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 attacking to the nucleus of the cell and it may be life-threatening. Overtime, this autoimmunity can lead to a series 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 vitamin D deficiency and SLE activity. 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.

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 [5,6]. 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 oversecretion of T cells which triggers 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 D3 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 sterol hormone plays in the progression of the disease remains unclear.

Methods

Articles excluded based on key words, such as vitamin D deficiency, SLE, Lupus Erythematosus, African American, and women

Results

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

<table>
<thead>
<tr>
<th>Authors/</th>
<th>Sample</th>
<th>Study Design</th>
<th>Results</th>
<th>Conclusion</th>
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<tbody>
<tr>
<td>Borba et al., 2009</td>
<td>36 patients with lupus</td>
<td>Cross-sectional: longitudinal regression analysis of 25(OH)D levels measured 29 years and 18.1% of African American patients and Hispanics</td>
<td>Patients with values &lt;80 ng/mL had a 4 times higher risk of developing SLE than patients with values ≥80 ng/mL.</td>
<td>Patients with values &lt;80 ng/mL had a 4 times higher risk of developing SLE than patients with values ≥80 ng/mL.</td>
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<tr>
<td>Zeid et al., 2012</td>
<td>68 female lupus patients</td>
<td>Case-control study: measured serum 25(OH)D levels between SLE patients and healthy controls</td>
<td>Patients with values &lt;40 ng/mL had a 1.8 times higher risk of developing SLE than patients with values ≥40 ng/mL.</td>
<td>Patients with values &lt;40 ng/mL had a 1.8 times higher risk of developing SLE than patients with values ≥40 ng/mL.</td>
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<tr>
<td>Li, W., Liu, M., &amp; Li, S. (2010)</td>
<td>198 recruited SLE patients.</td>
<td>Cross-sectional: determined the correlation between telomere length and vitamin D levels</td>
<td>Patients who had telomere values &lt;80 ng/mL and vitamin D levels lower than the normal range (&lt;17 ng/mL) had a significantly shorter telomere length than patients with values ≥80 ng/mL.</td>
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<tr>
<td>Ekins et al., 2013</td>
<td>123 patients with lupus</td>
<td>Cross-sectional: measured serum 25(OH)D levels in patients with SLE and healthy controls</td>
<td>Patients with values &lt;75 ng/mL had a 4 times higher risk of developing SLE than patients with values ≥75 ng/mL.</td>
<td>Patients with values &lt;75 ng/mL had a 4 times higher risk of developing SLE than patients with values ≥75 ng/mL.</td>
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<tr>
<td>Thudi, Yin, Wandstrat, Li, &amp; Olsen, 2008</td>
<td>198 recruited SLE patients.</td>
<td>Cross-sectional: determined the correlation between vitamin D levels and the expression of interferon gene signature.</td>
<td>Interferon gene expression was significantly higher in patients with values &lt;75 ng/mL than in patients with values ≥75 ng/mL.</td>
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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 propose a potential therapeutic role for vitamin D. There is general consensus that vitamin D helps in the treatment of SLE patients [25]. Vitamin D deficiency (<10 ng/mL) is extremely prevalent due to decreased sunlight exposure. These patients are photosensitive; therefore physician advice on photoprotection becomes imperative. 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 has a synergistic effect on 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 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. Inflammatory abnormalities in SLE may occur as a result of increased interferon alpha (IFNα), which is proteins that trigger protective defenses 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 supplementation to alleviate the clinical symptoms of SLE. While it is thought that 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 supplementation include hypercalcemia and increased renal disease [3]. 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 oversecretion of T cells which triggers 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.

Conclusion

According to the six studies 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 beneficial in maintaining telomere length and preventing cellular aging. Anti-telomere antibody levels may be biomarker of SLE status and disease activity. It is thought that 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 supplementation include hypercalcemia and increased renal disease [3]. 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 oversecretion of T cells which triggers 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.

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