The Role of Vitamin D Deficiency in African American Women with Systemic Lupus Erythematosus (SLE)

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Abstract

Background: Systemic lupus erythematosus (SLE) is a multi-organ, autoimmune disease that is mainly characterized by the overproduction of antibodies attaching to the nucleus of the cell and marking it for destruction. Overtime, this autoimmune response leads to an array of clinical manifestations by causing blood vessels to expand and leak fluid, resulting in swelling and inflammation of several parts of the body. The reported prevalence of SLE worldwide is 20 to 150 cases per 100,000, mostly affecting African American women, specifically those of childbearing age (20 to 40 years). Although SLE is a multifactorial disease, studies suggest a strong association between its progression and vitamin D deficiency. **Objective:** To investigate the role of vitamin D deficiency in disease activity of SLE among African American women. **Methods:** A structured literature review was conducted using PubMed, Google Scholar, and Lancet databases. An effective search strategy was developed to filter all appropriate and relevant studies on the effects of vitamin D deficiency in African American women with SLE. The inclusion criteria were vitamin D deficiency, systemic lupus erythematosus, African American, and women. The articles selected were peer-reviewed journals, published after 2000, and written in the English language. After several search parameters were conducted, six out of 42 articles remained and were used to support this study. **Results:** The selected scientific articles show that African American women affected by SLE have insufficient levels of 25-hydroxyvitamin D [25(OH)D]. This deficiency increases the severity of SLE and explains the abnormalities experienced by many patients with this disease. **Conclusion:** All of the articles reviewed suggest that vitamin D deficiency is associated with the progression of SLE in African American women.

Research Question

Is there an association between vitamin D deficiency and increased progression of systemic lupus erythematosus (SLE) in African American women?

Introduction

Systemic lupus erythematosus (SLE) is a multi-organ, chronic inflammatory disease that disproportionately affects African American women [1,2]. SLE predominantly affects women, with a female to male ratio of 9:1; moreover, studies have shown that African American women are 3 to 4 times likely to develop SLE than Caucasian women [3]. The exact etiology of SLE is unknown; however, multiple factors such as the environment, endocrine system and genetic information contribute to the development of the disease [4]. The progression of SLE is initiated when one's white blood cells (B cells) mistakenly overproduce antibodies that mark their own body cells for destruction [3,5]. When the antibodies attach to the normal cells, the white blood cells begin to attack them as if they are foreign antigens [4]. This results in the overdevelopment of T cells which creates proinflammatory pathways leading to inflammation, vasculopathy, and immune complex deposition [6]. The symptoms of SLE may result in the development of a butterfly shaped skin rash on the cheeks and nose, with progression it can lead to renal failure, heart problems, arthritis, pleural effusion, and fatigue [4]. While there's no cure for lupus, treatments can help control symptoms.

Vitamin D is known to have immunomodulatory properties, and it has been postulated that its actions can decrease immunoreactivity [6]. Vitamin D is a steroid hormone that plays a vital role in bone homeostasis and immune response [4]. The primary source (80%) of vitamin D is synthesized as vitamin D_3 in the skin upon exposure to ultraviolet B (UVB) radiation. It is metabolized in the liver to 25- hydroxyvitamin D [25(OH)D], which is the subtype that is usually measured to determine the patient's vitamin D status [4]. Generally, vitamin D deficiency is present in patients with SLE and severe forms of SLE may present in dark skinned populations such as African Americans [7]. This demographic is more at risk for lower levels of this vitamin, primarily due to the fact that pigmentation reduces vitamin D production in the skin [7]. Although it is known that SLE patients lack vitamin D, the role that this steroid hormone plays in the progression of the disease remains unclear.

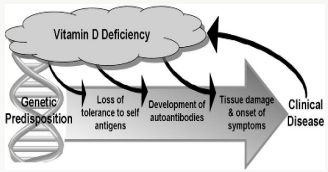

Figure 1. Conceptual model of the role of vitamin D deficiency in the pathogenesis of SLE.

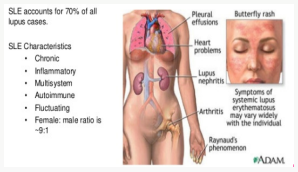

Figure 2. Clinical and Diagnostic Presentation of SLE

Methods

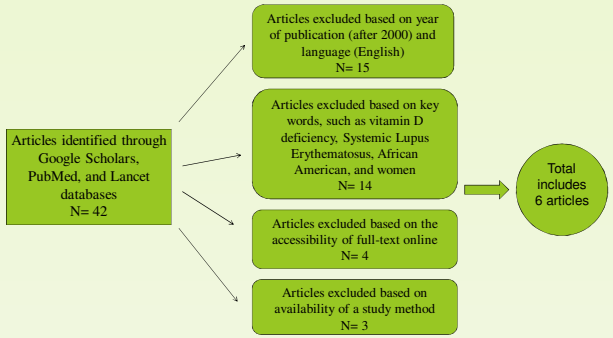

Figure 3. Visual representation of the methods process of structured literature review

Results

Table 1. Summary of the six articles used for this review

Author(s)	Sample	Study Design	Results	Conclusion
Petri, Bello, Fang, & Magder, 2013.	1,006 SLE patients. 91%:females (mean age: 49.6) 54%: Caucasian, 37%: African American, other ethnicity:8%	Longitudinal regression study: 25(OH)D and disease activity. SLE patients with low levels of 25(OH)D (<40 ng/ml) were given supplements of 50,000 units of vitamin D2 weekly + 200 units of calcium/vitamin D3 twice daily.	For those with levels of 25(OH)D less than 40 ng/ml, a 20-unit increase in 25-hydroxyvitamin D level was associated with a mean decrease of 0.22 (95% CI) (P=0.032) in the SELENA.	20-ng/ml increase in 25(OH)D level = a 21% decrease in having high disease activity score and a 15% decrease in having clinical proteinuria. There was no evidence of additional benefit of 25(OH)D beyond a level of 40 ng/ml.
Ben-Zvi et al., 2010.	198 recruited SLE patients.	25-OH vitamin D levels were measured. 29.3% and 11.8% of African American and Hispanic SLE patient had 25-D levels <10 ng/ml	The degree of vitamin D deficiency correlated inversely with disease activity; R=-0.234, p=0.002	Severe 25(OH)D deficiency in SLE patients: inverse correlation with disease activity. Suggest: vitamin D supplementation will contribute to restoring immune homeostasis in SLE patients.
Thudi, Yin, Wandstrat, Li, & Olsen, 2008.	37 female patients with lupus	Serum levels of 25(OH)D were measured using enzyme-linked immunoassay. Correlations with clinical and immunologic measures were determined.	65% of patients with SLE had values <80 nmol, which is accepted as the lower limit of vitamin D adequacy. 20%: 25(OH)D levels lower than the normal range (<47.7 nmol/L). Patients with these lowest level showed disease activity measures (p< 0.003).	Increased disease symptoms in patients with very low levels of vitamin D. Vitamin D supplements optimizes therapeutic outcomes. Possibility that such treatment could lead to increased autoantibody level requires further study.
Borba et al., 2009	36 patients with lupus	Cross-sectional: Group I-high activity: 12 patients, mean age 29.6 years, II-minimal activity: 24 patients, mean age 30.0 years, III- normal controls: 26 women, 32.8 years.	In group I, 25OHD levels were lower (P<0.05), which was related to the SLEDAI (R=-0.65, P<0.001). In multiple regression analysis, the 25OHD level was associated with SLEDAI.	A high prevalence of 25OHD deficiency in SLE patients indicates the need for vitamin D replacement, mainly during high disease activity periods.
Kamen et al., 2009.	123 recently diagnosed SLE patients and 240 controls were used	Population-based cohort study: compared serum 25(OH)D levels between recently diagnosed SLE cases and matched controls controlling for age, sex, season, and smoking.	Lower among African Americans (15.9 ng/ml) compared to Caucasians (31.3 ng/ml). Critically low vitamin D levels (<10 ng/ml) found in 22 SLE cases with renal disease being the strongest predictor (p<0.01) followed by photosensitivity.	These results suggest vitamin D deficiency as a possible risk factor for SLE and provide guidance for future studies looking at a potential role of vitamin D in the prevention and/or treatment of SLE.
Hoffecker, Raffield, Kamen, & Nowling, 2013.	African American female SLE patients and unaffected controls from the Sea Island region of South Carolina.	Serum 25(OH)D levels were measured using a nonchromatographic radioimmunoassay. Telomere length was measured in genomic DNA of peripheral blood by PCR.	Patients with SLE and vitamin D deficiency had shorter telomeres + higher anti-telomere antibody compared to age and gender matched unaffected controls.	Increasing 25(OH)D levels in African American patients with SLE may be beneficial in maintaining telomere length and preventing cellular aging. Anti-telomere antibody levels may be a biomarker of SLE status and disease activity.

Discussion

Results from all six studies suggest that there is an association between lower vitamin D levels and increased lupus activity, particularly in African American women. Two of these studies even proposed vitamin D deficiency as a trigger of SLE. There is general consensus that the lack of this vitamin leads to the breakdown of the regulation of immunological pathways and bone homeostasis, which are involved in the progression of SLE.

Vitamin D has anti-inflammatory properties that help to suppress immune cells that take part in the autoimmune reaction. Studies have shown that people with higher levels of vitamin D have fewer lupus symptoms; thus, people living in regions with more sunlight have a lower risk of developing autoimmune diseases. All studies propose that lack of vitamin D in SLE patients is extremely prevalent due to decreased sunlight exposure. These patients are photosensitive; therefore physicians recommend wearing high protective sunscreen, as well as avoid being outdoors. Moreover, the disease itself can induce an increase in metabolism and impair 25-hydroxylase, an enzyme used to convert vitamin D into 25[OH]D.

This deficiency was especially predominant in African American women and two studies suggest that low 25[OH]D levels among this demographic are present due to dermal pigmentation impeding the conversion of vitamin D. Evidence shows that melanin protects against the harmful effects of UV radiation at the expense of reduced vitamin D production. All studies discovered that African American women with SLE had lower levels of 25[OH]D than what is considered healthy (<20 ng/mL); three of these studies reported a large number of African American women with severe vitamin D deficiency (<10 ng/mL) compared to other racial groups. Studies have shown that levels lower than 10 ng/mL was associated with renal disease and proteinuria.

Several possible mechanisms contributing to the development of SLE were suggested. Four studies proposed that vitamin D insufficiency is associated with the production of autoantibodies and the interferon gene signature. Immunological abnormalities in SLE may occur as a result of increased activity of interferon alpha (IFNα), which are proteins that trigger protective defences of the immune system to eliminate all pathogens. Moreover, one study suggested that there is a relationship between vitamin D, telomere length, and anti-telomere antibodies in African American women with SLE. This study demonstrated that SLE patients have significantly shorter telomere length and higher anti-telomere antibodies than healthy individuals. Since immune function is highly dependent on these factors, this may lead to a decrease in adaptive immunity and an increased susceptibility to autoimmune diseases.

The results of this literature review support potential therapeutic benefits of using vitamin D supplements to alleviate the clinical symptoms of SLE. While it is thought that having enough vitamin D can help prevent flares in people affected by lupus. Further research is needed to explore this therapy, since some studies have determined that negative effects of vitamin D supplements include hypercalcemia (blood calcium levels are too high) and renal stones.

Limitations

There were a few limitations present in this literature review. There may have been an exclusion bias, since studies that were not written in English were not incorporated in this review. In addition, only studies that were accessible through the University of Ottawa database were used in this literature study due to monetary reasons. There was also a possibility of publication bias as articles that were not peer reviewed, such as the grey literature, were not included in this review. Lastly, it cannot be confirmed whether negative results were withheld from publication, thus the results of the study may be incorrectly skewed away from the null hypothesis.

Conclusion

According to the articles reviewed, there is growing evidence suggesting that vitamin D plays a key role in the increased disease activity of SLE in African American women. Lupus is a disease for which there are few effective treatment options. As shown in this review, vitamin D may be used as a beneficial therapeutic supplement. However, more research needs to be done on the benefits of using vitamin D to mitigate the clinical manifestations of SLE, due to its prevalence in society.

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