with >3,000 met-min/wk, while in the non-obese group, most (44%) did a light activity that was <600 met-min/wk (TABLE 1).

TABLE 1. Basic demographic, anthropometric, and laboratory parameters of research subjects with obesity and non-obesity

Variable	Obese (n=25)	Non obese (n=25)	p
Gender [n (%)]			
• Man	4 (16.0)	4 (16.0)	1.000
• Woman	21 (84.0)	21 (84.0)	
Gender (mean ± SD years)	39.12±8.22	36.00±8.25	0.187
Hypertension [n (%)]			
• Yes	10 (40.0)	3 (12.0)	0.024
• No	15 (60.0)	22 (88.0)	
Central obesity [n (%)]			
• Yes	24 (96.0)	4 (16.0)	0.001
• No	1 (4.0)	21 (84.0)	
Metabolic syndrome (NCEP ATP III) [n (%)]			
• Yes	12 (48.0)	1 (4.0)	0.001
• No	13 (52.0)	24 (96.0)	
Metabolic syndrome (IDF) [n (%)]			
• Yes	11 (44.0)	1 (4.0)	0.001
• No			
Outdoor activity (min)			
• <30	14 (56.0)	14 (56.0)	
• >30-60	4 (16.0)	8 (32.0)	0.231
• >60	7 (28.0)	3 (12.0)	
Working duration (h)			
• >8 h	14 (56.0)	7 (28.0)	0.045
• 4-8 h	11 (44.0)	18 (72.0)	
Physical activity category (IPAQ) [n (%)]			
• Light	8 (32.0)	11 (44.0)	
• Currently	8 (32.0)	5 (20.0)	0.558
• Heavy	9 (36.0)	9 (36.0)	

Variable	Obese (n=25)	Non obese (n=25)	p
SBP (mmHg)	120 (100-160)	108 (86-140)	0.002
DBP (mmHg)	80 (61-130)	70 (58-100)	0.001
Waist circumference (cm)	94.98 ± 9.24	75.56 ± 6.53	0.001
Body height (cm)	158 (150-170)	157 (149-176)	0.891
Body weight (cm)	75.93 ± 9.39	51.82 ± 5.24	0.001
BMI	28.68 (25.19-37.20)	20.83 (18.51-23)	0.001
FBG (mg/dL)	95 (69-185)	87 (58-103)	0.001
HDL cholesterol (mg/dL)	47.84 ± 9.19	50.80 ± 7.95	0.229
Triglycerides (mg/dL)	92 (63-289)	79 (59-135)	0.060
Hemoglobin (g/dL)	13.47 ± 1.56	12.42 ± 1.86	0.036
Leucocyte count ($x10^3$/uL)	6.96 (4.75-13.99)	6.47 (4.19-10.10)	0.060
Thrombocyte count ($x10^3$/uL)	302.90 ± 57.60	261.80 ± 80.68	0.044
Vitamin D intake (μg)	6.80 (1.50-28.90)	5.40 (2.70-28.30)	0.720
Total physical activity (MET-min/wk)	1668 (148.5-8130)	631(99-8370)	0.497

NCEP ATP III: National Cholesterol Education Program Third Adult Treatment Panel III; IDF: International Diabetes Federation; IPAQ: International Physical Activity Questionnaire; SBP: systolic blood pressure; DBP: diastolic blood pressure; BMI: body mass index; FBG: fasting blood glucose; HDL: high-density lipoprotein; MET: metabolic equivalent of task.

Analysis of serum vitamin D levels in the obese and non-obese groups

Results showed that most subjects (46%) had vitamin D insufficiency (TABLE 2). As many as 22 (44%) subjects had sufficient vitamin D levels, and 5 (10%) subjects had vitamin D deficiency. The prevalence of vitamin D deficiency was higher in the obese (12%) than in the non-obese (8%) group. In comparison, vitamin D insufficiency was more common in the non-obese (56%) than the obese (36%) group, but it was not statistically significant (p=0.365). Remarkably, this study found that more subjects with sufficient vitamin D were obese (52%) than non-obese (36%) (p>0.005). It is suspected that several factors can affect vitamin D insufficiency, which was found in the obese group more than in the non-obese group in this study.

TABLE 2. Comparative distribution of serum vitamin D levels in the obese and non-obese groups

Variable	Deficient (< 20 ng/mL)	Insufficiency (20-3 ng/mL)	Sufficient (>30 ng/mL)	
Obesity [n (%)]	3 (12)	9 (36)	13 (52)	0.365
Non-obesity (n (%)]	2 (8)	14 (56)	9 (36)	
Total	5 (10)	23 (46)	22 (44)	

Analysis of the factors that affect the sufficiency of vitamin D

TABLE 3 describes the factors influencing vitamin D deficiency/ insufficiency (<30 ng/mL) in the obese and non-obese groups. It was found that hypertension, metabolic syndrome, and wearing sunscreen significantly affected vitamin D levels < 30 ng/mL in the obese and non-obese groups (p<0.005). The average vitamin D levels in subjects with vitamin D deficiency/insufficiency (<30 ng/mL) and sufficient vitamin D (>30 ng/mL) were 25.72 and 33.93, respectively (p <0.001) (TABLE 4).

All variables in the bivariate analysis (TABLEs 3 and 4) that met the criteria of p < 0.25 were then continued to multivariate logistic regression analysis to determine the most powerful factor influencing the adequacy of vitamin D levels in the obese and non-obese groups.

The multivariate analysis (TABLE 5) found that only outdoor activity factors significantly affected the adequacy of vitamin D levels with p<0.05. Obese and non-obese subjects with outdoor activities <30 min had an increased risk of vitamin D deficiency/insufficiency, as much as 7.061 higher than subjects with outdoor activities >30 min (OR=7.061; 95% CI: 1.064-46.872; p=0.043).

TABLE 3. Bivariate analysis of demographic variables, sun exposure, and physical activity that affect vitamin D deficiency/insufficiency in all subjects

Variable	Vitamin D level < 30 ng/mL	Vitamin D level < 30 ng/mL	p
Gender [n (%)]			
• Man	2 (25)	6 (75.0)	0.116
• Woman	26 (61.9)	16 (38.1)	
Age (mean ± SD years)	36.82 ± 8.28	38.50 ± 8.42	0.484
Smoking [n (%)]			
• Yes	0 (0)	1 (100.0)	0.440
• No	28 (57.1)	21 (42.9)	
Exercise min/wk [n (%)]			
• <60	26 (61.9)	16 (38.1)	0.116
• >60	2 (25.0)	6 (75.0)	
Income (million/mo)/[n (%)]			
• <5	4 (36.4)	7 (63.6)	0.178
• >5	24 (61.5)	15 (38.5)	
Comorbid [n (%)]			
• Yes	2 (33.3)	4 (66.7)	0.385
• No	26 (59.1)	18 (40.90)	
Hypertension [n (%)]			
• Yes	4 (30.8)	9 (69.2)	0.033*
• No	24 (64.9)	13 (35.1)	
Central obesity [n (%)]			
• Yes	13 (46.4)	15 (53.6)	0.124
• No	15 (68.2)	7 (31.8)	
Metabolic syndrome (IDF) [n (%)]			
• Yes	2 (16.7)	10 (83.3)	0.002*
• No	26 (68.4)	12 (31.6)	

Variable	Vitamin D level < 30 ng/mL	Vitamin D level < 30 ng/mL	p
Outdoor activity (min)/[n (%)]			
• <30	19 (67.9)	9 (32.1)	0.057
• >30	9 (40.9)	13 (59.1)	
Hours exposed to the sun [n (%)]			
• Uncertain	5 (83.3)	1 (16.7)	0.211
• 07.00-16.00	23 (52.3)	21 (47.7)	
Working hours [n (%)]			
• Non-shift/morning	6 (75.0)	2 (25.0)	0.439
• Alternating shifts	22 (52.4)	20 (47.6)	
Working duration (hr)/ [n (%)]			
• >8	10 (47.6)	11 (52.4)	0.310
• 4-8	18 (62.1)	11 (37.9)	
The work environment is exposed to light [n (%)]			
• Yes	4 (50.0)	4 (50.0)	0.718
• No	24 (57.1)	18 (42.9)	
Body parts covered with clothes [n (%)]			
• >4	24 (61.5)	15 (38.5)	0.178
• 1-4	4 (36.4)	7 (63.6)	
Clothing material [n (%)]			
• Difficult to absorb sunlight	17 (51.5)	16 (48.5)	0.373
• Easy to absorb sunlight	11 (64.7)	6 (35.3)	
Wear a hat [n (%)]			
• Yes	0 (0.0)	3 (100.0)	0.079
• No	28 (59.6)	19 (40.4)	
Wear sunscreen [n (%)]			
• Yes	19 (70.4)	8 (29.6)	0.027*
• No	9 (39.1)	14 (60.9)	
MET category [n (%)]			
• Light	10 (52.6)	9 (47.4)	
• Currently	10 (76.9)	3 (23.1)	0.185
• Heavy	8 (44.4)	10 (56.6)	

TABLE 4. Bivariate analysis of anthropometric variables, dietary intake, and biochemical parameters that affect vitamin D deficiency/insufficiency in all subjects

Variable	Vitamin D level < 30 ng/mL	Vitamin D level < 30 ng/mL	p
SBP [median (min-max mmHg)]	116.5 (90-151)	120 (86-160)	0.430
DBP [median (min-max mmHg)]	74 (58-95)	76 (60-130)	0.562
Waist circumference (mean ± SD cm)	82.8 ± 12.7	88.41 ± 12.05	0.120
Body height [median (min-max cm)]	157 (149-166)	158 (150-176)	0.346
Bodyweight (mean ± SD kg)	61.37 ± 14.57	64.80 ± 11.97	0.377
BMI [median (min-max mmHg)]	22.81 (18.51-37.2)	26.37 (18.61-33.83)	0.374
Vitamin D levels [median (min-max ng/mL)	25.72 (14.38-29.97)	33.93 (30.08-101.71)	<0.001
FBG [median (min-max mg/dL)]	91 (67-146)	93 (58-185)	0.379
HDL cholesterol (mean ± SD mg/dL)	49.68 ± 7.52	48.86 ± 10.04	0.744
Triglycerides [median (min-max mg/dL)]	84.5 (59-289)	90.50 (64-228)	0.384
Hb (mean ± SD g/dL)	12.55 ± 1.78	13.45 ± 1.69	0.075
Leucocyte count [median (min-max x10^3/uL)]	6.86 (4.75-11.10)	6.52 (4.19-13.99)	0.611
Thrombocyte count (mean ± SD x10^3/uL)	287 ± 86.2	276 ± 51.5	0.562
NLR [mean (min-max)]	1.99 1.20-3.87)	1.72 (0.98-5.10)	0.197
BUN [(median (min-max mg/dL)]	8.55 (4.50-12.20)	8.80 (7.30-13.60)	0.120
Creatinine (mean ± SD mg/dL)	0.68 ± 0.16	0.76 ± 0.14	0.066
Uric acid [median (min-max mg/dL)]	4.50 (2.40-9.40)	4.70 (3.30-8.40)	0.423
Vitamin D intake [median (min-max μg)]	5.85 (2.40-24.60)	6.80 (1.50-28.90)	0.369
Calcium intake [median (min-max mg)]	343.9 (126-791)	299.5 (99.7-1375.3)	0.907
Magnesium intake [median (min-max mg)]	143.2 (52.2-321.6)	143.4 (46.9-453.9)	0.961
Phosphorus intake [median (min-max mg)]	630.3 (252.5-1433)	706.1 (246.5-1930.1)	0.333

SBP: systolic blood pressure; DBP: diastolic blood pressure; BMI: body mass index; FBG: fasting blood glucose; HDL: high-density lipoprotein; Hb: hemoglobin; NLR: neutrophil-lymphocyte ratio; BUN: blood urea nitrogen

TABLE 5. Multivariate logistic regression analysis of various factors that affect vitamin D deficiency/insufficiency in all subjects

	p	OR	95% CI
Outdoor activities			
• <30 min	0.043*	7.061	1.064-46,872
• >30 min			
Constant	0.715	6.550	

*p-value < 0.05: statistically significant; CI: confidence interval; OR: odds ratio

DISCUSSION

Baseline characteristics of obese and non-obese groups

In this study, there was no significant difference between the physical activity of the obese and non-obese groups (p>0.05). This finding follows the research conducted by Gupta *et al.*[14] that found there was no significant difference in physical activity between obese and non-obese children (p=0.139).[14] Although exposure to ultraviolet (UV)-B light can increase serum 25(OH)D levels, excessive UV radiation is not recommended to maintain adequate vitamin D production. The skin needs sun exposure to convert previtamin D3 to vitamin D. Physical activity can increase skin temperature. In contrast, high skin temperature can help produce vitamin D in the body.[12,15]

There was no significant difference in dietary intake of vitamin D, calcium, phosphorus, and magnesium between the obese and non-obese groups. This finding is consistent with the results of other studies, which showed no significant difference between dietary intake of vitamin D in the obese and non-obese groups.[14] Low dietary vitamin D intake [p=0.369; 5.85(2.40-24.60)] was associated with vitamin D deficiency and insufficiency, although this study did not prove statistical significance. Some of the reasons were the analysis of food diets in this study using a semi-quantitative Food Frequency Questionnaire which assesses the frequency of consuming foods containing vitamin D and only conducted one interview which should be done with more than one measurement. In addition, in this study, no daily diet recall was conducted, so the food intake analysis results were less than optimal. Another study conducted in North Sumatra, Indonesia demonstrated that vitamin D deficiency was significantly associated with low dietary vitamin D intake (p=0.046).[12] According to research by Masood and Iqbal *et al.*[16] the inability to buy food sources containing vitamin D causes vitamin deficiency, such as salmon and fish oil which are still considered expensive food sources in the market.[16]

There was a significant difference between SBP and DBP between the obese and non-obese groups in this study (p=0.002 and 0.001, respectively). This finding is similar with the research results by Alfawaz *et al.*,[17] that found there is a significant difference between SBP and DBP.[17] Research by Bugaz *et al.*,[18] reported a significant inverse relationship between hypertension and vitamin D levels, while in this study, a significant difference was found between hypertension and vitamin D (p=0.033). However, subjects with hypertension have higher levels of vitamin D sufficiency than those without hypertension. The difference in this relationship may be influenced by the fewer number of samples with comorbid hypertension, which was 26% of the total study sample. Several other studies found no significant difference between hypertension and vitamin D deficiency/insufficiency.[14,19]

This study showed a significant difference between metabolic syndrome and vitamin D levels (p = 0.001). The study by Karatas *et al.*[19] showed that vitamin D deficiency not only occurred in overweight/obese subjects with metabolic syndrome (72%) and without metabolic syndrome (69%) but also occurred in healthy subjects (49%).[19] Another study stated that inadequate vitamin D status will increase the risk of developing metabolic syndrome by 2.5 times (OR 2.5).[20] Previous studies have also shown that low levels of 25(OH)D are significantly associated with components of the metabolic syndrome such as increased blood pressure, increased triglycerides, decreased HDL, and increased abdominal circumference.[19-21] On the other hand, several studies have failed to demonstrate any significant association between vitamin D and metabolic syndrome.[22-24] The difference in results may be due to the studies were conducted in different populations, namely in the low-risk or high-risk groups.[20] Therefore, larger samples are needed for further research to assess the relationship between vitamin D status and metabolic syndrome, especially in Yogyakarta, Indonesia.

Analysis of vitamin D levels in the obese and non-obese groups

In this study, the prevalence of vitamin D deficiency was slightly higher in the obese than in the non-obese group. In contrast, vitamin D insufficiency was more common in the non-obese than the obese group, although it was not statistically significant (p=0.365). This result follows a study by Gupta *et al.*[14] which showed that the prevalence of vitamin D deficiency was significantly more common in obese children than in non-obese children. However, there was no significant relationship between serum levels of 25(OH) vitamin D3 with comorbid obesity. Research by South East Asian Nutrition Surveys (SEANUTS) revealed that there was no vitamin D deficiency (levels <25 nmol/L) in children in Indonesia.[10]

1.25(OH)2-D in human cells will stimulate adipogenesis by upregulating the gene expression such as fatty acid synthase (FASN), fatty acid-binding protein (FABP), and peroxisome proliferator activator receptor (PPAR)-γ, which play a role in the adipocyte differentiation. 1.25(OH)2-D also stimulates the translocation of glucose transporter 4 (GLUT4) that induces adiponectin secretion. 1.25(OH)2-D also induces leptin that promotes adiponectin secretion. Vitamin D regulates the adipokine secretion in adipocytes, such as adiponectin (an anti-inflammatory and insulin-sensitizing hormone), leptin, and resistin. Obesity is also associated with low-grade inflammation. Vitamin D also promotes lower chemokine and cytokine release by adipocytes and the chemotaxis of monocytes. Vitamin D deficiency will decrease mRNA levels of oxidation-related genes, resulting in an alternation of adipocyte metabolic metabolism and obesity progression. miR-146a, miR-150, and miR-155 have been identified as related to vitamin D.[25]

Several studies have found a significant inverse relationship between vitamin D and BMI.[14,26] However, in this study, there was no significant difference between BMI and vitamin D levels (p=0.374) (TABLE 4). Vitamin D insufficiency/deficiency occurred in normal BMI (mean BMI 22.81), while vitamin D sufficiency occurred in obese BMI (mean BMI 26.37). Following a study conducted on women in North Sumatra, Indonesia, BMI did not significantly affect the concentration of 25-hydroxyvitamin D. Vitamin D deficiency was detected in obese women in Indonesia and was also found in subjects with normal adiposity (subjects with normal adiposity) or non-obese.[27]

Another study conducted on men in Yogyakarta, Indonesia, also showed that the proportion of vitamin D deficiency and insufficiency was relatively high but was not significantly associated with obesity, lipid profile, and physical activity.[11] Several studies have found low 25(OH)D levels in women with high body fatness and normal and low body fatness subjects.[27,28] This shows that several other factors, apart from body fat composition, can cause subjects with high or normal body fat to experience vitamin D deficiency. BMI and body weight do not represent the body fat percentage; for example, athletes and other well-trained people may have a relatively high BMI (overweight or obese) but have a low total fat mass.[29] The BMI parameter is a method used to measure obesity, but BMI itself is not a good indicator of the amount or distribution of body fat. Body fat distribution influences metabolic health since central obesity or visceral fat accumulation is associated with cardiometabolic risk, while femoral-gluteal subcutaneous fat may protect against cardiovascular risk.[6]

Based on research conducted by SEANUTS in 2016, it was found that there is a relationship between BMI and level 25(OH)D in Malaysia, Thailand, and Indonesia.[10] A negative relationship between vitamin D and BMI or body fatness has also been reported in several studies, including in Indonesia.[30] Meanwhile, the positive correlation between 25(OH)D and BMI in Vietnam may be because children with obesity in Vietnam belong to a high socio-economic class, so their nutritional intake is better than non-obese subjects.[10] This is consistent with the results of our study, where dietary vitamin D intake in the obese group [6.80 (1.50-28.90)] was higher than in the non-obese group [5.40(2.7-28.30)], although it was not statistically significant. The high dietary vitamin D in the obese group is influenced by the higher educational status and income level in the obese group compared to the non-obese group (TABLE 1). This finding matches research conducted on the elderly in Indonesia, which also could not find significant evidence that the elderly who are obese are more at risk of malnutrition or vitamin D deficiency due to the social background of the subjects living in big cities where most of the subjects have a high level of education and economic status.[30]

Analysis of the factors that affect the sufficiency of vitamin D in all subjects

The high prevalence of vitamin D insufficiency in (sub)tropical countries requires a multifactorial approach, including promoting a lifestyle of outdoor activities with safe and adequate sun exposure and strategies to increase intake of foods containing high vitamin D.[10] Factors associated with vitamin D deficiency include the complexity of skin color, low sun exposure, vegetarian eating habits and low intake of fortified foods containing vitamin D.[14] This is following the results of the multivariate analysis (TABLE 5) which show that outdoor activities <30 min have a significantly higher risk by 7,061 times of having vitamin D deficiency/ insufficiency (vitamin D levels <30 ng/mL) compared to outdoor activities > 30 min (p = 0.043). Outdoor activities with the most prolonged duration (> 1 h) were found more in obese subjects than non-obese (TABLE 1), so many non-obese subjects in this study experienced vitamin D insufficiency. This result aligns with a study that found vitamin D deficiency in women in tropical countries is associated with exposure to sunlight for less than 1 h/d and having an indoor job.[27] Despite living in a tropical country rich in sunlight throughout the year, many subjects still do not get enough sun exposure. Most subjects only did physical activity for 15 min daily while wearing sunscreen, hijab, or hat.[30] A study showed that Indonesians should get a minimum of 25 min of direct sun exposure at 9-10 AM to obtain a blood concentration of 2,700 IU of vitamin D per exposure and at least 3 times a week to prevent vitamin D deficiency.[31]

There was no significant difference between hours exposed to the sun and body parts covered with vitamin D deficiency/insufficiency (p<0.05). This is due to the typical behavior in tropical countries to avoid direct sun exposure, for example, by walking on the edges of buildings to avoid direct sunlight and wearing sunscreen, hats, or umbrellas when doing outdoor activities.[10,27] Most of the population of Malaysia and Indonesia are Muslim. Most of the female Muslim population wears closed clothes covering the whole body except the face and palms. Research in Malaysia found a relationship between wearing closed clothes (Muslim wear) and low levels of vitamin D.[32,33] The non-obese group experienced more vitamin D insufficiency because they wore clothes that covered almost their entire body (>4 body parts) and wore hats more when doing outdoor activities, but this was not statistically significant (p>0.05). Research by Hidayat *et al.*[30] on the elderly population in Indonesia proved that sunscreen was significantly correlated with vitamin D deficiency (p=0.016). The finding is consistent with the results of this study, where subjects who used sunscreen (70.4%) had significantly more vitamin D deficiency/insufficiency than those who did not use sunscreen (39.1%) (p=0.027).[30]

Regional differences are the most significant source of variation in 25(OH) D levels across countries. Differences in 25(OH)D levels per region contributed to the significant difference in the prevalence of vitamin D insufficiency. The results showed that the population of Java island had a nine times higher risk for vitamin D deficiency compared to Sulawesi island, although still within the same country. These regional differences within a country have been observed previously in Thailand.[10,34]

Vitamin D deficiency in women in north Sumatra, Indonesia, is not associated with obesity but is more likely to be caused by a single nucleotide polymorphism.[12] Moreover, according to a trusted source study, people on the island of Java have a nine times higher risk of vitamin D deficiency than other islands in Indonesia.[34] Therefore, further research is needed to evaluate the relationship of vitamin D with obesity with a better method, such as a prospective cohort by considering vitamin D receptors' gene polymorphism, especially for Yogyakarta, Java Island. Genetic factors play a role in determining the concentration of 25(OH)-D in serum. Some research showed an association between Hydroxyvitamin D-1-α hydroxylase (CYP27B1), vitamin D 25-hydroxylase (CYP2R1), vitamin D binding protein (DBP/GC), vitamin D receptor (VDR), vitamin D 24-hydroxylase (CYP24A1), 7-dehydrocholesterol reductase (DHCR7), retinoid X receptors (RXR), calcium-sensing receptor (CASR), NPY, FOXA2, SSTR4, and IVL genes and serum 25(OH)-D Concentration.[25]

Remarkably, the differences between regions did not show a statistically significant relationship between the average hours of sun exposure and sun exposure per day. Some of the reasons include that the actual number of hours of sunshine in the area may differ from the annual mean value according to the meteorological department. In addition, hours of sunshine vary significantly throughout the year, and hours do not mean direct exposure to sunlight. People often like to stay indoors or in the shade or avoid direct sunlight by wearing clothes or an umbrella. The effectiveness of sun exposure may differ depending on factors such as air pollution, smog, and altitude. Additionally, Southeast Asians (including in Indonesia), especially women, tend to avoid sun exposure to maintain a fair skin tone because, culturally, white skin is a sign of beauty.[10,35]

Study limitations

This study has several limitations, including 1) the subjects were taken from health workers at a Central General Hospital in Yogyakarta, Indonesia, with a small number of samples so that the results cannot be generalized to the Indonesian population; 2) serum 25(OH) D levels were measured by the method ELISA, which is not the gold standard for measurement of vitamin D levels, but the technique of ELISA is currently the most widely used for research purposes since it is simpler and cheaper,[29] and 3) serum calcium and parathyroid hormone levels were not measured in this study. However, the strength of this study is that it analyzed various factors related to vitamin D levels, including demographic and anthropometric factors, lifestyle, dietary intake of food, physical activity, and factors of sun exposure which were relatively complete.

Despite the limitations of this study, the results of this study can be used as a preliminary study for further research to assess genomic studies of vitamin D (vitamin D receptor polymorphism), obesity, and metabolic syndrome in the population in Yogyakarta, Indonesia, as one of the developing countries in Southeast Asia. With the present results, it is recommended that metabolic disease prevention programs can be done, which will decrease the prevalence of metabolic diseases in the next decade.

CONCLUSIONS

The results found that there is no significant difference in vitamin D status among the obese and non-obese groups. Vitamin D deficiency/insufficiency (vitamin D levels < 30 ng/mL) is more common in non-obese subjects than obese subjects although it is not statistically significant. Various factors influence the difference in vitamin D levels in subjects. Outdoor activity <30 min is found to be a significant risk factor for vitamin D insufficiency/deficiency, despite living in a tropical country with abundant sunshine throughout the year.

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