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# Associations between Serum 25-Hydroxyvitamin D Levels and Metabolic Syndrome in Male Shift Workers

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#### **Abstract**

**Objective:** We investigated the association between serum 25-hydroxyvitamin D (25(OH)D) levels and metabolic syndrome (MetS) in male shift workers vulnerable to serum 25(OH)D deficiency.

Materials and methods: Laboratory measurements and self-questionnaire survey were conducted on 985 daytime and 755 shift workers. Shift workers comprised two-shift (n = 38) and three-shift (n = 717). Variables between daytime and shift workers were compared, the correlation between these variables and serum 25(OH)D levels and differences of variables according to quartiles of serum 25(OH)D levels were analyzed. Odds ratios (OR) of MetS and metabolic components depending on serum 25(OH)D levels were determined using multiple logistic regression analysis.

**Results:** The prevalence of Met S in daytime and shift workers was 24.7% and 23.8%, respectively. In daytime workers, mean serum 25(OH)D level was lower and age, the number of alcohol drinker, worker who lack exercise and sleep, married worker was higher than shift workers with significance. After correction of confounding factors including lifestyle, sociodemographic factors and seasonal variation, MetS (OR = 1.580, 95% CI = 1.004-2.488, P = 0.048) and waist circumference (OR = 1.915, 95% CI = 1.217-3.013, P = 0.005) were statistically significant in daytime workers, but not in shift workers. Both groups with serum 25 (OH) D deficiency showed hypertriglyceridemia regardless of MetS.

**Conclusions:** Associations between serum 25(OH)D levels and MetS in shift workers could be affected by confounding factors and working condition. Serum 25(OH) D deficiency is a risk factor of hypertriglyceridemia in male workers.

#### **Keywords**

Vitamin D, Shift, Daytime, Workers, Metabolic syndrome, Hypertriglyceridemia

### Introduction

Metabolic syndrome (MetS) includes abdominal obesity, hyperglycemia, low high-density lipoprotein cholesterol (HDL-C), high triglyceride (TG), hypertension and is related to cardiovascular disease, type 2 diabetes mellitus (DM), stroke, and cardiovascular mortality [1,2]. Insulin resistance (IR) related to abdominal obesity is the main cause of MetS, as well as lifestyle, environment, and genetic factors [3,4]. In South Korea, the prevalence of MetS increased from 24.5% in 2008 to 28.1% in 2017 in males and decreased from 20.5% to 18.7% in females [5].

For vitamin D synthesis, 7-dehydrocholesterol is converted into cholecalciferol in the skin keratinocyte from ultraviolet B of the sunlight and is absorbed by food intake. Next, 25-hydroxyvitamin D (25(OH)D) is produced by 25-hydroxylation in the liver, and then 1,25-dihydroxyvitamin D (1,25(OH) $_2$ D) is synthesized by 1 $\alpha$ -hydroxylation in the kidney. Additionally, 25(OH)D is a clinically useful measurement target because of its relatively longer half-life

than 1,25(OH),D [6].

Vitamin D is involved in bone metabolism and plays an essential role in cell differentiation control and cell proliferation, immune function, and anticancer effect, and its insufficiency causes rickets and osteoporosis [7]. Clinically, vitamin D is related to hypertension, cardiovascular disease, diabetes mellitus, cancer, and MetS.

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Vitamin D deficiency is one of the major health problems worldwide. In South Korea, vitamin D deficiency is considered as a serum 25(OH)D level of < 20 ng/mL, with 52.8% and 68.2% prevalence in males and females in 2008, which was 75.2% and 82.5% in 2014, respectively [8]. Decreased outdoor activities due to the increased urbanization cause inadequate sunlight exposure and decreased amount of ultraviolet B rays reaching the ground due to air pollution, leading to a decreased vitamin D synthesis in the skin [9].

Workers are affected by vitamin D concentration depending on working conditions, including indoor or outdoor, night or daytime, and office or manufacturing workers [10]. Shift work is a common form of work outside of working hours and varies depending on the duration of the shift, the change of working time, night or day, and the number of workers [11]. Circadian rhythm changes due to shift work cause various physical diseases, such as depression, cardiovascular diseases, and cancers [12]. Furthermore, developing type 2 DM is a risk with lifestyle factors, such as smoking, obesity, and lack of exercise [13]. Therefore, the development of MetS may be vulnerable to shift workers. However, many studies on the relationship between shift work and MetS have revealed inconsistent results [14].

This, this study aimed to compare the prevalence of MetS between daytime and shift workers and analyzed the relationship between serum 25(OH)D and MetS in two groups.

#### Methods

#### **Subjects**

This retrospective cross-sectional study included 2,003 workers who underwent an annual health check-up from March to December 2021. Of these, 243 females, 6 individuals who did not undergo clinical questionnaires or laboratory measurements, and 14 individuals taking vitamin D were excluded. A total of 1,740 males were finally enrolled. The numbers of daytime and shift workers were 985 and 755, respectively. Daytime workers refer to workers who never work at night in their usual work schedule. The time work schedule was from 09:00 to 18:00 h. Shift workers are divided into two-shift (n = 38) and three-shift workers (n = 717). The starting time of two-shift work is 08:00 h or 20:00 h, and the three-shift work begins at 08:00, 16:00, and 24:00 h. This study protocol was approved by the Institutional Review Board of Seoul National University Bundang Hospital, Seongnam-si, Gyeonggi-do, Korea (B-1703-385-003). Written informed consent was obtained from all participants.

#### Laboratory measurements

Blood collection of participants took place in the morning after fasting for at least 8 h. Weight, height, and blood pressure (BP) measurements were taken using standard techniques. Body mass index (BMI) was obtained by dividing weight (kg) by height squared (m²). Waist circumference (WC) was measured at the level midway between the lower ribs and the highest area of the iliac crest. Waist-BMI ratio (WBR) was calculated as WC in centimeters divided by BMI [15]. Fasting plasma glucose (FPG), HDL-C, TG, and serum

creatinine (Cr) levels were measured. Serum 25(OH)D (Atellica IM 1600 analyzer, Siemens, Germany) was measured using the Chemiluminescence immunoassay (CLIA) method. The seasonal data of serum 25(OH)D examination was categorized into four groups: Spring (March-May), summer (June-August), autumn (September-November), and winter (December-February).

#### **Definition of MetS**

We defined MetS by the 2009 harmonization criteria [16]. Subjects who meet at least three of the following criteria were diagnosed with MetS: (1) WC of  $\geq$  90 cm; (2) current use of anti-hypertensive medications or BP of  $\geq$  130/85 mmHg; (3) receiving treatment for previously diagnosed type 2 DM or FPG of  $\geq$  100 mg/dL; (4) HDL-C of < 40 mg/dL; (5) receiving medical treatment for elevated TG levels or TG of  $\geq$  150 mg/dL. The WC cut-off was set following the abdominal obesity criteria in Koreans under the Korean Society for the Study of Obesity [17].

## **Clinical questionnaires**

We conducted self-assessment questionnaire for the workers who participated in the study. Alcohol drinkers were defined as alcohol intake more than once a week. Smoking status was classified as current smoker, former smoker, and no smoker. The exercise was considered as aboverecommended physical activity (PA), including walking for 20 min daily; moderately intense activity (e.g., brisk walking or doubles tennis) for at least 20 min 5 days a week; or vigorously intense activity (e.g., jogging or singles tennis) for at least 20 min 4 days a week. Less intense levels were defined as below recommended PA. Sleep duration was classified into three groups, including 5 h, 6-7 h, and 8-9 h based on data answered for "In the past year, on average, how many hours per day did you sleep, including naps?" in the survey. The three subjects who slept more than 10 hours were included in the 8-9 h group. Marital status was classified as single or married. One worker was widowed and 12 workers who divorced were classified as single workers. Education level was divided into four levels: high school, college, university, and graduate school.

#### Statistical analysis

Continuous variables were expressed as mean ± standard deviation. The Kolmogorov-Smirnov test was performed for the normality of continuous variables. Student's t-test and Mann-Whitney U test were performed to determine differences between two groups for continuous variables, respectively and Chi-square test for categorical variables expressed as percentage or frequency. For the correlations between serum 25(OH)D level and variables, continuous variables were performed using the Spearman's correlation analysis. Serum 25(OH)D levels were logarithmically converted and categorized into quartiles (Q1, 1.91-2.72 ng/ mL; Q2, 2.73-2.99 ng/mL; Q3, 3.00-3.24 ng/mL; Q4, 3.25-4.29 ng/mL). Continuous variables according to the serum 25(OH)D levels were compared using the Kruskal-Wall is test and categorical variables using the Chi-square test. Multiple logistic regression analysis, including potential confounders,

was performed to analyze the relationship between serum 25(OH)D quartiles and the prevalence of MetS and its components. The Statistical Package for the Social Sciences for windows version 26.0 (SPSS Inc., Chicago, IL, USA) was used for all analyses. *P*-values of < 0.05 was considered statistically significant.

#### **Results**

# Characteristics of the study population

Table 1 shows the clinical characteristics of both daytime and shift workers. The prevalence of MetS was 24.7% and 23.8% in daytime and shift workers, respectively, but without

**Table 1:** Characteristics of daytime workers and shift workers.

Variables	Daytime workers (n = 985)	Shift workers (n = 755)	P value
Age (years)	41.15 ± 9.4	38.26 ± 10.10	< 0.001
BMI (kg/m²)	25.18 ± 2.99	25.39 ± 3.21	0.155
WC (cm)	84.96 ± 7.75	85.54 ± 8.19	0.116
WBR	3.39 ± 0.22	3.39 ± 0.22	0.694
SBP (mmHg)	122.10 ± 10.98	119.95 ± 10.98	< 0.001
DBP (mmHg)	75.23 ± 8.88	74.05 ± 7.86	0.005
FPG (mg/dL)	100.54 ± 16.17	101.09 ± 13.68	0.301
HDL-C (mg/dL)	53.05 ± 11.51	51.71 ± 10.45	0.074
TG (mg/dL)	141.92 ± 135.10	147.67 ± 107.12	0.538
Cr (mg/dL)	0.92 ± 0.15	0.88 ± 0.12	< 0.001
Serum (OH)2D (ng/mL)	20.61 ± 8.33	21.80 ± 7.73	< 0.001
≥ 20 (%)	451 (45.8)	416 (55.1)	< 0.001
< 20 (%)	534 (54.2)	339 (44.9)	
MetS component	1.58 ± 1.36	1.53 ± 1.29	0.647
MetS (%)			0.690
no	742 (75.3)	575 (76.2)	
yes	243 (24.7)	180 (23.8)	
Season (%)			< 0.001
spring	137 (13.9)	53 (7.0)	
summer	345 (35.0)	599 (79.3)	
autumn	390 (39.6)	85 (11.3)	
winter	113 (11.5)	18 (2.4)	
Marital status (%)			< 0.001
single	246 (25.0)	273(36.2)	
married	739 (75.0)	482(63.8)	
Education level (%)			< 0.001
high school	60 (6.1)	99 (13.1)	
college	17 (1.7)	52 (6.9)	
university	753 (76.4)	560 (74.2)	
graduate school	155 (15.7)	44 (5.8)	
Smoking status (%)			< 0.001
no smoker	459 (46.6)	353 (46.8)	
former smoker	339 (34.4)	188 (24.9)	
current smoker	187 (19.0)	214 (28.3)	
Alcohol consumption (%)			< 0.001
≤ once a week	765 (77.7)	<b>654</b> (86.6)	
> once a week	220 (22.3)	101 (13.4)	
Exercise (%)			0.019

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below recommended PA	705 (71.6)	501 (66.4)	
above recommended PA	280 (28.4)	254 (33.6)	
Sleep duration (%)			< 0.001
< 5 h	27 (2.7)	13 (1.7)	
6-7 h	868 (88.1)	565 (74.8)	
8-9 h	90 (9.1)	177 (23.4)	

Values are expressed as mean ± SD or number (%).

BMI: Body Mass Index; WC: Waist Circumference; WBR: Waist-BMI Ratio; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; FPG: Fasting Plasma Glucose; HDL-C: High Density Lipoprotein Cholesterol; TG: Triglyceride; Cr: Serum Creatinine; Mets: Metabolic Syndrome; PA: Physical Activity

Table 2: Bivariate analysis of the correlations between serum 25(OH)D levels and variables in daytime and shift workers.

Chausatauistiaa	Da	ytime workers	S	hift workers
Characteristics	Coefficient	P value	Coefficient	P value
Age (years)	0.055	0.086	0.119	0.001
BMI (kg/m²)	-0.107	0.001	-0.028	0.435
WC (cm)	-0.102	0.001	0.016	0.661
WBR	0.053	0.099	0.090	0.013
SBP (mmHg)	-0.057	0.076	-0.058	0.109
DBP (mmHg)	-0.062	0.050	-0.016	0.665
FPG (mmHg)	-0.019	0.552	0.088	0.016
HDL (mg/dL)	0.055	0.085	0.014	0.706
TG (mg/dL)	-0.176	< 0.001	-0.134	< 0.001
Cr (mg/dL)	0.044	0.166	0.086	0.019
Number of MetS component	-0.105	0.001	-0.003	0.928

BMI: Body Mass Index; WC: Waist Circumference; WBR: Waist-BMI Ratio; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; FPG: Fasting Plasma Glucose; HDL-C: High Density Lipoprotein Cholesterol; TG: Triglyceride; Cr: Serum Creatinine; Mets: Metabolic Syndrome

statistically significant differences (P = 0.690). Age, BP, HDL-C, and Cr were significantly increased in daytime workers. The mean serum 25(OH)D level (P = 0.002) was significantly lower, and the number of workers with serum 25(OH)D levels of < 20 ng/mL was higher in daytime workers than in shift workers (P < 0.001). Additionally, daytime workers showed significantly higher marital status, education level, alcohol consumption, lack of exercise, and short sleep of < 5h. The number of smokers and workers sleeping for 8-9 h was significantly higher in shift workers than in daytime workers.

# Relationships of clinical characteristics with serum 25(OH)D levels

The bivariate correlation analysis in TG revealed negative correlations in both groups (Table 2). Serum 25(OH)D levels in daytime workers showed significant negative correlations with BMI, WC and number of MetS component. Significant correlations were found between serum 25(OH)D and age, WBR, FPG and Cr levels in shift workers. We analyzed the difference in clinical characteristics according to serum 25(OH)D quartiles in two groups. BMI (P = 0.017), WC (P = 0.013), WBR (P = 0.020) and diastolic BP (P = 0.033) showed a significant difference in daytime workers, and TG (P < 0.001), the number of smokers (P = 0.043) and lack of PA (P = 0.034)

exhibited an inverse relationship with quartiles (Table 3). The season of data collection showed significant differences among quartiles (P < 0.001). In contrast, age (P = 0.016), FPG (P = 0.047), Cr (P = 0.031) and TG (P = 0.010) showed significant differences in shift workers (Table 4). Higher quartiles were positively related to age (P = 0.016). Lower MetS prevalence and higher MetS components were found in quartiles among daytime workers (Figure 1).

However, the prevalence of MetS was not statistically significant (P = 0.212), whereas the number of MetS components was statistically significant (P = 0.016). Quartiles did not show a significant relationship with the two variables in shift workers (Figure 1).

## Associations of MetS with serum 25(OH)D levels

The results of logistic regression analyses between serum 25(OH)D quartiles and MetS prevalence are shown (Table 5). The unadjusted odds ratio (OR) for MetS in each quartile of serum vitamin D in daytime workers did not show a significant association (model 1). Model 2, which was adjusted for age and Cr, revealed a statistical significance in the OR of MetS at the margin in the lowest quartile of serum 25(OH)D (OR = 1.528, 95% confidence interval [CI] = 0.997-2.342, P = 0.052). This did not change after additional adjustments for smoking

Table 3: Characteristics of participants based on serum 25(OH)D quartiles in daytime workers.

Characteristics	Q1	Q2	Q3	Q4	P trend
Participants (n)	281	253	233	218	
Age (years)	40.36 ± 9.25	41.29 ± 9.10	40.87 ± 9.68	42.32 ± 9.59	0.176
BMI (kg/m²)	25.52 ± 3.22	25.29 ± 2.95	25.16 ± 3.07	24.63 ± 2.61	0.017
WC (cm)	85.86 ± 7.97	84.87 ± 7.51	85.18 ± 7.91	83.70 ± 7.44	0.013
WBR	3.38 ± 0.22	3.37 ± 0.22	3.40 ± 0.22	3.41 ± 0.21	0.020
SBP (mmHg)	122.62 ± 11.37	123.03 ± 10.14	121.04 ± 11.75	121.47 ± 10.44	0.061
DBP (mmHg)	75.75 ± 8.99	76.13 ± 8.98	74.22 ± 9.19	74.57 ± 8.11	0.033
FPG (mg/dL)	101.99 ± 20.11	100.23 ± 15.90	99.34 ± 9.30	100.38 ± 16.52	0.777
HDL-C (mg/dL)	51.85 ± 11.31	53.57 ± 12.29	53.57 ± 11.60	53.37 ± 10.74	0.228
ΓG (mg/dL)	161.65 ± 131.5	152.14 ± 208.6	131.07 ± 72.80	118.00 ± 65.62	< 0.001
Cr (mg/dL)	0.91 ± 0.14	0.93 ± 0.16	0.94 ± 0.17	0.93 ± 0.13	0.185
Season (%)					< 0.001
spring	78 (27.8)	32 (12.6)	12 (5.2)	15 (6.9)	
summer	80 (26.5)	87 (34.4)	94 (40.3)	83 (38.1)	
autumn	80 (28.5)	104 (41.1)	101 (43.3)	106 (48.6)	
winter	43 (15.3)	30 (11.9)	26 (11.2)	14 (6.4)	
Marital status (%)					0.320
single	74 (26.3)	63 (24.9)	65 (27.9)	45 (20.6)	
married	207 (73.7)	190 (75.1)	168 (72.1)	173 (79.4)	
Education level (%)					
high school	16 (5.7)	13 (5.1)	18 (7.7)	13 (6.0)	0.896
college	6 (2.1)	4 (1.6)	4 (1.7)	3 (1.4)	
university	218 (77.6)	189 (74.7)	179 (76.8)	167 (76.6)	
graduate school	41 (4.2)	47 (4.8)	32 (3.2)	35 (3.6)	
Smoking status (%)					0.043
no smoker	132 (47.0)	136 (53.8)	99 (42.5)	91 (41.7)	
former smoker	90 (32.0)	70 (27.7)	92 (39.5)	87 (39.9)	
current smoker	59 (21.0)	47 (18.6)	42 (18.0)	40 (18.3)	
Alcohol consumption (%)					0.874
≤ once a week	220 (78.3)	199 (78.7)	181 (77.7)	165 (75.7)	
once a week	61 (21.7)	54 (21.3)	52 (22.3)	53 (24.3)	
Exercise (%)					0.034
below recommended PA	213 (75.8)	181 (71.5)	171 (73.4)	140 (64.2)	
above recommended PA	68 (24.2)	72 (28.5)	62 (26.6)	78 (35.8)	
Sleep duration (%)					0.674
5 h	10 (3.6)	6 (2.4)	6 (2.6)	5 (2.3)	
6-7 h	245 (87.2)	230 (90.9)	201 (86.3)	193 (88.5)	
8-9 h	26 (9.3)	17 (6.7)	26 (11.2)	20 (9.2)	

Values are expressed as mean ± SD or number (%).

BMI: Body Mass Index; WC: Waist Circumference; WBR: Waist-BMI Ratio; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; FPG: Fasting Plasma Glucose; TC: Total Cholesterol; HDL-C: High Density Lipoprotein Cholesterol; TG: Triglyceride; Cr: Serum Creatinine; Mets: Metabolic Syndrome; PA: Physical Activity

Serum 25(OH)D (ng/ml): Q1 (1.91-2.72), Q2 (2.73-2.99), Q3 (3.00-3.24), Q4 (3.25-4.29).

Table 4: Characteristics of participants based on serum 25(OH)D quartiles in shift workers.

Characteristics	Q1	Q2	Q3	Q4	P trend
Participants (n)	159	180	201	215	
Age (years)	36.52 ± 9.35	37.53 ± 10.20	38.69 ± 10.41	39.76 ± 10.09	0.016
BMI (kg/m²)	25.37 ± 3.37	25.55 ± 3.38	25.46 ± 2.96	25.23 ± 3.19	0.548
WC (cm)	85.03 ± 8.36	85.83 ± 8.44	85.51 ± 7.98	85.70 ± 8.08	0.658
WBR	3.37 ± 0.23	3.38 ± 0.23	3.37 ± 0.20	3.42 ± 0.24	0.147
SBP (mmHg)	119.87 ± 10.68	121.13 ± 10.15	118.81 ± 10.83	120.07 ± 11.92	0.078
DBP (mmHg)	73.99 ± 8.05	74.54 ± 7.59	73.29 ± 7.69	74.39 ± 8.10	0.332
FPG (mg/dL)	98.42 ± 9.79	101.06 ± 14.49	102.16 ± 14.82	102.09 ± 14.16	0.047
HDL-C (mg/dL)	51.40 ± 10.49	51.89 ± 10.16	51.62 ± 10.14	51.87 ± 10.99	0.924
TG (mg/dL)	155.19 ± 102.8	159.27 ± 104.6	142.01 ± 120.80	137.69 ± 97.72	0.010
Cr (mg/dL)	0.86 ± 0.12	0.89 ± 0.11	0.88 ± 0.13	0.90 ± 0.14	0.031
Season (%)					< 0.001
spring	36 (22.6)	9 (5.0)	3 (1.5)	5 (2.3)	
summer	99 (62.3)	137 (76.1)	172 (85.6)	191 (88.8)	
autumn	16 (10.1)	31 (17.2)	21(10.4)	17 (7.9)	
winter	8 (5.0)	3 (1.7)	5 (2.5)	2 (0.9)	
Marital status (%)					0.089
single	67 (42.1)	66 (36.7)	76 (37.8)	64 (29.8)	
married	92 (57.9)	114 (63.3)	125 (62.2)	151 (70.2)	
Education level (%)					0.175
high school	20 (12.6)	32 (17.8)	25 (12.4)	22 (10.2)	
college	13 (8.2)	8 (4.4)	10 (5.0)	21 (9.8)	
university	113 (71.1)	131 (72.8)	154 (76.6)	162 (75.3)	
graduate school	13 (8.2)	9 (5.0)	12 (6.0)	10 (4.7)	
Smoking status (%)					0.296
no smoker	85 (53.5)	84 (46.7)	96 (47.8)	88 (40.9)	
former smoker	31 (19.5)	44 (24.4)	49 (24.4)	64 (29.8)	
current smoker	43 (27.0)	52 (28.9)	56 (27.9)	63 (29.3)	
Alcohol consumption (%)					0.443
≤ once a week	140 (88.1)	160 (88.9)	168 (83.6)	186 (86.5)	
> once a week	19 (11.9)	20 (11.1)	33 (16.4)	29 (13.5)	
Exercise (%)					0.198
below recommended PA	106 (66.7)	122 (67.8)	142 (70.6)	131 (60.9)	
above recommended PA	53 (33.3)	58 (32.2)	59 (29.4)	84 (39.1)	
Sleep duration (%)					0.381
5 h	5 (3.1)	4 (2.2)	2 (1.0)	2 (0.9)	
6-7 h	111 (69.8)	136 (75.6)	158 (78.6)	160 (74.4)	
8-9 h	43 (27.0)	40 (22.2)	41 (20.4)	53 (24.7)	

Values are expressed as mean ± SD or number (%).

BMI: Body Mass Index; WC: Waist Circumference; WBR: Waist-BMI Ratio; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; FPG: Fasting Plasma Glucose; TC: Total Cholesterol; HDL-C: High Density Lipoprotein Cholesterol; TG: Triglyceride; Cr: Serum Creatinine; Mets: Metabolic Syndrome; PA: Physical Activity

Serum 25(OH)D (ng/ml): Q1 (1.91-2.72), Q2 (2.73-2.99), Q3 (3.00-3.24), Q4 (3.25-4.29).

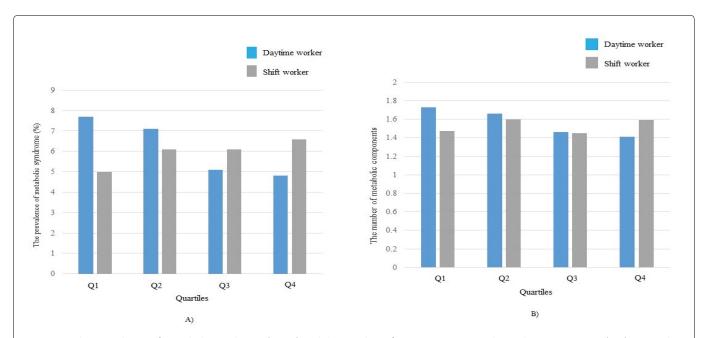


Figure 1: The prevalence of metabolic syndrome (MetS) and the number of MetS components depending on serum 25(OH)D quartiles in daytime and shift workers. (A) In shift workers, the prevalence of MetS showed no significant difference according to serum 25(OH)D quartiles (P = 0.933). The prevalence of MetS showed higher with lower serum 25(OH)D quartiles in daytime workers. However, there was no statistically significant difference (P = 0.212); (B) Significant differences between the number of MetS component and serum 25(OH)D quartiles were shown in daytime workers (P = 0.016), but not in shift workers (P = 0.446).

Table 5: Adjusted odds ratios of metabolic syndrome depending on serum 25(OH)D quartiles in daytime and shift workers.

		Shift workers						
	Q4 (n = 218)	Q3 (n = 233)	Q2 (n = 253)	Q1 (n = 281)	Q4 (n = 215)	Q3 (n = 201)	Q2 (n = 180)	Q1 (n = 159)
Model 1	1.000				1.000			
Exp(B)		0.994	1.392	1.349		0.979	1.133	1.036
Lower		0.634	0.910	0.889		0.620	0.715	0.640
Upper		1.558	2.127	2.046		1.546	1.796	1.679
<i>P</i> value		0.979	0.127	0.159		0.929	0.596	0.885
Model 2	1.000				1.000			
Exp(B)		1.060	1.481	1.528		1.048	1.316	1.293
Lower		0.670	0.960	0.997		0.654	0.815	0.780
Upper		1.676	2.285	2.342		1.679	2.123	2.145
<i>P</i> value		0.805	0.076	0.052		0.845	0.261	0.319
Model 3	1.000				1.000			
Exp(B)		1.065	1.520	1.530		1.068	1.318	1.321
Lower		0.671	0.981	0.995		0.666	0.815	0.794
Upper		1.689	2.356	2.352		1.715	2.130	2.197
<i>P</i> value		0.790	0.061	0.053		0.784	0.260	0.284
Model 4	1.000				1.000			
Exp(B)		1.009	1.513	1.580		1.050	1.317	1.239
Lower		0.633	0.971	1.008		0.651	0.809	0.721
Upper		1.608	2.358	2.476		1.693	2.144	2.127
<i>P</i> value		0.971	0.067	0.046		0.842	0.269	0.438
Model 5	1.000				1.000			
Exp(B)		1.022	1.524	1.599		1.106	1.375	1.281

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Lower		0.640	0.976	1.018		0.681	0.838	0.740
Upper		1.632	2.379	2.511		1.796	2.257	2.219
P value		0.928	0.064	0.041		0.685	0.208	0.377
Model 6	1.000				1.000			
Exp(B)		1.018	1.480	1.580		0.999	1.284	1.202
Lower		0.636	0.945	1.004		0.609	0.773	0.687
Upper		1.630	2.316	2.488		1.637	2.132	2.104
P value		0.941	0.087	0.048		0.996	0.334	0.519

Model 1, crude odds ratio; Model 2, adjusted for age, serum creatinine; Model 3, adjusted for model 2 plus alcohol consumption and smoking status; Model 4, adjusted for model 3 plus exercise and season; Model 5, adjusted for model 4 plus marital status, education level and sleep duration; Model 6, adjusted for model 5 plus waist-BMI ratio. BMI, body mass index. Serum 25(OH)D (ng/ml): Q1 (1.91-2.72), Q2 (2.73-2.99), Q3 (3.00-3.24), Q4 (3.25-4.29).

Table 6: Adjusted odds ratios of metabolic syndrome components depending on serum 25(OH)D quartiles in daytime and shift workers.

	Daytime workers					Shift workers				
	Q4 (n = 218)	Q3 (n = 233)	Q2 (n = 253)	Q1 (n = 281)		Q4 (n = 215)	Q3 (n = 201)	Q2 (n = 180)	Q1 (n = 159)	
High WC	1.000					1.000				
Exp(B)		1.443	1.564	1.915			0.881	1.144	1.036	
Lower		0.907	0.993	1.217			0.561	0.723	0.625	
Upper		2.296	2.462	3.013			1.385	1.810	1.717	
<i>P</i> value		0.122	0.053	0.005			0.584	0.565	0.890	
High BP	1.000					1.000				
Exp(B)		0.869	1.389	1.270			0.945	1.388	1.231	
Lower		0.572	0.932	0.847			0.578	0.852	0.714	
Upper		1.319	2.070	1.904			1.548	2.259	2.124	
P value		0.509	0.106	0.248			0.824	0.188	0.455	
High FPG	1.000					1.000				
Exp(B)		0.951	0.951	1.161			1.041	1.039	0.670	
Lower		0.641	0.645	0.786			0.690	0.678	0.417	
Upper		1.411	1.404	1.715			1.572	1.593	1.076	
P value		0.803	0.809	0.453			0.848	0.861	0.097	
Low HDL-C	1.000					1.000				
Exp(B)		1.366	1.412	1.910			1.159	1.267	1.421	
Lower		0.679	0.708	0.973			0.587	0.632	0.678	
Upper		2.750	2.818	3.750			2.287	2.538	2.979	
P value		0.382	0.328	0.060			0.671	0.505	0.352	
High TG	1.000					1.000				
Exp(B)		1.853	2.144	2.909			0.947	2.006	1.693	
Lower		1.198	1.398	1.894			0.604	1.273	1.029	
Upper		2.866	3.290	4.466			1.485	3.160	2.785	
P value		0.006	< 0.001	< 0.001			0.812	0.003	0.038	

High WC,  $\geq 90$  cm; High BP,  $\geq 130/85$  mmHg or current use of antihypertensive medication; High FPG,  $\geq 100$  mg/dl or receiving treatment for previously diagnosed type 2 DM; Low HDL-C, < 40 mg/dl; High TG,  $\geq 150$  mg/dl.

WC: Waist Circumference; BP: Blood Pressure; FPG: Fasting Plasma Glucose; HDL-C: High Density Lipoprotein Cholesterol; TG: Triglyceride. Serum 25(OH)D (ng/ml): Q1 (1.91-2.72), Q2 (2.73-2.99), Q3 (3.00-3.24), Q4 (3.25-4.29).

status and alcohol consumption (model 3). The OR of MetS was significantly increased in the lowest quartile after adjusting for exercise and season (model 4) (OR = 1.580, 95%Cl = 1.008-2.476, P = 0.046). This statistical significance remained after adjusting for marital status, education level, and sleep duration (model 5) (OR = 1.599, 95%Cl = 1.018-2.511, P = 0.041) and WBR (model6) (OR = 1.580, 95%Cl = 1.004-2.488, P = 0.048). By contrast, unadjusted and adjusted OR for MetS in any model in shift workers were not significantly associated.

# Associations of individual components of MetS with serum 25(OH)D levels

The association of serum 25(OH)D quartiles with each MetS component was assessed after adjusting for age, Cr, smoking status, alcohol consumption, PA, season, marital status, education level, sleep duration and WBR (Table 6). WC

in daytime workers showed significant association with Q1 quartile (OR = 1.915, 95% CI = 1.217-3.013, P = 0.005). The adjusted OR for high TG level of MetS components showed significant association in each quartile of serum 25(OH)D in model 6, and the OR was the highest in the lowest quartile (OR = 2.909, 95% CI = 1.894-4.466, P < 0.001). High BP, high FPG, and low HDL-C levels showed no significant association in each quartile. The adjusted OR for high TG level of MetS components showed significant association in the Q1 quartile (OR = 1.693, 95% CI = 1.029-2.785, P = 0.038) and Q2 quartile (OR = 2.006, 95% CI = 1.273-3.160, P = 0.003) in shift workers in model 6, respectively while the others did not. In addition, the lowest (Q1) and second (Q2) quartiles of Serum 25(OH) D levels showed significant associations with high TG levels regardless of MetS (Table 7).

**Table 7:** Adjusted odds ratios of metabolic components when serum 25(OH)D levels are ≥ 20 ng/mL or < 20 ng/mL in daytime and shift workers.

		Daytime	workers			Shift w	vorkers	
	Serum 25(C	DH)D ≥ 20 ng/mL	Serum 25(0	OH)D < 20 ng/mL	Serum 25(OH)D ≥ 20 ng/mL		Serum 25(0	DH)D < 20 ng/mL
	MetS (-)	MetS (+)	MetS (-)	MetS (+)	MetS (-)	MetS (+)	MetS (-)	MetS (+)
High WC	1.000				1.000			
Exp(B)		11.002	1.156	14.533		10.354	0.900	16.056
Lower		6.303	0.739	8.866		5.809	0.561	8.587
Upper		19.205	1.808	23.820		18.454	1.444	30.020
P value		< 0.001	0.525	< 0.001		< 0.001	0.662	< 0.001
High BP	1.000				1.000			
Exp(B)		8.767	1.253	11.571		8.319	1.157	12.077
Lower		5.092	0.869	7.163		4.646	0.690	6.622
Upper		15.095	1.807	18.693		14.896	1.940	22.026
P value		< 0.001	0.226	< 0.001		< 0.001	0.580	< 0.001
High FPG	1.000				1.000			
Exp(B)		8.566	0.876	8.649		6.913	0.856	3.757
Lower		4.628	0.632	5.254		3.721	0.588	2.149
Upper		15.857	1.216	14.236		12.842	1.244	6.568
P value		< 0.001	0.430	< 0.001		< 0.001	0.414	< 0.001
Low HDL-C	1.000				1.000			
Exp(B)		24.875	1.330	19.301		13.789	2.203	12.398
Lower		10.494	0.543	8.771		5.939	0.921	5.172
Upper		58.966	3.256	42.473		32.014	5.269	29.720
P value		< 0.001	0.533	< 0.001		< 0.001	0.076	< 0.001
High TG	1.000				1.000			
Exp(B)		9.285	1.701	14.086		11.214	1.985	23.599
Lower		5.431	1.170	8.676		6.250	1.290	11.887
Upper		15.873	2.472	22.870		20.119	3.053	46.851
P value		< 0.001	0.005	< 0.001		< 0.001	0.002	< 0.001

High WC, ≥ 90 cm; High BP, ≥ 130/85 mmHg or current use of antihypertensive medication; High FPG, ≥ 100 mg/dl or receiving treatment for previously diagnosed type 2 DM; Low HDL-C, < 40 mg/dl; High TG, ≥ 150 mg/dl. WC: Waist Circumference; BP: Blood Pressure; FPG: Fasting Plasma Glucose; HDL-C: High Density Lipoprotein Cholesterol; TG: Triglyceride; Mets: Metabolic Syndrome. 20 ng/mL of serum 25(OH) D corresponds to 2.99 ng/mL of logarithmically transformed serum 25 (OH)D.

#### Discussion

Our study revealed a higher MetS prevalence in daytime workers than in shift workers. The relationship between obesity and vitamin D deficiency was observed in daytime workers, and the association between vitamin D deficiency and MetS and abdominal obesity remained even after adjusting for potential confounding factors. A significant association was found between vitamin D and TG levels in both groups.

Circadian rhythm misalignment occurs due to shifting work, destroying the sleep/wake cycle, and changing meal times, which causes obesity due to excessive appetite and high-calorie food intake due to poor balance of leptin and ghrelin, which are hormones that suppress and stimulate, respectively [18,19]. Additionally, most vitamin D synthesis occurs in the skin, and obesity, less external activity, and less sunlight exposure reduce vitamin D levels [20]. Shift workers may be more vulnerable to vitamin D deficiency than daytime workers, due to less sunlight exposure time, irregular meal times, and lack of vitamin D intake due to instant food. The circadian rhythm misalignment is related to sleep disturbance. Short sleep is associated with weight gain, impaired glucose tolerance, dyslipidemia, high BP, IR, and MetS [21]. This study revealed a higher number of 8-9 h of sleep duration in shift workers than in daytime workers, and the number of daytime workers with < 5h of sleep was significantly higher than that of shift workers. Sleep quality as a crucial determinant of the development of MetS with sleep duration has shown an inverse correlation with MetS; however, this study did not investigate sleep quality [22]. The occurrence of sleep disturbance along with sleep/wake cycle disruption is also related to vitamin D deficiency because vitamin D receptors are expressed in brain areas that regulate the sleep/wake cycle [23].

Shift work has various types, and the impact on the health of shift workers may vary according to the working schedule, the number of nights worked per month or year, and rotation direction [14,24]. Our study included rotating shift workers who do not work only at night, such as night shift workers, but alternatively, work day and night. Therefore, circadian misalignment and lifestyle risks were less in night shift workers. Clockwise rotation (morning-afternoon-night) is a working schedule that changes from day to night, and the opposite is called anticlockwise rotation (afternoon-morning-night) [25]. Clockwise rotation is known to have fewer health hazards than anticlockwise rotation. However, the rotation schedule for the shift pattern was not obtained, and leptin and ghrelin levels were not measured.

Lifestyle factors, such as smoking, alcohol, and lack of exercise, can accelerate the risk of MetS. Smoking increases the risk of hypertriglyceridemia, low HDL-C, and IR and is associated with MetS development [26,27]. Serum vitamin D levels decreased through a specific mechanism by an endocrine disruptor contained in tobacco smoke [28]. Increased ionized calcium caused by smoking inhibits parathyroid hormone (PTH) levels and affects serum vitamin D levels [29]. This study revealed a significantly increased number of smokers

in shift workers compared to daytime workers, but it showed an inverse relationship with serum 25(OH)D levels in daytime workers. However, calcium and PTH levels were not measured and the smoking duration and number of smoked cigarettes were not investigated. Alcohol consumption showed a significant increase in daytime workers. Excessive alcohol consumption is associated with hypertension, dyslipidemia, and obesity [30]. Alcohol intake that exceeds 5 g per day was associated with hypertension, hypertriglyceridemia, and low HDL-C [31]. Conversely, those who consumed 0.1-5g of alcohol per day had a significantly lower prevalence of MetS than those who consumed no alcohol. Additionally, proper amount or timing and the type of alcohol consumption rather reduced MetS prevalence [32]. Our study has not obtained the amount of alcohol consumption. Alcohol consumption showed no significant relationship with serum 25(OH)D levels in both groups. Studies have shown positive or negative associations between alcohol consumption and vitamin D levels, which remain controversial [33]. Exercise improves insulin activity and lowers BP by controlling fat and glucose metabolism [34]. Serum 25(OH)D level is related to muscle function and immune response and showed a positive relationship according to the quartiles group of exercise [35], which was consistent with our study. The exercise may have relatively decreased while working indoors for a long time, and the shift worker may have had active time outside of work. A study revealed an increased risk of MetS in daytime workers than in shift workers, with lack of exercise as a risk factor [36].

As age increases, vitamin D levels decreases by reduced outdoor activities and lack of vitamin D synthesis due to skin atrophy, various food intake changes, and decreased renal function [37]. Daytime workers showed a significant increase in the mean age than shift workers. However, there was no significant correlation between age and serum 25(OH)D levels and significant difference in age according to vitamin D level changes in daytime workers. In contrast, positive correlation was found between age and serum 25(OH)D levels in shift workers. These findings may be because of the absence of the elderly population above 50 years. Positive relationships were found in age and Cr according to quartiles of serum 25(OH)D levels in shift workers. Another study also showed that age and 25 (OH)D level were proportional to healthy individuals with normal renal function [38].

Studies revealed a higher MetS prevalence due to relatively reduced healthcare system access in adults with low education levels than in adults with high education levels [39]. Our study revealed a significantly lower educational level in shift workers. The increased MetS prevalence in daytime workers is due to lifestyle and age differences in both groups despite the higher educational level than shift workers. The married group is less exposed to smoking, alcohol, and stress than the divorced or unmarried group, resulting in a lower MetS prevalence [40]. Stress reduction due to mental and emotional support, improvement of cardiovascular disease mortality and morbidity, and better health behavior were reported [41]. MetS prevalence in daytime workers was higher than in shift workers although there were more

married people in shift workers than in daytime workers because many of the daytime workers are married but live apart from their spouses due to their working environment. The positive or inverse relationship between income and MetS was reported [42]. However, this factor has no available information.

Similar to our study, some studies revealed no difference between the two groups, or rather, the prevalence of MetS was lower in shift workers. One study for healthcare workers showed no significant difference between shift and daytime workers for the risk of MetS after adjustment of potential confounders [24]. This result may be explained by the clockwise rotation of shift workers or the reverse causation hypothesis that the healthier they are, the more they prefer to work in shifts. Another study revealed a lower risk of MetS for nurses working in shifts than daytime working nurses engaged in management because of increased PA in patient care [43]. Another study revealed a lower prevalence of MetS in shift workers of car-manufacturing companies compared with daytime workers [36]. The shift workers comprised twoshift (n = 1,125) and three-shift workers (n = 182), unlike our study. This result was not clearly explained because of workrelated information, including shift rotation, psychological stress, work duration, economic status, and academic career. Additionally, they considered the possible effect of health workers as one of the causes.

We found many potential involved confounders in serum 25 (OH)D levels and vitamin D deficiency as potential risk factors for MetS. Vitamin D is fat-soluble and distributed in fat cells, thus vitamin D decreases as obesity increases [20]. WC is an indicator of abdominal obesity and is related to IR [44]. WC showed significant differences among quartiles of serum 25 (OH)D levels, with significant associations in daytime workers. However, our study did not measure insulin concentration and investigate the association between IR and MetS. Additionally, an inverse relationship between vitamin D levels and BMI was found in daytime workers and without a significant difference with shift workers. Previous studies revealed an inverse relationship between vitamin D levels and obesity indicators, such as BMI and WC [20]. Actually, the second quartile (Q2) showing significant association with MetS is quartiles of serum 25(OH)D levels of approximately below 20 ng/mL, and WC showed significant association in Q1 and Q2, and the criteria for vitamin D deficiency in this study was 20 ng/mL. Therefore, intervention is needed to prevent MetS for workers with vitamin D levels below 20 ng/mL.

Our study revealed that serum 25 (OH)D level plays an important role in lipid metabolism, such as TG. The mechanism is unclear, but increased intestinal absorption of calcium by serum vitamin D reduces intestinal absorption of fatty acids and synthesis and secretion of TG in the liver [45]. Calcium increases bile acid secretions, which reduces cholesterol levels [46]. Low serum 25(OH)D levels increase PTH, and this hormone reduces lipolysis, lipoprotein lipase activity, and peripheral TG removal [47]. Impaired  $\beta$ -cell function and IR by vitamin D deficiency are related to hypertriglyceridemia and decreased HDL-C [48].

Seasonal variation showed significant differences among quartiles of serum 25(OH)D levels in both groups. Vitamin D levels are the lowest in winter and the highest in summer and autumn in blood collection [49,50]. This study revealed a higher number of shift workers who underwent blood sample examinations in the summer and vice versa in autumn. The number of daytime workers was higher than shift workers in winter, which may have lowered serum 25(OH)D levels. However, since there were relatively more workers who received blood collection in the autumn than shift workers, it is not clear whether seasonal variation affected the association between serum 25(OH)D levels and MetS.

This study has several limitations. First, cross-sectional design limits the determination of the causal relationship between variables and MetS. Second, generalizing our study results is difficult due to the small sample size. Third, information, such as alcohol consumption, smoking status, exercise, and sleep duration, depended on the self-rating questionnaire, so they are subject to recall bias. Fourth, data such as sun exposure time, working outdoors, and dietary regimen information were unavailable. Fifth, calcium, PTH, and IR, which could have affected the serum 25(OH)D level, were not measured.

#### Conclusion

In conclusion, shift workers may have different health effects depending on their working conditions and environment, lifestyle factors, and sociodemographic status. Serum 25(OH)D deficiency is a risk factor for MetS and hypertriglyceridemia in male workers. However, a prospective study with a large population is necessary.

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