

Original article

Effects of Vitamin D Insufficiency on Hemoglobin Levels and Skin Infections Among Libyans of Various Ages

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ABSTRACT

This study explores the effects of vitamin D deficiency on hemoglobin levels and skin infections in 138 Libyan men and women across various ages. A cross-sections study was done in Al-Ajilat city, during the period from June to September 2024. A total of 63 (45.35 %) males and 75 (54%) females were included in this study, with different skin infections from different ages. A hematological blood analyzer (Sysmex KX-21N) was used to evaluate the hemoglobin concentration (HGB) in venous blood samples obtained in EDTA tubes. A competitive ELISA-based immunoassay was also used to assess vitamin D (25-hydroxycholecalciferol) in the patients' serum. Vitamin D insufficiency was more prevalent in men (60.3%) than in women (49.3%), though the difference was not statistically significant ($p = 0.263$). Hemoglobin levels were higher in men (mean: 14.2 g/dL) than women (mean: 12.5 g/dL), reflecting potential gender-specific biological differences. Male participants also exhibited greater variability in vitamin D and inflammatory marker (CRP) levels. Infection patterns revealed gender-related trends, with fungal infections being more common in men and viral infections in women. However, the association between infection types and gender was not statistically significant ($p = 0.137$). Gender significantly influenced CRP and hemoglobin levels but had no apparent effect on vitamin D levels. No strong linear correlations were observed between vitamin D, CRP, hemoglobin, or age. The findings highlight gender differences in vitamin D status, immune responses, and infection types, although most differences lacked statistical significance. The study underscores the need for further research to elucidate vitamin D's role in skin infections and its potential interplay with hemoglobin levels and immune markers

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INTRODUCTION

In the last few years, numerous researches examining the connection between vitamin D and certain skin disorders have been published as a result of the increased interest in the role this vitamin plays in skin illness. From keratinocyte proliferation, differentiation, and apoptosis to barrier maintenance and immunoregulatory activities, vitamin D influences a variety of skin functions [1]. More excitingly, vitamin D actively acts on the skin itself and is produced by keratinocytes in reaction to sun exposure. The photoendocrine system of vitamin D is the term given to this two-way process [2]. Additionally, vitamin D inhibits neoangiogenesis and oncogenesis and plays a role in cell differentiation, maturation, and senescence [3].

Physiologically, like a hormone, vitamin D controls the metabolism of calcium, phosphorus, and parathyroid hormone (PTH), which has significant effects on the skeletal system's integrity. A renewed interest in the functions of vitamin D has resulted from the identification of vitamin D receptors (VDRs) in the majority of body cells and the existence of enzymes that manufacture 1,25-dihydroxyvitamin D [1,25(OH) 2 D], the active form of vitamin D, in non-renal locations such as the skin [4]. Currently, dermatologists are interested in vitamin D because of its cutaneous production and its use in treating common skin conditions like psoriasis. Research suggesting that vitamin D functions as an immunomodulator has made it possible to learn more about its potential therapeutic benefits for psoriasis, atopic dermatitis, and skin cancer [5]. Additionally, vitamin D deficiency persists as common; according to a study of teenagers in numerous European nations, 80% of participants had vitamin D levels below the adequate range. Furthermore, more than 40% were deemed inadequate or really inadequate [6]. The vitamin D status of the general European population, where vitamin D deficiency is common and particularly common in dark-skinned subgroups [7], and estimates of dietary intakes in Europe, which were usually low in vitamin D [8], are in line with this. Poor vitamin D deficiency is prevalent even in more southern nations like India [9].

According to the recent studies, inflammatory illnesses have been linked to changes in vitamin D status in recent decades [10,11]. As demonstrated by numerous investigations that found either a deficiency or insufficiency of serum vitamin D in psoriatic patients, vitamin D plays a crucial role in psoriasis in this setting [12-14]. Serum 25(OH)D levels in psoriatic patients were significantly lower than those in controls, according to several case-control studies, and there was an inverse relationship between serum 25(OH)D and the severity of the condition [15-17].

Epidemiologically, living at higher latitudes and being more susceptible to vitamin D deficiency has been shown to significantly increase the risk of several fatal tumors, such as those of the breast, esophagus, prostate, colon, etc. [18,19] Higher latitudes also raise the likelihood of developing autoimmune disorders including multiple sclerosis, type I diabetes, hypertension, and other autoimmune diseases, as well as infectious diseases like influenza and tuberculosis [20]. Moreover, in addition to its immunomodulatory properties, vitamin D can also promote the production of filaggrin. Adult and pediatric hypovitaminosis D has been linked to atopic dermatitis (AD) [21]. In the same context, while AD usually gets better in the summer, poor wintertime sun exposure may contribute to the disease exacerbations that frequently happen in the colder months. Furthermore, decreased skin levels of LL-37 peptide, whose synthesis is triggered by vitamin D [22], are linked to an increased risk of *Staphylococcus aureus* infections in AD.

On the other hand, children with ichthyosis congenita have low levels of 25(OH)D and high levels of PTH, according to Sethuraman et al. [23]. In that study, vitamin D supplementation with 60,000 IU of oral cholecalciferol for 10 days, followed by a maintenance regimen of 400 to 600 IU/d, produced a quick response, with a discernible improvement in the dermatological symptoms by the fifth day in terms of stiffness and scaling. Six of the seven kids in the study had serum 25(OH)D levels less than 4 ng/mL

With regard to acne, it is known currently that there was an inverse correlation found between vitamin D levels and the frequency and severity of inflammatory acne lesions, and the vitamin D levels of the acne patients were lower than those of the healthy controls [24]. A correlation between vitamin D and decreased production of interleukin (IL) 6, IL-8, and metalloproteinase-945a, as well as a decrease in IL-17 expression due to its effect on Th17 cells, may account for the vitamin's role in acne [25].

Since low hemoglobin levels were reported in 42.71% of the control group, 62.5% of pneumonia patients, and 56.25% of bronchiolitis cases, they were determined to be a risk factor for acute lower respiratory tract infections (ALRTIs) ($P = 0.044$) [26]. These findings were consistent with the Harris et al. study [27]. They looked at air pollution and anemia as potential risk factors for ARLTIs. Compared to healthy, non-anemic children, they discovered that anemic children are more likely to be hospitalized for acute respiratory infections. Poor tissue oxygenation is the primary pathophysiological deficiency in ARTIs, and anemia reduces oxygen delivery on its own, they explained their findings. On the other hand, some of other studies show an association between anemia and vit. D deficiency in heart failure (HF) patients. It might be because patients with anemia and worse kidney function had lower vit. D. In other research, correlations between patients slated for coronary angiography and heart surgery were discovered [27-29]. Conversely, in randomized controlled trials, vitamin D had no effect on anemia in two studies [30, 31], but it had a positive effect on the dosage of erythropoietin-stimulating drugs in two studies conducted in CKD [32, 33].

Accordingly, because many of the previous studies have demonstrated the implication of Vit. D deficiency in many of skin infection diseases, and in occurrence of anemia, this study has designed to explore the role of low levels of vit. D in skin infection among Libyan men and women of different ages as well as the possible implication of vit. D deficiency in the variation of hemoglobin concentration among the same population.

METHODS

Study design and setting

This cross-sections study was done in Al-Ajilat city (west region of Tripoli (-Libya, during the period from June to September 2024. A total of 63 (45.35 %) males and 75 (54%) females were included in this study. Male and female patients with different skin infections from different ages were included in this study, while those with chronic liver disorders or those who taking any treatments that might affect the bone metabolism or liver function were excluded in the current study.

Blood tests

A hematological blood analyzer (Sysmex KX-21N) was used to evaluate the hemoglobin concentration (HGB) in venous blood samples obtained in EDTA tubes. The CRP GEN4-250 test Reagent for Roche Cobas Integra 400/400+ was used to evaluate C-reactive protein (CRP). A competitive ELISA-based immunoassay was also used to assess vitamin D (25-hydroxycholecalciferol) in the patients' serum. All mentioned investigations were achieved in Yashfeen laboratory department, Al-Ajelat central clinic.

Data analysis

Following the organization and entry of all data into an Excel file (Microsoft Office version 2019), SPSS (Statistical Software for Social Analysis-version 23) was used for statistical analysis. The data has been subjected to several statistical measurements, including correlation between some significant parameters, mean value, standard deviation, and P value. To make the various metrics more understandable, the results are shown in tables and figures. When the P-value was less than 0.05, the measurements were deemed statistically significant.

RESULTS

The current study included 138 patients in total, of whom 75 (54%) were female and 63 (45.35%) were male (Table 1).

Table 1. Total number of participants included in the study.

Sex	Patients number	Percent %
Male	63	45.65 %
Female	75	54.35 %
Total	138	100 %

Potential gender disparities in vitamin D levels among participants with skin infections are suggested by the data in table 2. In the current study, vitamin D insufficiency was surprisingly more common in men than in women. Notably, 37 female patients had a percentage of vitamin D deficiency (49.3%), while 38 male patients represent (60.32%) had levels below the deficiency threshold. Consequently, the significance value (p-value < 0.05) is usually less than the p-value (0.263) obtained. This implies that the percentage of vitamin D insufficiency in males and females is not statistically different.

Table 2. The percentage of study participants with skin infections who were vitamin D deficient.

Vit. D level (ng/ml)	Male	Female
Vit. D level < 25 ng/ml	38 (60.32%)	37 (49.3%)
Vit. D level > 25 ng/ml	25 (39.68%)	38 (50.67%)
Total	63 (100%)	75 (100%)

P-value = 0.263

The frequencies of males and females with vitamin D levels in two categories—less than 25 ng/mL and greater than or equal to 25 ng/mL—as well as the overall frequencies for all participants are graphically compared in figure (1). This figure indicates that the distribution of Vitamin D levels below and above the 25 ng/mL threshold is relatively similar between males and females. Nonetheless, the group with Vitamin D \geq 25 ng/mL and the entire sample are marginally more likely to be female. This could indicate that women are more likely to have adequate vitamin D levels.

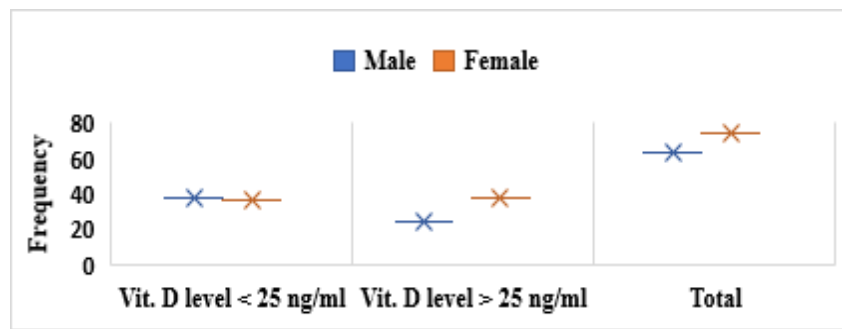


Figure 1. Vitamin D deficiency among participants (skin infected patients) included in the study.

Table 3 shows some differences between genders across different variables, with males generally having higher inflammation (CRP), higher hemoglobin levels, but with greater variability in CRP and Vitamin D levels. Females, on the other hand, have slightly older average ages and lower CRP and hemoglobin levels with less variability in those markers. For most variables (especially CRP and Vitamin D), males tend to show higher variability. This means that male participants in the study may have more diverse responses or conditions related to these parameters than females. Both genders show relatively precise means for most variables, with smaller standard errors (e.g., age, CRP, Vitamin D), suggesting reliable estimates for the group averages.

This table provides insights into the different physiological profiles and immune responses between males and females with skin infections. The higher variability in males for some parameters could suggest different underlying factors or treatments influencing their health status.

Table 3. Average value, standard deviation, and standard error of age and other variables for individuals with skin infections.

Parameters	Gender	N	Mean	±SD	± Std. Error
Age	Female	75	41.4 Ys	21.8	2.5
	Male	63	37.3 Ys	19.4	2.4
CRP	Female	75	3.7 mg/dl	3.5	0.4
	Male	63	5.6 mg/dl	6	0.7
Vit. D	Female	75	25 ng/ml	9.1	1
	Male	63	24.9 ng/ml	10	1.2
HGB	Female	75	12.5 g/dl	1.2	0.14
	Male	63	14.2 g/dl	1.49	0.18

The distribution of different illnesses by pathogen type and gender is shown in table 4. Although bacterial diseases tend to be well balanced, viral infections are more common in females, and some fungal infections (such Tinea cruris and athlete's foot) seem to affect males solely or primarily. This raises the possibility of exposure patterns or vulnerabilities unique to a given gender for various illnesses. In more details, the number of males and females affected by specific infections varies significantly, with some infections (e.g., Herpes zoster and Warts) being more common in females, while others (e.g., Impetigo and Athlete's foot) are more frequent in males.

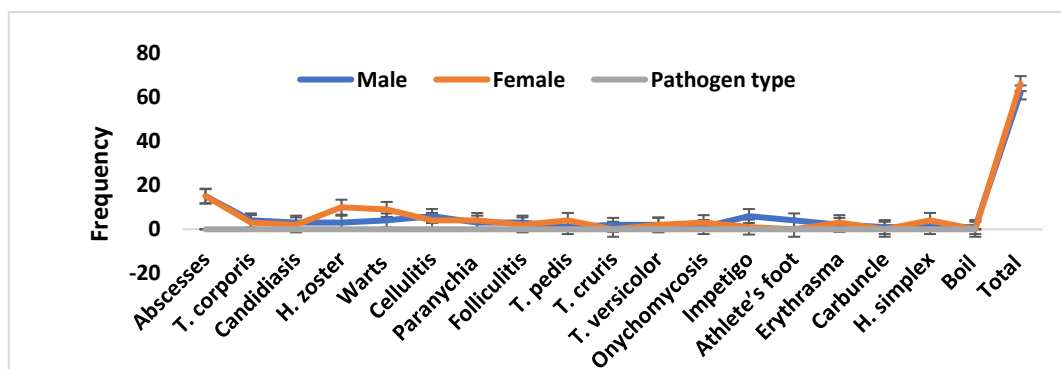


Figure 2. Total number of participated patients suffering from different infections and pathogen types.

Table 4. Total number of participated patients suffering from different infections and pathogen types.

Infection type	Male	Female	Pathogen type
Abscesses	15	15	B
T. corporis	4	3	F
Candidiasis	3	2	F
H. zoster	3	10	V
Warts	4	9	V
Cellulitis	6	4	B
Paronychia	3	4	B
Folliculitis	3	2	B
T. pedis	1	4	F
T. cruris	2	0	F
T. versicolor	2	2	F
Onychomycosis	1	3	F
Impetigo	6	1	B
Athlete's foot	4	0	F
Erythrasma	2	3	B
Carbuncle	1	0	B
H. simplex	1	4	V
Boil	1	0	B
Total	62	66	

B: Bacteria, V: Virus, F: Fungi.

Based on the information shown in table 5, the chi-square test's p-value of 0.137 is greater than the traditional significance level of 0.05. This implies that there is no statistically significant relationship between the kind of infection and gender among participants with vitamin D deficiency. The proportions do vary somewhat by gender, but this difference is not statistically significant (Figure 3).

Table 5. Relationships between various infection factors and vitamin D deficiency (< 25 ng/ml).

Gender	Bacterial infection	Viral infection	Fungal infection	Total
Males with vit. D < 25 ng/ml	21	6	9	36
Females with vit. D < 25 ng/ml	17	15	9	41
Total	38	21	18	77

P value = 0.137

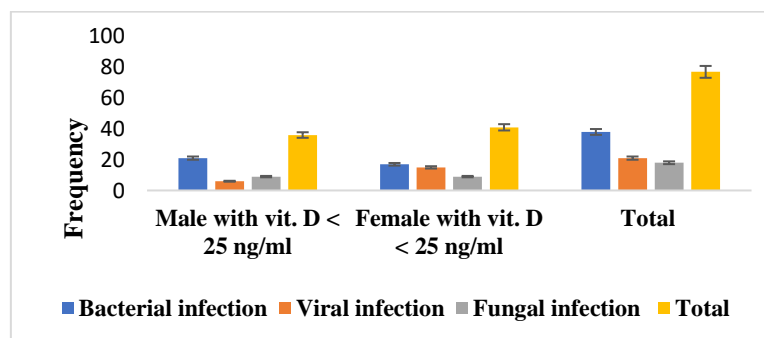


Figure 3. Relationships between various infection factors and vitamin D deficiency (< 25 ng/ml)

Using Pearson's correlation coefficient, table (5) shows a statistical examination of the relationship between vitamin D3 (VIT D3) levels in males and females. The association is statistically significant because $p < 0.05$. There is a weak positive association between male and female vitamin D3 levels, as indicated by the value of $r = 0.269$.

Accordingly, the sample population (N = 138) does not exhibit any significant linear associations between Age, CRP, VIT D3, and HGB. In other words, changes in one variable are not highly correlated with changes in another, according to the weak and non-statistically significant correlations that were found. In contrast, the findings of an analysis of variance (ANOVA) evaluating the influence of the independent variable (e.g., gender) on three dependent variables—

CRP, VIT D3, and HGB—indicate that gender is a significant factor in determining the levels of CRP and HGB, with a greater effect for HGB and no apparent impact for VIT D3.

Table 6. Correlation Between Vitamin D3 Levels in Females and Males

Vitamin D3 Levels		VIT D3 in Females	VIT D3 in Male
VIT D3 in Females	Pearson Correlation	1	.269*
	Sig. (2-tailed)		.032
	N	75	63
VIT D3 in Male	Pearson Correlation	.269*	1
	Sig. (2-tailed)	.032	
	N	63	63

*. Correlation is significant at the 0.05 level (2-tailed).

DISCUSSION

As a secosteroid, vitamin D was first identified for its involvement in the skeleton, but in recent years, its roles in several organs have come to light. Although risk factors like obesity, smoking, and/or having a high skin phototype make some people more vulnerable to low levels of vitamin D than others, there is currently a widespread concern about vitamin D deficiency in both the healthy and the sick population worldwide [34-37].

Although a previous study found that women were more likely to suffer from vitamin D insufficiency, a survey of 15,804 people in the United States indicated that vitamin D deficiency was more common among men [38, 39]. Similar findings to our study were found in another study by Albuloshi et al. [40] carried out in Kuwait, which found that vitamin D deficiency was somewhat more common in male participants than in female participants. They explained this finding by pointing out that more women may be taking vitamin D supplements than men [40].

Related to the possible relation between HGB concentration among males and females and the deficiency of Vitamin D, the current study found that Mean Hemoglobin concentration of females was 12.5 g/dL \pm 1.2, which was within the normal range for females but on the lower end (normal: 12.0–15.5 g/dL) and the variability in HGB level was low. Conversely, HGB concentration mean was 14.2 g/dl \pm 1.49, which was within the normal range (normal: 13.5–17.5 g/dL) (table 3). Remarkably, both males and females have borderline deficient vitamin D levels (around 25 ng/ml). Despite similar Vitamin D levels, males exhibit higher mean hemoglobin levels (14.2 g/dL) than females (12.5 g/dL). This suggests that gender-related biological differences in hemoglobin (e.g., hormonal differences) may outweigh the influence of Vitamin D deficiency.

Internationally, a cross-sectional meta-analysis found that the incidence of anemia was positively correlated with vitamin D deficiency [41]. According to this study, which had 5183 people, those who were vitamin D deficient were 64% more likely to develop anemia than those who were vitamin D sufficient [41]. In contrast to that, Vitamin D therapy in iron-deficient participants did not improve their clinical outcomes, such as hemoglobin and ferritin levels, according to another meta-analysis by Basutkar et al. [42]. Similarly, there was no discernible effect of varying vitamin D dosages on hemoglobin and ferritin levels in the clinical studies reviewed by Arabi et al. [43].

Additionally, the current study found that, in relation to the effects of vitamin D deficiency, females experience slightly more infections overall than males. The observed differences in infection types between males and females with vitamin D insufficiency are not statistically significant at the traditional $p < 0.05$ level, according to the p -value of 0.137. In this context, published studies consistently report a potential link between Vitamin D deficiency and increased susceptibility to infections, particularly bacterial and respiratory infections. Vitamin D is known to play an important role in modulating the immune system, enhancing the production of antimicrobial peptides, and reducing inflammation [44].

On the other hand, in agreement with the results of the current study, some studies suggest that males are more prone to bacterial infections due to differences in immune system function, while females may have higher rates of viral infections, potentially linked to hormonal and immune system variations [45, 46]. The results in table (5) align with these findings to some extent but are not statistically significant. As a result, opinions on whether vitamin D levels are related to the severity of atopic dermatitis lesions vary. The factors that led to this outcome are still being investigated. The potential correlation between CRP and vitamin D levels in male and female patients with various skin illnesses is covered in Table (3). According to this study, men have higher mean CRP levels than women (5.6 mg/dL vs. 3.7 mg/dL), which may indicate that men have a higher inflammatory load. According to certain research, males' greater CRP levels may be caused by comorbidities, smoking prevalence, or higher body mass index (BMI). Notably, published evidence suggests an inverse relationship between Vitamin D levels and CRP. Lower Vitamin D levels are associated with higher CRP and systemic inflammation, as Vitamin D modulates immune responses and reduces inflammation [47, 48].

CONCLUSION

The results of this study, which looked at how vitamin D deficiency affected skin infections and hemoglobin levels in Libyan men and women, showed that although vitamin D deficiency was more common in men than in women, the difference was not statistically significant. Adequate vitamin D levels were marginally more common in women. In addition, compared to females, males had higher levels of hemoglobin, the inflammatory marker CRP, and more variation in CRP and vitamin D levels. Although they displayed less variation in these measurements, females tended to have lower hemoglobin and CRP levels. Furthermore, there were tendencies in the types of skin diseases by gender, with some fungal infections primarily affecting men and viral infections being more prevalent in women. However, the association between infection type and gender was not statistically significant. No strong linear relationships were found between age, CRP, vitamin D levels, and hemoglobin in the overall sample. Gender was a significant factor affecting CRP and hemoglobin levels, with a stronger impact on hemoglobin. Vitamin D levels showed no significant influence from gender. Overall, the study highlights notable differences in vitamin D status, immune responses, and infection patterns between genders, though many observed disparities were not statistically significant. Dependently, these results recommend more investigations and researches should be done to explore the relation of vitamin D level with different variables related to the skin infection.

Author Contributions

All authors participated in writing, review, editing. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest.

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آثار نقص فيتامين د على مستويات الهيموجلوبين والالتهابات الجلدية لدى الليبيين في مختلف الأعمار

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المستخلص

تتناول هذه الدراسة تأثير نقص فيتامين د على مستويات الهيموجلوبين والالتهابات الجلدية لدى 138 رجل وامرأة ليبي في مختلف الأعمار. أجريت دراسة مقطعية في مدينة العجيلات، خلال الفترة من يونيو إلى سبتمبر 2024. تم تضمين إجمالي 63 (45.35%) من الذكور و 75 (54%) من الإناث في هذه الدراسة، مع التهابات جلدية مختلفة من مختلف الأعمار. تم استخدام محلل الدم الدموي لتقييم تركيز الهيموجلوبين في عينات الدم الوريدي التي تم الحصول عليها في أنابيب EDTA. كما تم استخدام اختبار المناعة القائم على ELISA التنافسي لتقييم فيتامين د (25-هيدروكسي كوليالكالسيفيرول) في مصل المرضى. كان نقص فيتامين د أكثر انتشاراً لدى الرجال (60.3%) منه لدى النساء (49.3%)، على الرغم من أن الفرق لم يكن ذا دلالة إحصائية (ص = 0.263). كانت مستويات الهيموجلوبين أعلى لدى الرجال (متوسط: 14.2 جم / ديسيلتر) من النساء (متوسط: 12.5 جم / ديسيلتر)، مما يعكس الاختلافات البيولوجية المحتملة بين الجنسين. أظهر المشاركون الذكور أيضاً تبايناً أكبر في مستويات فيتامين د والعلامات الالتهابية. كشفت أنماط العدوى عن اتجاهات مرتبطة بالجنس، حيث كانت العدوى الفطرية أكثر شيوعاً لدى الرجال والعدوى الفيروسية لدى النساء. ومع ذلك، فإن الارتباط بين أنواع العدوى والجنس لم يكن ذا دلالة إحصائية (ص = 0.137). أثر الجنس بشكل كبير على مستويات العلامات الالتهابية والهيموجلوبين ولكن لم يكن له تأثير واضح على مستويات فيتامين د. لم يتم ملاحظة أي ارتباطات قوية بين فيتامين د أو العلامات الالتهابية أو الهيموجلوبين أو العمر. تسلط النتائج الضوء على الاختلافات بين الجنسين في حالة فيتامين د والاستجابات المناعية وأنواع العدوى، على الرغم من أن معظم الاختلافات تفتقر إلى الدلالة الإحصائية. تؤكد الدراسة على الحاجة إلى مزيد من البحث لتوضيح دور فيتامين د في التهابات الجلد وتفاعله المحتمل مع مستويات الهيموجلوبين والعلامات المناعية.

الكلمات الدالة: نقص فيتامين د، عدوى الجلد، تركيز الهيموجلوبين، 25 هيدروكسي فيتامين د.