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Letter

Association between serum 25(OH)D levels and cancer in adults with psoriasis: A cross-sectional study

Dear Editor,

Psoriasis, a chronic inflammatory cutaneous condition, is characterized by the development of red plaques with silvery scales, significantly affecting patients' quality of life and mental health[1]. This condition is thought to affect approximately 2% of the Western population, with diagnosis peaking in early adulthood[2]. Vitamin D, a fat-soluble vitamin, is essential for phospho calcium metabolism, calcium homeostasis, and bone health. It exists in two primary forms: vitamin D_3 (cholecalciferol) and vitamin D_2 (ergocalciferol). Both forms play critical roles in preventing rickets, bone demineralization, hypertension, cancers, and autoimmune disorders[3]. Epidemiological studies have shown a correlation between low vitamin D levels and the development or progression of certain diseases, including psoriasis[4]. Furthermore, individuals with psoriasis have been found to have an increased risk of cancer, particularly keratinocyte cancer, lymphomas, lung cancer, and bladder cancer[5]. The present study aimed to explore the association between serum 25(OH)D levels and cancer among U.S. adults with psoriasis, as this relationship has not been previously investigated.

The National Health and Nutrition Examination Survey (NHANES) is an American cross-sectional survey that collects data on the health and nutrition of the general population through stratified multistage random sampling (https://www.cdc.gov/nchs/nhanes/). This analysis included data from five two-year NHANES survey cycles (2003–2004, 2005–2006, 2009–2010, 2011–2012, and 2013–2014), which are the cycles that collected psoriasis prevalence information. Participants aged 20 years or older were included, while those with missing or implausible data regarding psoriasis, cancer, or serum 25(OH)D levels, as well as those without psoriasis (n = 15 570), were excluded (***Fig. 1***). A radioimmunoassay kit (DiaSorin, Stillwater, MN, USA) was used to measure serum 25(OH)D levels at the National Center for Environmental Health (Atlanta, GA, USA). The diagnoses of psoriasis and cancer were based on self-reported physician diagnoses. To generate unbiased estimates from the complex NHANES sampling design, we used appropriate sampling weights in our analyses. All analyses were performed using R software (version 4.4.1; R Foundation for Statistical Computing, Vienna, Austria) and EmpowerStats software (X&Y Solutions Inc., Boston, MA, USA). A P value < 0.05 was considered statistically significant.

A total of 456 psoriasis patients were included, among whom 69 had cancer. Multivariate logistic regression analysis was used to investigate the association between serum 25(OH)D levels and cancer. ***Table 1*** shows the baseline characteristics of psoriasis patients with and without cancer. Significant differences were observed between the two groups in age, race, diabetes, hypertension, waist circumference, and 25(OH)D levels. In ***Table 2***, model 1 was adjusted for no covariates, model 2 was adjusted for age, sex, and race, and model 3 was adjusted for age, sex, race, hypertension, and waist circumference. In model 3, the serum 25(OH)D level as a continuous variable was associated with a 1% increased risk of cancer (odds ratio [OR] = 1.01, 95% confidence interval [CI]: 1.00–1.03, P = 0.035 5). For the categorical analysis, the vitamin D-deficient group (< 30 nmol/L) served as the reference category. The > 100 nmol/L group exhibited the highest relative odds of cancer, with an OR of 8.56 (95% CI: 2.77–26.41, P = 0.000 7) in model 3.

High doses of vitamin D have been demonstrated to effectively and safely treat psoriasis by increasing serum 25(OH)D levels and improving Psoriasis Area

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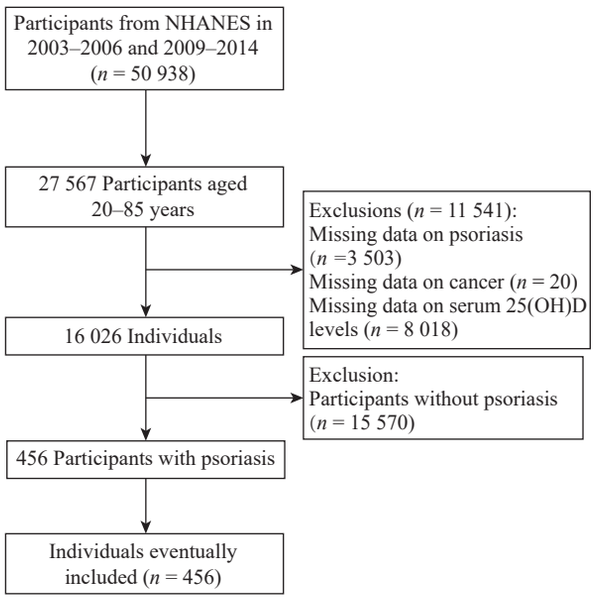

Fig. 1 **Flow chart showing the selection of study participants.**

and Severity Index scores without signs of toxicity[4]. Our analysis revealed a positive association between higher serum 25(OH)D levels —particularly levels exceeding 100 nmol/L—and cancer risk in individuals with psoriasis. This finding appears to contradict the majority of prior literature, which suggests a protective role of vitamin D against several types of cancer[6]. Furthermore, analysis of the baseline characteristics showed that psoriasis participants with cancer had significantly higher mean serum 25(OH)D levels than those without cancer (85 nmol/L *vs.* 71 nmol/L, $P = 0.011$; ***Table 1***), which also contrasts with earlier studies that reported lower vitamin D levels in cancer patients[7]. Although our findings differ from previous studies, all analyses were conducted following the NHANES analytic guidelines, including appropriate use of sampling weights, covariate adjustments, and sensitivity analyses, ensuring the scientific rigor and

Table 1 **Baseline characteristics of psoriasis participants with and without cancer**

Characteristics	Overall (N = 19 413 044)[2]	Cancer (N = 3 007 031)[2]	Without cancer (N = 16 406 013)[2]	P-value
Age [years, *n* (%)][1]				< 0.000 1
> 60	155 (27)	44 (57)	111 (21)	
20–60	301 (73)	25 (43)	276 (79)	
Sex [*n* (%)][1]				0.863 0
Female	237 (52)	38 (50)	199 (52)	
Male	219 (48)	31 (50)	188 (48)	
Race [*n* (%)][1]				0.008 0
Mexican American	39 (4)	3 (1)	36 (5)	
Other Hispanic	42 (5)	5 (3)	37 (5)	
Non-Hispanic White	269 (80)	53 (91)	216 (78)	
Non-Hispanic Black	51 (5)	6 (4)	45 (6)	
Other race	55 (6)	2 (1)	53 (7)	
Diabetes [*n* (%)][1]				0.042 0
Yes	79 (14)	15 (18)	64 (13)	
No	362 (84)	50 (74)	312 (85)	
Borderline	15 (3)	4 (8)	11 (2)	
Hypertension [*n* (%)][1]				0.000 1
Yes	210 (42)	48 (63)	162 (38)	
No	246 (58)	21 (37)	225 (62)	
Alcohol use [*n* (%)][1]				0.976 6
Yes	315 (74)	51 (78)	264 (74)	
No	141 (26)	18 (22)	123 (26)	
BMI (kg/m^2, mean ± SD)	30 ± 7	30 ± 7	30 ± 7	0.371 3
Waist circumference (cm, mean ± SD)	102 ± 15	106 ± 15	101 ± 15	0.006 8
25(OH)D (nmol/L, mean ± SD)	73 ± 28	85 ± 34	71 ± 27	0.005 8

P-values were calculated using Pearson's Chi-square test with Rao & Scott adjustment for categorical variables, and design-based Kruskal–Wallis test for continuous variables [BMI, waist circumference, and 25(OH)D].
[1]Unweighted counts (*n*) and weighted percentages (%); continuous variables are presented as weighted mean ± SD.
[2]Weighted population estimates (*N*).
Abbreviations: BMI, body mass index; SD, standard deviation.

Table 2 **Odds ratio (OR) for cancer by total 25(OH)D levels in participants with psoriasis**

$25(OH)D_2+25(OH)D_3$[a]	*n*/*N*	Model 1		Model 2		Model 3	
		OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Continuous (nmol/L)	456/456	1.02 (1.01, 1.03)	0.003 5	1.01 (1.00, 1.02)	0.052 2	1.01 (1.00, 1.03)	0.035 5
Category (nmol/L)							
⩽ 30	30/456	Reference		Reference		Reference	
31–50	99/456	2.43 (0.93, 6.36)	0.076 9	3.89 (1.26, 12.08)	0.024 2	3.48 (1.19, 10.21)	0.029 5
51–75	156/456	1.45 (0.61, 3.46)	0.403 7	1.86 (0.72, 4.84)	0.208 8	1.94 (0.80, 4.66)	0.149 5
75–100	119/456	3.55 (1.73, 7.27)	0.001 3	3.38 (1.36, 8.37)	0.012 6	3.90 (1.55, 9.80)	0.006 5
> 100	52/456	7.66(3.06, 19.22)	0.000 1	7.49 (2.46, 22.85)	0.001 1	8.56 (2.77, 26.41)	0.000 7
P for trend		0.006 7		0.057 1		0.034 7	

Model 1 was adjusted for none. Model 2 was adjusted for age, sex, and race. Model 3 was adjusted for age, sex, race, hypertension, and waist circumference.
[a]The criteria for grouping serum 25(OH)D levels refer to the Institute of Medicine (IOM) and the Endocrine Society's classification criteria for the five classifications, with the IOM considering 25(OH)D < 30 nmol/L to be vitamin D-deficient, 30–50 nmol/L to be vitamin D-insufficient, and ⩾ 50 nmol/L to be vitamin D-sufficient. According to the Endocrine Society, 25(OH)D < 50 nmol/L is vitamin D-deficiency, 50–75 nmol/L is vitamin D insufficiency, and 25(OH)D ⩾ 75 nmol/L is vitamin D-sufficiency.

reproducibility of our results. These inconsistencies may be attributed to the cross-sectional design of NHANES, which limits causal inference and raises the possibility of reverse causality. It is possible that individuals with cancer were more likely to receive vitamin D supplementation or phototherapy, leading to elevated serum levels. Additionally, unmeasured confounding factors, such as sun exposure, supplement use, geographic location, and seasonal variation, may have biased the observed associations.

These findings underscore the importance of cautious interpretation when evaluating vitamin D's role in psoriasis and cancer. While vitamin D supplementation holds therapeutic promise, excessive use may not confer additional benefits and could potentially increase cancer risk. Therefore, individualized monitoring is essential to ensure optimal vitamin D levels and minimize potential harm.

The main strength of our study is the use of a large, nationally representative U.S. sample, enhancing the generalizability of the findings. However, several limitations should be acknowledged. First, as a cross-sectional study, it cannot establish the temporal relationship between psoriasis and cancer, leaving causal direction unclear. Second, due to the diversity of cancer types, our study did not analyze specific cancer subtypes. Nevertheless, our findings provide valuable insights into the potential implications of vitamin D supplementation for psoriasis patients with cancer, thereby highlighting the need for further research.

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Yours sincerely,

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