

RESEARCH LETTER

Melasma is Associated with Lower Serum Vitamin D Concentrations as Compared to Healthy Controls

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ABSTRACT

Background: Melasma is a common, chronic skin condition of hyperpigmentation involving the appearance of symmetric and irregular light brown macules and patches, mainly on sun exposed skin of the head and neck. Though the pathogenesis is not fully understood, hyperfunctional melanocytes are known to deposit excess melanin in the epidermis and dermis. Vitamin D has been shown to influence melanogenesis via its influence on the vitamin D receptor. Due to the avoidance of ultraviolet light recommended to patients with melasma, vitamin D supplementation is recommended. Given the known influence of vitamin D on the skin, and the large prevalence of melasma in the public, the association between vitamin D and melasma will be examined further.

Methods: A retrospective review was performed utilizing the TriNetX platform to query de-identified patient data from the Medical University of South Carolina's Electronic Health Record system over a 9-year period from January 2013 to May 2022. Calcidiol (25-hydroxy-vitaminD) was utilized as a surrogate for vitamin D level. Statistical analyses were performed using t-testing.

Results: Of 1,962 patients diagnosed with melasma, 840 had a serum calcidiol level measured following diagnosis. The majority of these patients were female (77%) and had an average age of 60.3 ± 19.2 years. Melasma patients were most commonly Caucasian (81%), followed by African American (15%) and Hispanic or Latino (3%). Patients with melasma had an average serum calcidiol of 33.8 ± 15.8 ng/mL (reference range: 25 – 80 ng/mL). This was significantly lower than comparison to 2,146 dermatology patients not diagnosed with melasma (36.8 ± 15.8 ng/mL, p-value <0.0001%).

Conclusion: Vitamin D has been demonstrated to be critical in the skin, including differentiation and proliferation of melanocytes. Our results suggest that patients with melasma, who have significantly lower levels of serum vitamin D than their healthy counterparts, may benefit from vitamin D supplementation. Future studies investigating improvement in melasma symptoms following vitamin D supplementation are needed.

Melasma is a common, chronic skin condition of hyperpigmentation involving the appearance of symmetric and irregular light brown macules and patches on sun exposed skin.¹⁻³ Melasma affects 5-6 million women in the US, including 50-70% of pregnant women.² Though the pathogenesis is not fully understood, hyperfunctional melanocytes are known to deposit excess melanin in the epidermis and dermis.² Vitamin D has been shown to stimulate melanogenesis, and to regulate the activation, proliferation, and migration of melanocytes.

Vitamin D deficiency has a prevalence of 40% in the US, with the highest rates seen in African Americans (82.1%) and Hispanic (69.2%) patients.^{2,4} Melasma is also disproportionately prevalent in those with Fitzpatrick skin types IV-VI, making it a common problem experienced by African American, Hispanic, and Asian populations.² Common treatments include avoidance of UV light.³ It is due to this avoidance of UV light that vitamin D supplementation is recommended, though the susceptibility of patients with higher Fitzpatrick skin types to develop vitamin D deficiency should also be considered.⁵ This is especially true given that these higher skin types are prone to develop melasma. Due to the known influence of vitamin D on melanocytes,⁶ and the high prevalence of both melasma and vitamin D deficiency, we aimed to further examine the association between vitamin D status and melasma.

After receiving IRB Approval, a retrospective review was performed utilizing the TriNetX platform to query de-identified patient data from January 2013 - May 2022. Serum calcidiol (25-hydroxy-vitamin D) concentration was utilized to indicate vitamin D status. Statistical analyses were performed using t-testing.

Of 1,962 patients diagnosed with melasma, 840 had a serum calcidiol level measured following diagnosis. Most patients were female (77%) with a mean age of 60.3 ± 19.2 years. Melasma patients were Caucasian (81%), followed by African American (15%) and Hispanic or Latino (3%). Patients with melasma had an average serum calcidiol of 33.8 ± 15.8 ng/mL (range: 3.2 – 101) (reference range: 25 – 80 ng/mL). This was significantly lower in comparison to 1,044 ethnicity and sex matched controls (36 ± 15.3 ng/mL, range: 2.5 – 149.6, p-value <0.0270) (Table 1).

Table 1. Patient Demographics and Calcidiol Concentration.

	Melasma Patients	Control Patients	p-value
Number of patients	1,992	1,044	
Age (years)¹	60.2 ± 19.2	64.7 ± 15.2	<0.0001
Sex²			
Female	1,530 (77%)	833 (80%)	0.602
Male	462 (23%)	211 (20%)	0.602
Ethnicity²			
Hispanic or Latino	41 (2%)	13 (1%)	0.1074
Not Hispanic or Latino	1,936 (97%)	1,022 (98%)	0.2442
Unknown	15 (1%)	10 (1%)	0.5530
Serum calcidiol^{1,3}	33.8 ± 15.9 (range 3.2-101)	36.0 ± 15.3 (range 2.5 – 149.6)	0.0270

¹mean ± SD ²count (%) ³reference range: 25–80ng/mL

Vitamin D is known to have major influence in the skin.⁶ It enacts its effects via the vitamin D receptor (VDR). This receptor is expressed in both melanocytes and keratinocytes, with the highest level of VDR expression is at the

basal layer of the epidermis.^{1,6} Activation of VDR causes inhibition of growth of both normal and malignant melanocytes.¹ Epidermal proliferation and differentiation also occurs via VDR in keratinocytes.⁶ It has also been suggested that VDR may influence androgen and estrogen activation, which are proposed to play a role in the pathogenesis of melasma.¹ Given this understanding of the VDR, one would expect vitamin D levels to be normal or even elevated in patients with melasma, a disease characterized by overactive melanocytes, and that is especially prevalent in pregnant women. However, patients in our cohort had significantly lower levels of serum calcidiol. Our results are consistent with a 2018 study that also observed a significant correlation between melasma and low serum calcidiol levels.⁷ This expected pattern may differ for individuals who receive little to no sun exposure or consistently utilize sun protective measures.

To date, no studies have investigated changes in melasma symptoms with vitamin D supplementation. However, the significantly lower serum calcidiol levels observed in the melasma cohort underscores the need to provide vitamin D supplementation to such patients, given that avoidance of UV light remains a treatment of choice.⁸

Melasma is a common condition with significant impact on quality of life due to the emotional and psychosocial consequences of its physical symptoms.² Vitamin D has been demonstrated to be critical in the skin, with involvement in the differentiation and proliferation of melanocytes. Our results suggest that patients with melasma may benefit from vitamin D supplementation. Larger, multi-center studies investigating the correlation between serum calcidiol and melasma, and future studies exploring

changes in melasma symptoms following vitamin D supplementation, are warranted.

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