Correlation between serum 25(OH)D levels with severity of work-related hand eczema among healthcare workers: a cross-sectional study

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Abstract

Hand eczema (HE) is a common condition seen in medical facilities, particularly during the COVID-19 pandemic. The effects of vitamin D on skin inflammation are diverse. The purpose of this study is to examine the relationship between vitamin D levels in healthcare workers as determined by serum 25(OH)D and the severity of HE. In Indonesia, between September and October of 2022, a cross-sectional design was employed for this analytical descriptive study. The hand eczema severity index was used to determine the severity of HE. Out of the 44 healthcare workers who had HE, the findings indicated that 29 had mild HE, 11 had moderate HE, and 4 had severe HE. Subjects with mild, moderate, and severe HE had mean serum 25(OH)D levels of 17.85 ng/mL, 16.45 ng/mL, and 17.87 ng/mL, respectively, falling into the vitamin D deficiency category. Serum 25(OH)D levels and the severity of HE did not significantly correlate (r=-0.056; p=0.359). Serum 25(OH)D levels did not significantly differ between subjects with mild, moderate, and severe HE. The degree of HE was not negatively correlated with serum 25(OH)D levels.

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Introduction

Hand eczema (HE) is a work-related skin inflammation of the hands with heterogeneous etiology and morphology.[1] Based on a systematic review of 66 studies ranging from 1964 to 2019, the lifetime prevalence of HE in the general population reached 14.5%.[2] It is more prevalent in workers who do frequent handwashing, but everyone with frequent and repeated exposure is at risk.[3] The COVID-19 pandemic has led to increased awareness of hand hygiene around the world. Hand hygiene has become a widely accepted principle as an effort to prevent the transmission of COVID-19 and other diseases. The Centers for Disease Control and Prevention recommend washing hands with soap and water for 20 seconds or using a hand sanitizer that contains at least 60% alcohol. The habit and frequency of hand washing can affect the integrity and function of the skin barrier, thereby increasing the risk of developing HE.[4] Sawitri *et al*.[5] have also found that the incidence of contact dermatitis increases with the increasing frequency and duration of exposure to personal protective equipment and hand hygiene (HH) practices during the COVID-19 pandemic. The occurrence of HE is influenced by cell proliferation and differentiation, skin barrier conditions, and immune function. Vitamin D, a fat-soluble vitamin, has a role in regulating these processes and is closely related to the skin due to its function of tissue repair, disease prevention, and immunomodulation.[6] Vitamin D deficiency has been reported in various inflammatory skin diseases. This claim raises the suspicion that a person's vitamin D status can modulate skin inflammation, including HE.[7] In Indonesia, studies regarding vitamin D levels are still limited. Suryadinata *et al*.[8] found that the mean vitamin D levels of adults in Surabaya, Indonesia was in the insufficiency category, or under 30 ng/mL.

In recent years, various instruments have been developed to assess the severity of HE. One of the most widely used instruments is the hand eczema severity index (HECSI), which assesses the severity of HE based on six different symptoms, as well as the

area involved.[9] This research was conducted to study the correlation of serum 25(OH)D levels, which is a form of vitamin D circulating in the blood, with the severity of HE among healthcare workers in our institution.

Materials and Methods

This is a descriptive analytic study with a cross-sectional design conducted in our hospital from September to December 2022. The research subjects were selected using the consecutive sampling method according to the study criteria. All subjects were asked to sign an informed consent form prior the participation in the study. This research has received ethical approval from the Health Research Ethics Committee of the Faculty of Medicine Universitas Indonesia.

The inclusion criteria included healthcare workers, defined as medical doctors, nurses, and lab personnel, aged 18-59 years, and were diagnosed with HE based on history and physical examination. Exclusion criteria included having skin infection, autoimmune disease with lesions in the hand area (*e.g.*, psoriasis and autoimmune bullous disease), skin disorders caused by chemotherapy drugs in the hand area, body mass index (BMI) that is classified as obese based on the Asia Pacific BMI Classification, having a disease or condition that can affect serum 25(OH)D levels (*e.g.*, kidney disease, liver disease, cystic fibrosis, celiac disease, or Crohn's disease), taking supplements containing vitamin D2 or D3 in the past month, taking immunosuppressants within the past month, using topical corticosteroids or moisturizers in the past week, and are pregnant or currently taking oral contraceptives containing estrogen (if the subject is female).

Examinations carried out on the subject included anamnesis, dermatological examination, and examination of serum 25(OH)D levels. The severity of HE in subjects was calculated using the HECSI instrument.[9] Subjects' hands were inspected in five areas, namely fingertips, fingers, palms, backs of hands, and wrists. The intensity of each area was assessed with six clinical signs in the form of erythema, induration/papules, vesicles, fissures, scales, and edema. The final HECSI score was calculated by multiplying the area of involvement of each site by the sum of the intensities for each clinical sign, then adding these together to obtain a disease severity score. Total HECSI score has a range from 0 to 360, with a score of 1-16 classified as mild, 17-37 classified as moderate, 38-116 classified as severe, and ≥117 classified as very severe. Peripheral venous blood was collected by a lab officer and the sample was sent to the Clinical Pathology Laboratory for examination of serum 25(OH)D levels using the chemiluminescence immunoassay method. Measurement of quality of life was also performed using a validated Indonesian version of the dermatology life quality index (DLQI) questionnaire.

All data were analyzed using Statistical Package for the Social Sciences (SPSS) for Windows version 21.0. The Pearson test was used to assess the correlation of serum 25(OH)D levels with the severity of HE if data distribution was normal while the Spearman test was used if the distribution was not normal. The statistical significance value of the research results was determined based on $p<0.05$.

Results

Sociodemographic characteristics

The median age of the subjects in this study was 36 years, with the youngest being 23 years and the oldest being 59 years. The majority of subjects in this study were women and nurses (72.7%) followed by doctors (25%). The sociodemographic characteristics of the subjects are shown in Table 1.

Clinical characteristics

The median duration of HE experienced by the subjects was 52 weeks, with 72.7% having a history of previous HE. The average BMI of subjects was 23.35 kg/m^2 which belonged to the overweight category. Based on the HECSI score, 65.9% of subjects had mild HE. The median DLQI score is 10 which indicated a moderate effect on subjects' life quality. The clinical characteristics of the subjects are shown in Table 2.

Serum 25(OH)D levels

The mean serum 25(OH)D level of all subjects was 17.50 ng/mL which belonged to the vitamin D deficiency category. Serum 25(OH)D level of subjects based on the severity of HE was shown in Table 3.

Correlation of serum 25(OH)D levels with the severity of hand eczema

There was no significant correlation between serum 25(OH)D levels and HE severity as measured using HECSI (r=-0.056; p=0.359). The correlation between serum 25(OH)D levels and the total HECSI score are shown in Figure 1.

Table 1. Sociodemographic characteristics of healthcare workers with hand eczema (n=44).

Characteristics	N (%)
Age in years, median (min-max)	36 (23-59)
Sex	
Male	3 (6.8)
Female	41 (93.2)
Occupation	
Doctor	11 (25.0)
Nurse	32 (72.7)
Lab personnel	1 (2.3)
Frequency of handwashing (per day)	
≤10 times	9 (20.5)
>10 times	35 (79.5)
Type of soap	
Antiseptic	41 (93.2)
Non-antiseptic	3 (6.8)
Frequency of using handrub (per day)	
≤10 times	10 (22.7)
>10 times	34 (77.3)
Type of handrub	
Alcohol-based	44 (100)
Non-alcohol-based	0 (0)
History of using occlusive gloves >2 hours per day	
Yes	28 (63.6)
No	16 (36.4)
History of wetwork activity >2 hours per day	
Yes	28 (63.6)
No	16 (36.4)

N, number of subjects.

Discussion

Sociodemographic characteristics

In this study, the median age of subjects with HE was 36 years. Based on a study in Korea, HE was most commonly found in the age group of 20-39 years.[10] Other studies by Safizadeh *et al.*[11] in Iran and Georgieva,[12] in Bulgaria, also found similar results, with a mean age of 32.38 years and 34.14 years, respectively. The age mentioned above was a productive age so there was a lot of exposure to irritants from work. The number of female subjects in this study was far more than the male subjects (93.2% *vs*. 6.8%). Studies in other countries also found that there were more women with HE than men.[10,12] More women experiencing HE might be caused by exposure to irritant factors from household work, including wetwork activities at home.[10] The greater number of female subjects with HE in this study could also be due to the higher percentage of women among the healthcare workers working in the hospital compared to men.

Among healthcare workers who experienced HE, the highest HE incidence was found in the nursing profession (70.4%) in this study. Among healthcare workers, nurses were the group with the highest risk of experiencing HE, with an estimated prevalence of 18-30%.[13] The high prevalence of HE in nurses was caused by frequent handwashing and poor hand-drying techniques.[13] Moreover, there has been an increase in HH practices among healthcare workers during the COVID-19 pandemic era.[14] 79.5% of subjects had a habit of washing hands with water and soap more than 10 times per day, which was a risk factor for the occurrence of HE.[15] Other studies have also shown that washing hands at least 8-10 times per day significantly increases the risk of HE.[16] The habit of washing hands too frequently can cause skin barrier damage and induced HE.[14] As much as 93.2% of the soap used by the subjects was antiseptic soap. The antiseptic soap used in the hospital environment contained chlorhexidine gluconate 4% in water. Chlorhexidine is an antiseptic and disinfectant that is widely used, especially in the hospital environment. The incidence of HE was known to increase with increasing concentration of chlorhexidine used. Chlorhexidine at high concentrations can irritate the skin and mucous membranes, causing irritant contact dermatitis. Irritant contact dermatitis can occur at chlorhexidine concentrations of 4% and above.[17] The use of hand sanitizers with a frequency of >10 times per day was found in 77.3% of subjects and all subjects used alcohol-based hand sanitizers. However, the frequency of using hand sanitizers was reported to be not related to the incidence of HE.[18] This finding was supported by other studies by Kodik *et al*.,[19] Alkhalifah,[20] and Loh *et al*.,[16] which obtained similar results. The use of alcohol-based hand sanitizers was less likely to cause dry skin than washing hands with water and soap.[19]

A total of 63.6% of subjects used occlusive gloves for >2 hours a day and performed wetwork activities for >2 hours per day. The daily use of occlusive gloves was associated with the incidence of HE in the general population.[20] In healthcare workers, the use of non-sterile occlusive gloves >2 hours per day was associated with the incidence of HE.[21] Similar results were also supported by Techasatian *et al*.[15] The use of occlusive gloves will allow heat and moisture to be trapped inside. The function of the skin barrier can be further disrupted due to the effects of the occlusion.[22] Wetwork has been known to be a risk factor for HE, especially in nurses. The main risks associated with HE from wetwork were related to the duration and frequency of exposure. Water is a potential irritant and can penetrate the *stratum corneum* quite easily. Frequent exposure to water causes swelling and shrinkage of the *stratum corneum* which can lead to HE.[22]

Table 2. Clinical characteristics of healthcare workers with hand eczema (n=44).

Characteristics	N (%)
HE duration in weeks, median (min-max)	52 (1-416)
Previous history of HE	
Yes	32 (72.7)
No	12 (27.3)
Body weight in kg, mean ± SD	59.57±5.93
Body height in cm, mean ± SD	159.68±4.49
BMI in kg/m^2, mean ± SD	23.35±2.12
BMI category	
Underweight	2 (4.5)
Normal	11 (25.0)
Overweight	31 (70.5)
HECSI score, median (min-max)	12 (5-41)
HE severity	
Mild	29 (65.9)
Moderate	11 (25)
Severe	4 (9.1)
Very severe	0 (0)
DLQI score, median (min-max)	10 (0-24)
DLQI score category	
No effect on patient's life	4 (9.1)
Small effect on patient's life	7 (15.9)
Moderate effect on patient's life	15 (34.1)
Very large effect on patient's life	14 (31.8)
Extremely large effect on patient's life	4 (9.1)

N, number of subjects; HE, hand eczema; BMI, body mass index; HECSI, hand eczema severity index; DLQI, dermatology life quality index.

Table 3. Serum 25(OH)D levels of subjects based on the severity of hand eczema calculated using the hand eczema severity index (n=44).

	Hand eczema severity			p
	Mild (n=29)	Moderate (n=11)	Severe (n=4)	
Serum 25(OH)D level (ng/mL), mean ± SD	17.85±9.30	16.45±5.16	17.87±4.63	0.741[a]

n, number of subjects; SD, standard deviation; aKruskal-Wallis test.

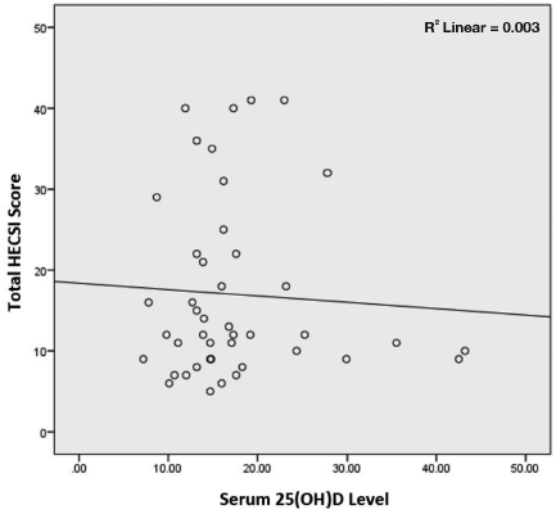

Figure 1. Correlation of serum 25(OH)D levels with the severity of hand eczema as measured using the hand eczema severity index.

Clinical characteristics

The median duration of HE in subjects in this study was 52 weeks, with variations ranging from 1 week to 8 years. Based on the literature, the duration of HE can vary with fluctuating symptoms and can last up to several years. A study conducted in Korea found HE duration to be varied from less than 1 month to 3 years, but 33.2% experienced HE for a year or more.[10] Another study conducted in Iran obtained similar results with 45.5% of HE cases lasting for 1 year or more.[11] Continued exposure to irritants and lack of adequate treatment contributed to the chronic course of HE.[10] The above studies yielded results similar to those obtained in this study. As many as 72.7% of subjects in this study had a history of previous HE. A history of previous HE was strongly associated with an increased risk of HE, especially during the COVID-19 pandemic.[15] The mean weight and height of subjects were 59.57 kg and 159.68 cm. The average BMI of subjects was 23.35 kg/m^2, with 70.5% of subjects belonging to the overweight category. Research by Loman *et al*.[23] found that overweight and obesity BMI may have a positive relationship with the incidence of HE. Obesity and high waist circumference were shown to be related to the incidence of HE. Increased visceral fat can work as an endocrine organ that activates macrophages and releases pro-inflammatory cytokines that can lead to immune dysregulation.[23]

The severity of HE in this study was measured using the HECSI score. The median HECSI score was 12 which indicated mild HE, with a minimum score of 5 and a maximum of 41. Research by Charan *et al*.[24] obtained an average HECSI score of 14.46 which also indicated mild HE. Mahajan *et al*.[25] obtained an average HECSI score that indicated moderate HE, which was 18.54. However, a study by Varma *et al*.[26] obtained an average HECSI score of 48.81 and a median of 44 which indicated severe HE. The degree of severity of HE varied in various existing studies, suggesting a wide spectrum of HE that depends on exposure factors.

A median DLQI score of 10 was obtained from this study, indicating a moderate impact of HE on patients' lives. Based on the DLQI score category, 34.1% of subjects experienced a moderate impact on life from HE, and 31.8% had a severe impact. Research on the impact of HE on quality of life has been quite extensively researched previously. Three studies regarding the impact of HE on patients' quality of life found that the average DLQI score of HE patients indicated a moderate impact on their quality of life.[24-26] This was consistent with the results obtained in this study and also previous studies, which showed a significant negative impact on the quality of life of HE patients.

Serum 25(OH)D levels

The mean serum 25(OH)D level in subjects in this study was 17.50 ng/mL. This average value belonged to the category of vitamin D deficiency, which was below 20 ng/mL. A study by Amon *et al*.[7] in Germany found an average serum 25(OH)D level in HE patients of 25.3 ng/mL. This level was higher than the number obtained in this study, although it still belonged to the category of vitamin D deficiency. Low serum 25(OH)D level was reported to correlate with inflammatory skin disease activity, indicating that a person's vitamin D status may have a modulatory function against inflammatory skin diseases. By increasing the expression of antimicrobial peptides and having a positive effect on skin barrier function, vitamin D plays a role in stabilizing the skin's immunological integrity. The further vitamin D-mediated effects on immune and inflammatory responses suggested that there may be at least a partial role of vitamin D in acute or chronic inflammatory skin conditions.[7] Amon *et al*.[7] also compared serum 25(OH)D levels in HE patients with the normal population, and obtained a mean serum 25(OH)D level of 44.1 ng/mL which was much higher than in HE patients. The average serum 25(OH)D level in HE patients in this study was found to be lower than a study conducted in Germany, but existing studies showed that serum 25(OH)D levels in the normal population in Indonesia were also relatively low. Suryadinata *et al*.[8] obtained an average serum 25(OH)D level in young adults in Indonesia of 20.52 ng/mL, which belonged to the insufficiency category. Low vitamin D levels are thought to be caused by insufficient exposure to sunlight, low vitamin D intake, or polymorphisms in the vitamin D receptor gene.[27]

The average serum 25(OH)D level in subjects with mild HE was 17.85 ng/mL, higher than the moderate HE group with an average serum 25(OH)D level of 16.45 ng/mL. However, the mean serum 25(OH)D level in the severe HE group was 17.87 ng/mL, which was slightly higher than the mild and moderate HE groups. Research by Methkal *et al*.[28] in Ukraine found serum 25(OH)D levels in mild, moderate, and severe HE patients of 33.8 ng/mL, 30.6 ng/mL, and 28.6 ng/mL, respectively. This was more consistent with the theory which states that vitamin D levels are associated with skin inflammation, including HE. Future research can be carried out by considering the balance of numbers between subjects with mild, moderate, and severe HE.

Correlation of serum 25(OH)D levels with the severity of hand eczema

There was no statistically significant correlation between serum 25(OH)D levels and HE severity as measured using the HECSI score. However, based on the scatter plot, there was a slight graphic trend of inverse correlation between serum 25(OH)D levels and the total HECSI score. The higher the serum 25(OH)D level, the lower the total HECSI score, although statistically there was no significant correlation (r=-0.056; P=0.359). Research by Methkal *et al*.[28] obtained similar results with no statistically significant correlation found between serum 25(OH)D levels and the severity of HE. A systematic review by Huang *et al*.[29] found a significant inverse correlation between vitamin D levels and atopic dermatitis severity in 10 of 16 studies, although HE was not specifically mentioned. The tendency of an inverse correlation between serum 25(OH)D levels and HE can be explained based on their effects on the skin. Vitamin D decreases the expression of proinflammatory cytokines and increases the expression of regulatory cytokines, causing a decrease in T cell activation. In addition, vitamin D also has a direct role in epidermal differentiation and skin barrier permeability.[29]

In this study, no significant correlation was found between serum 25(OH)D levels and the severity of HE, possibly because most subjects had serum 25(OH)D levels in the category of deficiency and insufficiency. There were only 6.8% of subjects in this study with vitamin D sufficiency status. In addition, HE is a multifactorial condition, so the degree of severity is likely to be influenced by many factors other than serum 25(OH)D levels. Factors that can affect the severity of HE based on the literature include atopy, wetwork, contact with irritants, and stress.[30] Serum 25(OH)D levels are only one of the various factors that can affect HE severity, so no significant correlation can be found in this research.

Conclusions

There was no significant difference in serum 25(OH)D levels between subjects with mild, moderate, and severe HE. Serum 25(OH)D level was not inversely correlated with HE severity.

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