VITAMIN D STATUS IN PATIENTS WITH PLAQUE PSORIASIS: RELATION TO DISEASE SEVERITY

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ABSTRACT

Background: There is increasing evidence on the association between vitamin D insufficiency and plaque psoriasis, but the impact of vitamin D status on disease severity and vice versa has not been well reported. The present study was aimed to investigate the level of 25-hydroxyvitaminD [25(OH)D] and the prevalence of vitamin D abnormalities in patients with plaque psoriasis and in those without psoriasis and to study the association between vitamin D level and disease severity.

Materials and Methods: This case-control study was conducted at the Dermatology Outpatient Clinic, Azadi Teaching Hospital from November2018 to March 2019, which included 77adult patients with plaque psoriasis and109 healthy individuals. The two groups were matched for age, sex and BMI. The Psoriasis Area and Severity Index (PASI) of disease were determined and categorized as follow: Mild-to-Moderate: PASI score <12 and severe – PASI score >12.Vitamin D status was assessed by measurement of serum 25(OH)D concentrations.

Results: Significantly lower 25(OH)D levels($p<0.001$) were found in psoriatic patients compared to healthy individuals. The mean 25(OH)D was lower in patients with severe disease state in comparison with that for mild or mild-to-moderate severity ($P=0.170$ and $p= 0.057$, respectively).Patients with insufficient 25(OH)D <20 ng/ml had a higher PASI score compared to those with adequate 25(OH)D >20 ng/ml (16.30 vs. 11.35, $p=0.032$).The vitamin D deficiency quantitated by 25(OH)D<10 ng/ml was detected in 19(24.7%) of patients with plaque psoriasis as compared to 13(11.9%) in healthy individuals($p<0.010$).

Conclusions: A low vitamin status is present in the majority of patients with plaque psoriasis, particularly among those with severe disease.

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Keywords: …….

Vitamin D deficiency has been shown to play an important role in the incidence and unfavorable prognosis of a wide range of diseases including cardiovascular, cancer, infectious diseases and autoimmunediseases[1], of The autoimmune diseases that related to low vitamin D levels are rheumatoid arthritis[2], multiple sclerosis[3], diabetes mellitus[4], systemic lupus erythematosus[5] and psoriasis[6]. Plaquepsoriasis is considered to be a chronic inflammatory disease. This disease involves the innate and acquired immune system. The role of immune-regulatory of vitamin D impacts both the innate and adaptive immune system results in the immune tolerance of self-structures. The data regarding association of vitamin D deficiency and plaque psoriasis severity are controversial[7]. On the other hand, the effectiveness of vitamin D analog to treat psoriasis plaques is a matter of

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investigation by dermatologists and other physicians[8]. Hence, it is essential to know the level of serum vitamin D and the prevalence of vitamin D deficiency among patients with plaque psoriasis. As data on the subject is scared particularly in the population of Kurdistan region, Iraq[9]. To gain into the association between vitamin D and psoriasis, we measured serum 25(OH)D level and analyzed its relation to PASI score in a sample of patients with plague psoriasis.

MATERIALS AND METHODS

Patients and study design

This case-control study was performed at the Dermatology Outpatient Clinics, Azadi General Teaching Hospital in Duhok, Kurdistan Region, Iraq, from November 2018 to March 2019. It had been formally approved by the Research Ethics committee; Directorate of Health of Duhok and the Institutional Review Board of Duhok College of Medicine with the reference number of (27032018-2). Chronic plaque psoriasis of varying severity who attended the Outpatient Clinic was included in this study. The healthy individuals as a control group were recruited from the staff and workers of the same hospital and matched for age, gender, and BMI.A verbal consent was taken from all patients and healthy individuals. Inclusion criteria were patients with clinical chronic plaque psoriasis and apparently healthy individuals with negative family history of psoriasis. Patients with renal impairment, chronic liver disease, and patients who received topical vitamin D analogue and systemic supplement for the last two months and exposed to phototherapy for the last six months were excluded from the study.

Diagnosis and Severity of Psoriasis

The diagnosis of psoriasis was based on the criteria of Canadian Psoriasis Guidelines Committee, 200910. The severity of the disease was measured using the Psoriasis Area and Severity Index (PASI), categorized as follows: Mild-to-Moderate - PASI score <12 and severe –PASI score >12.

Data collection

The general and anthropometric information was taken from all patients and healthy individuals that included age, sex, height, weight, metabolic diseases, family history of psoriasis and drug history. Body Mass Index (BMI) was calculated by dividing weight in Kg by squared height in meter. The category of BMI was arranged as follows: healthy weight 18.5–24.9 kg/m^2, overweight 25 – 29.9 kg/m^2 and obese more than 30 kg/m2[11].

Assessment of vitamin D status

The vitamin D status was assessed according to the following criteria; severe deficiency-serum 25(OH)D concentration below 10 ng/ml. insufficency10-30 ng/ml and sufficiency>30 ng/ml. A cutoff point of<20 ng/ml of 25 (OH)D was used to classify patients as on low vitamin D status.

Sample Collection

Morning Blood samples were collected between 9.00-11.30 AM at the Lab Department of Clinical Biochemistry at Azadi General Teaching Hospital. About 5ml of blood was withdrawal by venipuncture using vacutainer from the antecubital vein and collected in BD Vacutainer System CAT-plain tubes; the serum was separated by centrifugation at 3000 rpm for 10 minutes. Then, the serum was used for analysis of serum 25(OH) D.

Biochemical Analysis

Cobas 6000 Roche (open, automated, discrete and random-access measured serum concentration of 25(OH) D depending on electrochemiluminescence immunoassay. The measurement was performed through employing vitamin D Binding protein (VDBP) in capturing both 25-hydroxyvitamin D3 and D2. This assay for quantitative determination of total vitamin D sufficiency.

Statistical analysis

Values were expressed as mean ± standard deviation, a significance level of difference was determined using the student's t-test.

Intergroup comparison analyzed by one-way analysis of variance (ANOVA). P<0.05 was considered statistically significant. The statistical calculations were performed by Statistical Package for Social Science SPSS version 24 (SPSS 24; IBM Corp; USA).

RESULTS

This study included 77 patients with plaque psoriasis and 109 healthy individuals as controls. Moderate-to-severe psoriasis was observed in 93.5% of the patients (n=72). The general information of the patients with psoriasis and the controls has been described in [Table 1]. Fifty-seven (74.0%) patients were on drugs for disease treatment, and 22 patients (28.6%) had a family history of psoriasis. The mean value of the PASI score was 14.56 (Interquartile Range [IQR]: 26.60), ranged between 6.0 and 56.0. The mean disease duration 4.0 years, ranged between half and 30 years. The serum 25(OH) D concentration was significantly lower in patients compared to controls (14.60 +7.82 vs. 23.91+10.68 ng/ml), P<0.001.

Table 1- General information of patients and controls

Variables	Cases	Controls	*P*-value
Number	**77**	**109**	
Age (year)	36.56±14.60 Range: 18-70 years	36.13±11.79 Range: 18-74 years	0.825*
Sex			0.730**
Male	38 (49.4)	51 (46.8)	
Female	39 (50.6)	58 (53.2)	
BMI (Kg/m^2)	27.38±6.48 Range: 15.56-46.56	27.07±4.62 Range: 17.75-37.10	0.723*
Drug history	57 (74.0%)	-	
Family history	22 (28.6%)	-	
Disease duration (year)	4.00±9.50 Range: half-30	-	
Disease severity PASI score	14.56±27.55 Range: 6.0-56.0	-	
25(OH)D (ng/mL)	14.60±7.82 Range :4.43-38.68	23.91±10.68 Range:7.50-52.70	<0.001*

*Independent t-test and **Chi-square tests were performed for statistical analyses.
The data for disease duration, disease severity, and PASI score are median (Interquartile range). Other data are in Mean ± Standard deviation.

The prevalence of low vitamin D status (25(OH)D <20 ng/ml) was found among 64.9% patients with plaque psoriasis compared to 37.6% in the controls, p<0.001. Severe vitamin D deficiency [25(OH)D<10 ng/ml was found in 24.7%of patients compared to 11.9%, p<0.001in healthy controls [Table2].

Table 2- Vitamin D level in patients with psoriasis and controls

25(OH) D (ng/ml)	Cases (n=77) n (%)	Controls (n=109) n (%)	*P*-value
< 20 (Deficiency)	50 (64.9)	41 (37.6)	<0.001
20-30 (Insufficiency)	23 (29.9)	35 (32.1)	
30 – 100 (Normal)	4 (5.2)	33 (30.3)	
< 10 (Severe Deficiency)	19 (24.7)	13 (11.9)	<0.001
10-30 (Insufficiency)	54 (70.1)	63 (57.8)	
30 – 100 (Normal)	4 (5.2)	33 (30.3)	

Table 3illustratesthe mean ± SD of age, BMI, disease duration and PASI score stratified by 25 (OH) D cutoff points of 20 ng/ml. Patients with 25(OH) D levels < 20

ng/ml had significantly higher PASI score and lower age compared to those with 25(OH) D >20 ng/ml (P=0.032 and p=0.036, respectively). No statistically significant differences were found in the sex distribution, BMI, drug history, family history and disease duration.

Table 3- Baseline characteristics in psoriasis patients with 25(OH)D less and more than 20 ng/mL

Variables	25 (OH)D <20 ng/ml	25 (OH)D ≥20 ng/ml	*P*-Value
Number	50	27	
Age (year)	29.5±26.5	42.0±20.0	0.036*
Sex			0.09**
Male	21 (42.0)	17 (63.0)	
Female	29 (58.0)	10 (37.0)	
BMI (Kg/m^2)	25.69±12.68	27.82±4.98	0.173*
Drug History			0.591**
yes	38 (76.0)	19 (70.4)	
no	12 (24.0)	8 (29.6)	
Family History			0.880**
yes	14 (28.0)	8 (29.6)	
no	36 (72.0)	19 (70.4)	
Disease duration (year)	4.5±9.5	4.0±9.0	0,871*
PASI Score	16.30±29.20	11.35±24.85	0.032*

* Mann-Whitney U-test and ** Pearson Chi-Square test were performed for statistical analyses.

Table 4 illustrates mean +SD of 25(OH)D in patients with different disease severity. Patients with severe disease state had a lower vitamin D level compared with that of mild or mild to moderate severity, but the difference was not significant, (P=0.170 and p= 0.057, respectively).

Table 4- Serum 25(OH) D levels in patients with different disease severity

Disease state	Number	25 (OH)D (ng/ml)	*P*-value
Mild (PASI Score <7)	5	18.32±8.26	0.170*
Moderate (PASI Score 7-12)	28	15.20±7.06	
Severe (PASI Score >12)	44	13.81±6.15	
PASI Categories			0.057**
Mild-Moderate (PASI Score ≤12)	33	15.67±6.86	
Severe (PASI Score >12)	44	13.81±6.15	

*ANOVA-One way and **Independent t-tests were performed for statistical analyses.

DISCUSSION

The results of this study showed significantly higher prevalence of severe vitamin D deficiency together with lower mean 25(OH)D levels in patients with plaque psoriasis in Duhok compared to healthy individuals. The results confirm an association between low vitamin D status and disease severity, as the mean PASI score observed in patients with low vitamin D status [25(OH)D<20 ng/ml] was significantly higher than that observed in patients with[25(OH)D>20ng/ml]to include specifics on how they align with previous studies. It is important to note that the majority of the patients enrolled in the present study had moderate-to-severe disease, and with low vitamin D status, suggesting that vitamin D status play an important mechanism through which severe deficiency can influence higher risk of psoriasis and may be the main determinant of disease severity. In agreement with this finding, a study by Pokharel and his colleagues12have reported a link between low concentration of vitamin D and disease severity in patients with plaque psoriasis. Other studies have supported this observation, reporting that vitamin D

deficiency results in a positive impact on disease severity13,14. The level of serum vitamin D in psoriasis patients compared to in healthy individual has been assessed in other settings as well. For example, Atwaand his colleagues2 conducted a cross-sectional study in Saudi Arabia from March to September 2012. In contrast with our findings, they did not find a link between low concentration of vitamin D and disease severity in patients with psoriasis. But they also found that vitamin D levels were significantly lower in psoriasis patients compared to their matched controls. This lower level of the vitamin was found even after adjustment for confounding factors. The low levels of 25(OH)D have been shown to associate with C-reactive protein and BMI and patients with a BMI greater than 27 kg/m2 had a higher risk of 25(OH)D insufficiency15.The association of BMI and 25(OH)D was studied, and the results showed that BMI nearly similar in patients with different vitamin D status. These results are in agreement with previous studies 16,17.

The link between age and vitamin D status has been studied, but the results are controversial yet. Nayak and his colleagues18observed a direct correlation between age and vitamin D, While others did not find this kind of association19, 20.The results confirm a link between age and vitamin D status, with the lowest serum 25(OH)D levels found in younger psoriasis patients, which is similar to results of other studies22.

The potential mechanism behind vitamin D function may involve in the high levels of vitamin D receptor (VDRs) that found on dendritic cells, T and B lymphocytes, and macrophages. These cells are functionally affected by the binding of activated 1, 25(OH)D23. Furthermore, there is some evidence that emphasized vitamin D has a regulatory role in immune system. The presence of vitamin D receptors (VDRs) has been found in most immune cells, such as activated CD4+ and CD8+ lymphocytes, and dendritic cells24,25. Thus, the levels of vitamin D and its cell receptor could be an important mechanism in reducing disease severity in autoimmune disease. Accumulative evidence supports a wide array of immune-regulatory effects by vitamin D, including anti-inflammatory effects among patients with plaque psoriasis26, 27.

As expected, severe psoriasis is associated with lower levels of 25(OH)D and unfavorable changes in disease severity. This finding may confirm that a low vitamin status is present in the majority of patients with plaque psoriasis, particularly among those with severe disease. This may reflect the additive effect of vitamin D status on disease severity. A limitation of our study is the small sample size and the limited number of settings from which participants were drawn in addition; the inadequate number of mild cases observed in the study is another limitation. Consider suggesting that future studies include larger sample sizes and account for additional variables such as socioeconomic status, dietary factors, and seasonal variations. Infectious diseases and types of treatments may play interacting roles with vitamin D status that predispose psoriasis.

CONCLUSION

This study indicated that approximately two thirds of the patients with psoriasis were with low vitamin D status. This lower vitamin D status appeared to be more prevalent in those with severe psoriasis, but it was no significant association between 25(OH) D concentration and disease severity.

RECOMMENDATION

The patients with psoriasis are required to be screened for concentration of vitamin D in the routine clinical practice.

The vitamin D supplementation could be suggested as an effective public health intervention in general population.

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پوختە

دۆخی ڤیتامین D لە نەخۆشانی تووشبوو بە پلاکی سەدەف: پەیوەندی بە تووندی نەخۆشییەکە

پێشەکی و ئارمانج: کێم بونا ڤیتامین دی بەیوەندی دگەل هەژمارەکا مەزن یا نەخوشی یان هەیە . سۆرایسس نەخۆشیە کا ئیلتیهابی یە کو سیستە می ئیمناهیا زکماکی و نە زکماکی پەیوەندیار دکە ت .

ئارمانجا فەکۆلینا مە دڕوست کرنا زانیاری بین دە ستبیکی لسە رە وشا فیتامین دی دە ف کومە ك ز نە خوششین سورایسس ل بازیری دهوکی.

شێوە : ئە ف فەکۆلینە نەخۆش- کۆنترۆل ل پشکا پێستی ناسی ل نەخۆشخانەیا ئازادی یا فیرکرنی د نافبە را هە یفا ئە بریل و ئوکتوبە را 2018 هاتیە پەنجام دان . فەکۆلین لناف ئە و نە خوشیین کو ب سورایسس هاتن ناسین ب دزواری بین جوداجودا هاتە ئە نجام دان .نە خوشییا سورایسس ب با سی سکور هاتە بیفان . زمارە یا کیمتر ز 12 وە کو نە خوشیا سفك / نا فە ند و زید ە تر ز 12 وە کو نە خوشییا دزوار هاتە نیاسین .

ئەنجام : تە مە نی نە خوشان 36.56 دنافبە را 18-70 سالّ ل هە مبە ر 36.13 دنافبە را 18-74 سالّ لناف کونترول .نەخۆشین بە ر لە 4 سالان نە خوش کە تبوون دزواریا نە خوشی یا ئە وان 15.0 بو . فە کولینا مە نیشان دا کو ریزیا فیتامین دی لناف نە خوشان ب شیوە یە کی بە رجاف ل هە مبە ر کونترولان کیمترە , 16.90 ل هە مبە ر 23.91 .هیج بە یوە ندیە کا بە رجاف دنا فبە را دزواریا نە خوشی یا سورایسس وفیتامین دی بە یدا نە بو

د ە رئە نجام : فەکۆلینا مە بیشنیا ر دکە ت ریزیا ڤیتامین دی لناف نەخۆشیین سۆرایسس لهمبە ر کە سین ساخلە م کیمترە

پەیڤێن سەرەکی : ڤیتامین دی، سورایسس، دژواریا نەخۆشیئ

الخلاصة

حالة فيتامين د لدى المرضى الذين يعانون من الصدفية اللويحية: العلاقة مع شدة المرض

الخلفية والأهداف: لقد تبين أن نقص فيتامين (د) يساهم في الاصابة والتشخيص لمجموعة واسعة من الأمراض . الصدفية هي مرض التهابي مزمن يتضمن الجهاز المناعي الفطري والمكتسب . الغرض من هذه الدراسة هو أنشاء بيانات أساسية عن حالة فيتامين (د) في عينة من المرضى الذين يعانون من الصدفية في مدينة دهوك .

الطريقة : كانت هذه دراسة الحالات والشواهد التي أجريت في عيادات الأمراض الجلدية الخارجية – مستشفى أزادي التعليمي بين أبريل وأكتوبر 2018. تم تسجيل المرضى البالغين الذين يعانون من الصدفية الذين تم تشخيصهم مع شدة مختلفة في هذه الدراسة . تم تعيين الضوابط الصحية المتطابقة للعمر والجنس ومؤشر كتلة الجسم من شركاء أو أقارب المرضى ألذين ليس لديهم مرض الصدفية. تم قياس شدة المرض عن طريق مؤشر الصدفية ومنطقة الشدة (PASI SCORE) وتصنيفها على النحو التالي: درجة معتدلة PASI SCORE < 12 - والنتيجة الشديدة PASI > 12 -SCORE

النتائج: كان متوسط عمر المرضى 36.56 (SD:1460) تراوحت 18-70 سنة مقارنة ب 36.13 :SD) (11.79 تراوحت بين 18- 74 عاما في الأشخاص الأصحاء. كان متوسط مدة المرض للمرضى الذين يعانون من الصدفية 4.0 سنوات .و كان متوسط شدة المرض 15.0 . كان المرضى الذين يعانون من الصدفية تركيز أقل بكثير من فيتامين D في الدم) 16.90 SD:7.82) نانوجرام / مل (مقابل23.91(SD:10.68) .

P <0.001 . 16.30 لم تجد الدراسة العلاقة الكبيرة بين شدة المرض وتركيز فيتامين د. (P= 0.611)

الأستنتاجات : تشير الدراسة الحالية الى أن المرضى الذين يعانون من الصدفية لديهم تركيز أقل بكثير من فيتامين (د) مقارنة مع الضوابط الصحية المتطابقة مع تقدم العمر .

كلمات مفتاحية : فيتامين د . الصدفية ، شدة المرض