Journal of Medical & Pharmaceutical Sciences
Volume (6), Issue (3) : 30 Jun 2022
P: 40 - 51
ISSN: 2522- 333X
مجلة العلوم الطبية والصيدلانية
المجلد (6)، العدد (3) : 30 يونيو 2022 م
ص: 40 - 51

Evaluation of serum Calcium level in psoriatic patients

Noura Shokri Jomah
Mohamad Adel Ismaiel
Jamal Khadam
Faculty of Medicine || Tishreen University || Syria

Abstract: Background: Psoriasis is a chronic immune- mediated skin disease, with a genetic predisposition. Many factors can trigger or exacerbate psoriasis. Recently, some studies found that psoriasis was associated with hypocalcemia. So we did this study to find this association in our patients.

Objective: To evaluate serum calcium level in psoriatic patients and compare it with controls.

Methods: This case- control study included 160 subjects (80 patients with psoriasis and 80 controls) admitted to dermatology clinic at Tishreen University Hospital, Latakia, Syria, from 2020- 2021. Serum calcium and serum albumin levels were estimated in all patients.

Results: Calcium levels were significantly lower in psoriatic patients than in the control group (mean = 8.98±0.5 in patients vs 9.48±0.5 in controls, p- value<0.001). Calcium levels were significantly lower in patients with severe types of psoriasis (p-value<0.05). There was an inverse correlation between serum calcium levels and PASI score (r =- 0.3, p- value<0.05). There was also an inverse correlation between serum calcium levels and each of age and disease duration.

Conclusion: In this study, a low calcium level was observed in psoriatic patients. Hypocalcemia may be a marker for the severity of psoriasis. In addition, Calcium seems to have a role in the pathogenesis of psoriasis.

Keywords: psoriasis, hypocalcemia, calcium, serum level, PASI score.

تقييم مستوى الكالسيوم المصلي عند مرضى الصداف

نورا شكري جمعة
محمد عادل إسماعيل
جمال خدّام
كلية الطب البشري || جامعة تشرين || سوريا

المستخلص: خلفيّة الدّراسة: الصداف هو مرض جلدي التهابي مزمن مع تأهب وراثي للإصابة. هناك العديد من العوامل التي يمكن أن تحرّض الصداف أو تفاقمه. مؤخراً وجدت بعض الدراسات أن الصداف يترافق مع نقص مستوى الكالسيوم المصلي. لذلك قمنا بهذه الدراسة لكشف هذا الترافق عند مرضانا.

الهدف: قياس مستوى الكالسيوم المصلي لدى مرضى الصداف ومقارنته مع مستوياته عند الشّواهد.

الطرق: الدراسة الحالية من نمط حالة- شاهد، شملت 160 مريضاً (80 مصاباً بالصداف و80 شاهداً) من مراجعي العيادة الجلديّة في مشفى تشرين الجامعي- اللاذقية- سوريا، بين عاميّ (2020- 2021). تم تقييم مستوى الكالسيوم والألبومين المصلي عند كل المرضى.

النتائج: أظهر مرضى الصداف قيماً أخفض للكالسيوم المصلي مقارنةً بمجموعة الشواهد (بلغ متوسط قيم الكالسيوم عند المرضى 8.98±0.5 مقابل 9.48±0.5عند الشواهد، p- value<0.001). كانت مستويات الكالسيوم المصلي أقل بشكل واضح في الأشكال الخطيرة

للصداف(p- value<0.05) . كانت هناك علاقة ارتباط عكسية بين مستوى الكالسيوم المصلي وشدّة الصداف مقدرة ب PASI score (r =- 0.3, p- value<0.05). أظهرت الدراسة أيضاً علاقة ارتباط عكسية بين مستوى الكالسيوم المصلي وكلّ من العمر ومدة الإصابة بالصداف.

الخلاصة: تم ملاحظة وجود نقص في مستوى الكالسيوم المصلي عند مرضى الصداف في هذه الدراسة، كما أن نقص كلس الدم قد يكون مشعراً لشدة الصداف. بالإضافة لذلك، يبدو أن للكالسيوم دوراً في إمراضية الصداف.

الكلمات المفتاحية: صداف، نقص كلس الدم، كالسيوم، المستوى المصلي، شدة الصداف مقدرة ب PASI score.

INTRODUCTION.

Psoriasis is a group of common, chronic, inflammatory and proliferative conditions of the skin, associated with systemic manifestations in many organ systems. The most characteristic lesions consist of red, scaly, sharply demarcated, indurated plaques, present particularly over the extensor surfaces and scalp. The point prevalence rises during childhood, and in adults. [1] Psoriasis affects approximately 2–3% of general population. Isolated studies have reported on the incidence of psoriasis in the Middle East, including a small, Single- Centre study, that found the incidence of psoriasis to be 1.5% and 3.4%, in south- western and eastern Saudi Arabia, respectively. [2]

Psoriasis is characterized histologically by cutaneous inflammation, increased epidermal proliferation, hyperkeratosis, angiogenesis, abnormal keratinization, shortened maturation time and parakeratosis. [3]

Five main types of psoriasis have been reported: plaque psoriasis, guttate psoriasis, inverse psoriasis, pustular psoriasis; and erythrodermic psoriasis. [4]

A number of risk factors have been recognized in the etiopathogenesis of psoriasis, including family history and environmental risk factors, such as diet, obesity, smoking, stress and alcohol consumption. [3]

The activation of innate and adaptive inflammatory cellular immune responses is considered to be the main trigger factor of the epidermal changes in psoriatic skin. However, the molecular players that are involved in enhanced proliferation and impaired differentiation of psoriatic keratinocytes are only partly understood. One important factor that regulates differentiation on the cellular level is Ca^{2+}. In normal epidermis, a Ca^{2+} gradient exists that is disturbed in psoriatic plaques, favoring impaired keratinocyte proliferation. [5] This leads to parakeratosis and abnormal desquamation and permeability barrier in psoriasis. [6]

It has been observed that there is disturbance in the metabolism of calcium in few cases with psoriasis. “Pustular psoriasis of Von Zumbush” has been found to be associated with mild hypocalcemia. [7]

Reportedly, Hypoparathyroidism, which may be primary or may be due to surgical removal, is found to aggravate the condition of psoriasis. Even pseudo hypoparathyroidism has also been found to be associated with psoriasis. [8]

Prescribing some calcium channel blockers such as diltiazem to some patients have resulted in developing psoriasiform rashes. The leisions have recovered after stopping the drugs consumption. [9]

Moreover, we showed that topical application of 1- 25, dihydroxyvitamin D, a well- known calcitropic hormone, improved skin lesions of psoiatic patients. [10]

Although vitamin D plays an important role in regulating the level of serum calcium, the main goal of this study was to look for a possible association between hypocalcemia and psoriasis regardless of the level of vitamin D.

IMPORTANCE OF THE STUDY:

Depending on the previous factors, several studies have approved the close relation between hypocalcemia and psoriasis. So we did this study to investigate the presence of this relationship in our patients.

If this relationship is proven, calcium can be considered as a risk factor for psoriasis in our country. A routine blood test for calcium level should therefore be performed in all psoriatic patients. Accordingly, calcium supplements are recommended to treat the disease.

AIM of the study:

The main objective of this study was to evaluate the serum calcium level in psoriatic patients in comparison with controls, and correlate it with the severity of psoriasis (PASI score).

The secondary objective was to study the correlation between serum calcium level in psoriatic patients and each of the following variables: age, sex, type of psoriasis and disease duration.

MATERIALS AND METHODS.

Study design: this case control study was carried out in department of dermatology and venereology, Tishreen University hospital, Latakia, Syria over period of March 2020 to March 2021.

Size of sample: The study enrolled 160 subjects of either sex with different age groups.

Group 'A' (Cases) involved 80 Patients of chronic psoriasis of different age and sex who attended Department of Dermatology and Venereology over a period of 1 year.

Group 'B' (Controls) included 80 age and sex matched healthy individuals without psoriasis.

Inclusion criteria: Inclusion criteria were only clinically and histopathologically diagnosed cases of psoriasis.

Exclusion criteria: Exclusion criteria were patients of psoriasis suffering from any chronic medical disease; thyroid or parathyroid disease; patients of psoriasis on current consumption of vitamin D (within two months); patients receiving concomitant treatments with the ability to influence serum calcium; pregnancy and lactation.

Study tools: All the patients underwent a medical questioning, clinical examination and laboratory tests.

Testing of blood samples were conducted in biochemistry laboratory in Tishreen University Hospital, Latakia, Syria. About 5 ml of blood sample was collected using a sterile capped tube, and serum calcium and albumin levels were measured. Normal range of serum calcium was accepted 8.8–10.3 mg/dl.

Serum Calcium was assessed by Colorimetric method. Calcium ions reacts with Arsenazo III to form an intense purple coloured complex. In this method the absorbance of calcium- Arsenozo III complex measured biochromatically at 660/700nm. The resulting increase in absorbance of the reaction mixture is directly proportional to calcium concentration in the sample. [11]

In patients found to have hypoalbuminemia, calcium levels were corrected prior to interpretation by the following equation:

Corrected calcium (mg/dl) = total calcium (mg/dl)+ 0.8* (standard albumin level- serum albumin). [12]

The data regarding age, sex, symptoms, duration of disease, treatment history, smoking and alcohol, family history, history of chronic diseases were recorded in the Form. A detailed general physical examination was conducted. Type and distribution of lesions were noted. PASI (Psoriatic Area Severity Index) Scoring index was used to evaluate the severity of the disease and categorized into mild (PASI <10), moderate (PASI 10- 20) and severe (PASI >20). [13]

Data Processing and Statistical Analysis: A packaged computer analysis program, statistical package for the social science (IBM SPSS statisticsVersion20) will be using for statistical analysis of this data. Chi- square test was used to find the significance of study parameters on categorical scale and Pearson test was used to find correlation. The coefficient of correlation r signifies the amount of co-variation between two variables which can range from +1 to- 1. One- way ANOVA was used for normally distributed parametric variables when comparing three groups. Variables were presented as the mean ± standard deviation, and median and range in the parenthesis where appropriate. P- value < 0.05 was considered statistically significant.

Ethical considerations: Written consent was obtained from the participants who agreed to participate in this study.

RESULTS.

The present study involved 80 patients of psoriasis (41 males and 39 females) and 80 controls (41 males and 39 females). The ages ranged between 7 and 76 years, the median age was 43.

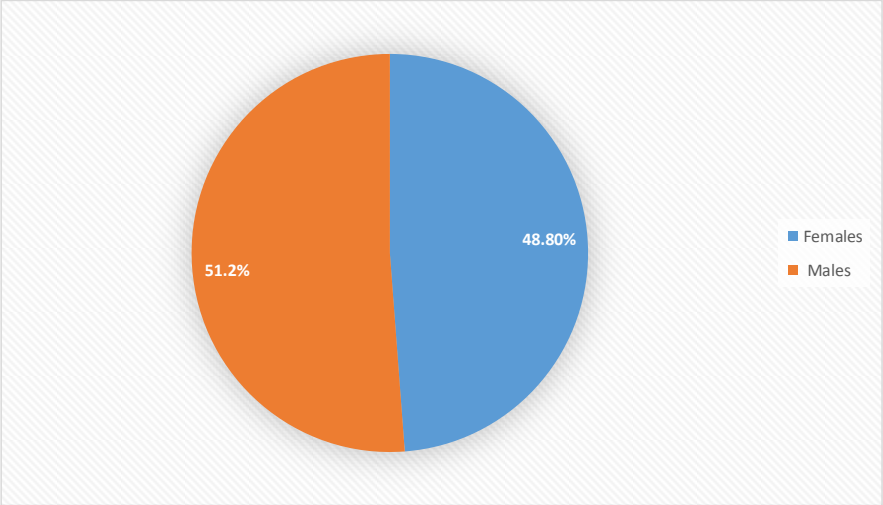

Figure (1) Distribution of study sample according to sex.

Table (1) gives the distribution of 80 cases of psoriasis and 80 controls according to sociodemographic variables.

	Cases	Controls	p- value
Sex Males Females	 41 (51.3%) 39 (48.8%)	 41 (51.3%) 39 (48.8%)	1
Age	43.5[7- 76]	43[7- 74]	0.9

Cases and controls had similar distribution according to age and sex.

The duration of psoriasis ranged from 6 months to 45 years with an average duration of 10 years.

Table (2) gives the distribution of 80 cases of psoriasis according to disease duration.

Duration of disease	Number	Percentage
< 5 yr	17	21.25%
5- 15 yr	40	50%
> 15 yr	23	28.75%

The previous table showed that in 50% of psoriatic patients, the duration of psoriasis was 5- 15 years.

Table (3) gives the distribution of 80 cases of psoriasis according to type of psoriasis.

Type of psoriasis	Number	
Plaque Psoriasis	25	65%
Palmoplantar Psoriasis	11	13.8%
Nail Psoriasis	8	10%
Scalp Psoriasis	6	7.5%
Erythrodermic Psoriasis	4	5%
Generalized Pustular Psoriasis	2	2.5%

Type of psoriasis	Number	
Localized Pustular Psoriasis	2	2.5%
Guttate Psoriasis	2	2.5%
Inverse Psoriasis	1	1.3%
Psoriatic Arthritis	1	1.3%

The previous table showed that 65% of cases suffered from plaque psoriasis, followed by 13.8% suffered from Palmoplantar psoriasis; knowing that the patient may have more than one type of psoriasis.

PASI score ranged from 1 to 66 with average score of 10.3.

Table (4) gives the distribution of 80 cases according to severity of psoriasis.

Severity of psoriasis	Number	Percentage
Mild (PASI<10)	38	47.5%
Moderate (PASI=10- 20)	26	32.5%
Severe (PASI>20)	16	20%

The previous table showed that 47.4% of psoriatic patients were with mild severity, followed by 32.1% with moderate severity.

Table (5) Mean serum calcium levels in psoriatic patients compared with controls is presented in table 5.

	N	Mean±SD (Ca)	Range	p- value
Cases	80	8.98±0.5	7.80 – 10.10	0.0001
Controls	80	9.48±0.5	8.40 – 12.10	

As a result of this study, serum calcium levels were lower in psoriatic patients compared to the controls with significant differences.

Hypocalcemia was found in 27 psoriatic patients by 33.75%, while in controls hypocalcemia was found in 6 cases by 7.5% and hypercalcemia in 2 cases by 2.5%.

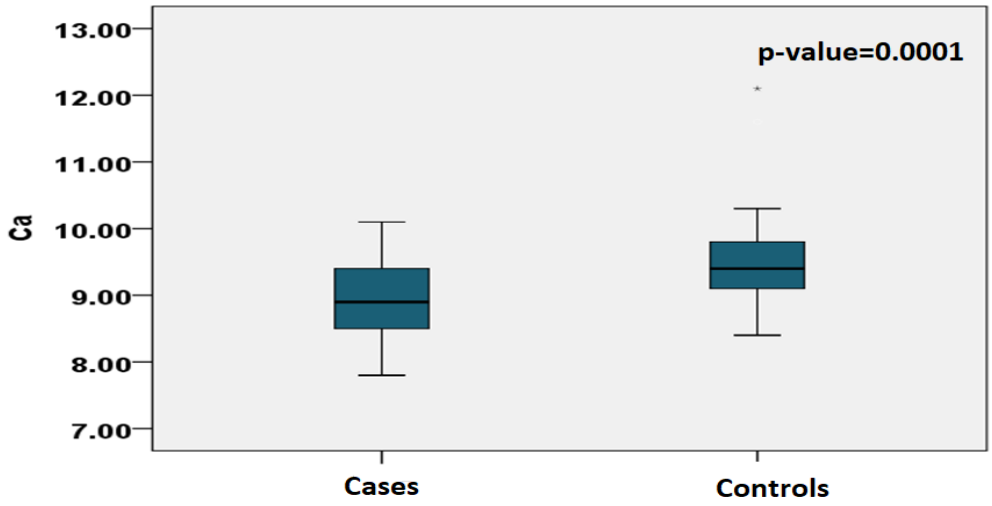

Figure (2) Mean serum calcium levels in cases and controls

Relationship between serum calcium level and sex in psoriatic patients:

The relationship between serum calcium level and sex was studied using the Independent t student test. The serum calcium level was lower in males compared to females with no statistically significant differences (p- value>0.05).

Table(6) Mean serum calcium levels in psoriatic patient according to sex is presented in table 6.

Sex	N	Mean ± SD	Range	p- value
Males	41	8.90±0.5	7.80 – 10.10	0.2
Females	39	9.06±0.6	7.90 – 10.10	

Relationship between serum calcium level and age in psoriatic patients:

The relationship between serum calcium level and age was studied using the Pearson Correlation coefficient and the value of the correlation coefficient was r =- 0.3, and therefore there was an inverse correlation between the two variables studied. Therefore, the older the age, the lower the serum calcium levels in psoriatic patients with p- value=0.009.

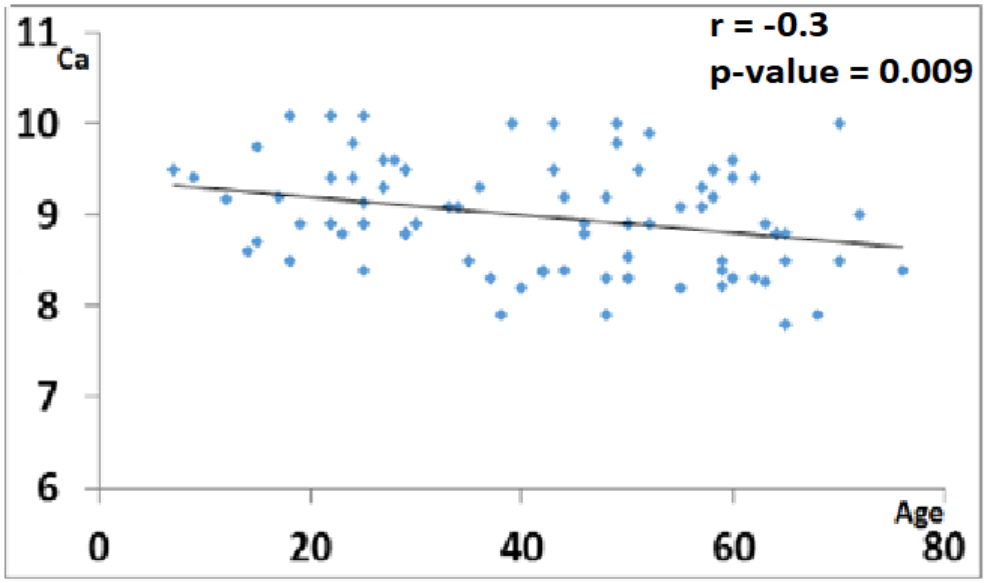

Figure (3) Relationship between serum calcium level and age in psoriatic patients.

Relationship between serum calcium level and duration of psoriasis:

The relationship between the serum calcium level and the duration of psoriasis was studied using the Pearson Correlation coefficient and the value of the correlation coefficient was r =- 0.3, and therefore there was an inverse correlation between two variables. Therefore, as the duration of psoriasis increases, serum calcium level decreases with p- value=0.04.

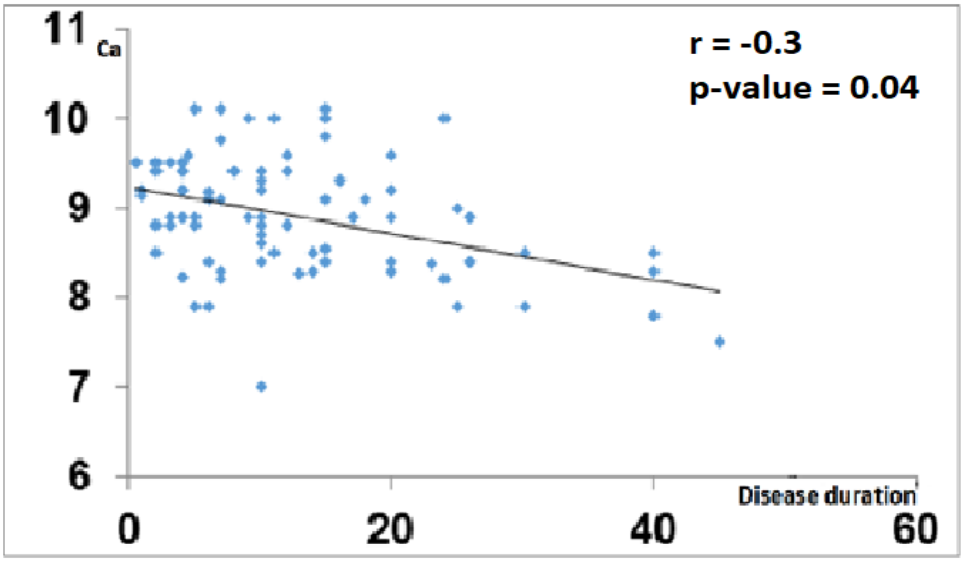

Figure (4) Relationship between serum calcium level and duration of psoriasis.

Relationship between serum calcium level and PASI score in psoriatic patients group:

The relationship between serum calcium level and PASI score was studied using the Pearson Correlation coefficient, and the value of the correlation coefficient was r =- 0.3, and therefore there was an inverse correlation between two variables. Therefore, as PASI score increases, the serum calcium level decreases with p- value=0.008.

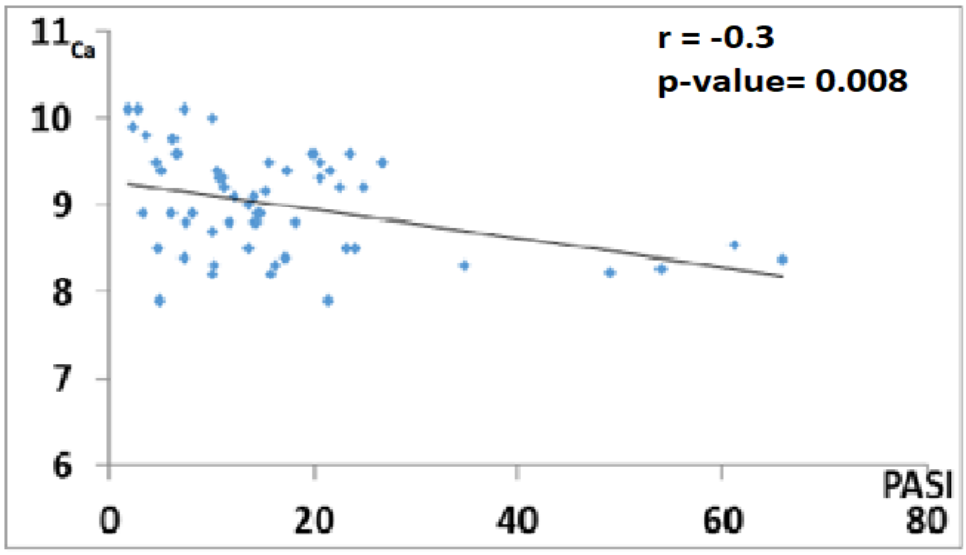

Figure (5) Relationship between serum calcium level and PASI score.

Relationship between serum calcium level and severity of psoriasis:

The relationship between serum calcium level and the severity of psoriasis was studied using the One Way ANOVA test, which showed that serum calcium level decreases as the severity of psoriasis increases and there were statistically significant differences. The statistically significant differences were between mild and severe psoriasis with p- value=0.02.

Table (7) Mean serum calcium level in psoriatic patients according to severity of psoriasis is presented in table 7.

Severity of psoriasis	N	Mean ± SD (Ca)	Min – Max	P- value
Mild	38	9.09±0.6	7.90- 10.10	0.04
Moderate	26	8.95±0.4	8.20- 10	
Severe	16	8.75±0.5	7.80- 9.60	

Relationship between serum calcium level and the type of psoriasis:

The relationship between serum calcium level and the type of psoriasis was studied using the One Way ANOVA test, which showed that the lowest mean calcium levels were in patients with severe forms of psoriasis (generalized pustular psoriasis, erythrodermic psoriasis and joint psoriasis) with statistically significant differences (p- value<0.05). Hypocalcemia was found in 100% of patients with these types.

Table (8) Mean serum calcium level in psoriatic patients according to the type of psoriasis is presented in table 8.

Type of psoriasis	N	Mean ± SD (Ca)	Min – Max	Number of patients with hypocalcemia (%)
Plaque Psoriasis	52	9.07±0.5	7.90- 10.10	12 (23.1%)
Palmoplantar Psoriasis	11	8.82±0.6	7.90 – 10	5 (45.4%)
Erythrodermic Psoriasis	4	8.35±0.1	8.22- 8.54	4 (100%)
Generalized Pustular Psoriasis	2	8.10±0.4	7.80- 8.40	2 (100%)
Localized Pustular Psoriasis	2	10±0	10- 10	0 (0%)
Psoriatic Arthritis	1	8.20±0	8.20- 8.20	1 (100%)
Guttate Psoriasis	2	9.45±0.07	9.40- 9.50	0 (0%)
Inverse Psoriasis	1	8.70±0	8.70- 8.70	1 (100%)
Scalp Psoriasis	6	8.85±0.5	8.30- 9.80	3 (50%)
Nail Psoriasis	8	9.09±0.4	8.50- 9.20	2 (25%)

Discussion.

Psoriasis is categorized as hyperproliferation disorder, as epidermal basal cells exhibit increased frequency of mitosis in the disease. Considering available reasons of psoriasis, the main reason is not known but several factors such as family records and accompanying with human leukocytes antigens (HLA) have been mentioned. [14]

Several studies have indicated to calcium role in controlling cellular multiplication and differentiation. On the other hand, measuring epidermal calcium concentration in patients suffering from psoriasis demonstrated low level of calcium and justify parakeratosis in such conditions. [15]

According to the result of the present study, hypocalcemia was more common in patients with psoriasis compared with controls (33.75% vs 7.5%). Serum calcium level was compared across severity of psoriasis and the association was found to be statistically significant. Correlation between disease duration and serum calcium was significant. Hypocalcaemia was significantly associated with pustular psoriasis, erythrodermic psoriasis and psoriatic arthritis. The results are in correspondence with other researches. Most of the studies reported an association between hypocalcemia and psoriasis.

Chaudhari S et al [13] analyzed serum calcium levels in patients of psoriasis and correlated with severity of psoriasis in comparison with control subjects. They observed the same that mean Serum calcium levels were significantly lower in psoriasis patients than in controls. However, correlation with disease severity was not found to be significant statistically. In addition, correlation between age and serum calcium was not significant, which is contrary to the results of the present study.

Qadim et al [16] conducted a study on hospitalised patients of psoriasis and reported hypocalcaemia to be present in 37.5% of their patients. This was similar to the results in our study. 19 (50%) patients of pustular psoriasis, 4 (100%) patients of erythroderma and 14 (24.5%) of patients of psoriasis vulgaris had hypocalcaemia in their study, which is consistent with the results of our study.

In the study of Bijina et al, [17] Hypocalcemia was noted in 38% of patients. There was no correlation observed between the duration of the disease and hypocalcemia, which is contrary to the results of the present study.

Rawat et al [3] found hypocalcaemia in 21% of their patients. All patients of erythroderma, psoriatic arthritis and pustular psoriasis had hypocalcemia, which was similar to our study.

In the study of Basha et al, [18] level of serum calcium was lower in patients with psoriasis vulgaris compared with controls, which is consistent with the results of the present study.

Morimoto et al [19] studied association between serum vitamin D and calcium levels with severity of skin lesions in psoriasis vulgaris. Calcium levels were compatible between the two groups with no statistically significant differences. This may be attributed to the small size of the studied sample. There was also no significant difference in the mean basal values of 25OHD and 1,25- (OH) 2D in groups of psoriatic patients and controls but a significant negative correlation was found between the serum levels of 1,25- (OH) 2D and the severity of skin lesions.

Zhai et al [20] determined pre- treatment calcium levels before administration of methotrexate to patients with severe plaque type psoriasis. They found significantly better improvement in patients who were treated with calcium before methotrexate. A positive correlation was also found between pre-treatment calcium.

Limitation of the study:

1- Financial obstacles prevented us from increasing the sample size, as well as from repeating the test to the same patient to assess calcium level after clinical improvement and after treatment.

2- Lack of patients suffering from non- plaque psoriasis types. So larger and longer- term studies should be carried out in order to collect a greater number of patients from all psoriasis types.

Conclusion.

In our study, Serum calcium levels were lower in the patients with Psoriasis when compared with the controls. Serum calcium can be used as a marker for severity of Psoriasis. Serum calcium level was lower in sever forms of psoriasis when compared with other forms. Thus, correcting the calcium levels by dietary or oral supplements might prove to be beneficial in providing a better outcome and preventing progression of mild, stable disease to severe forms.

Recommendations.

1- Screening tests for serum calcium level in psoriatic patients of all types.

2- It is better to include dairy as calcium resource in daily diet of patients suffering from psoriasis.

3- In case of intensification of psoriasis lesions, it is important to pay attention to hypocalcemia as an important factor.

References.

1- David Burden A and Brian Kirby. Inflamatory Dermatoses, Rook's Textbook of Dermatology (2016), Chapter 35; 1134- 1180.

2- Abdulghani M, Al Sheik A, Alkhawajah M, et al. Management of psoriasis in Africa and the Middle East: a review of current opinion, practice and opportunities for improvement. *J Int Med Res*. 2011;39 (5):1573- 1588.

3- Rawat L, Kothiwala R, Mehra A, et al. India. Serum calcium level in patients suffering from psoriasis and its correlation with severity of psoriasis: A case control study. *International Multispecialty Journal of Health (IMJH)*. 2019; 2395- 6291.

4- Wolf- Henning Boehncke, Michael P Schön. Psoriasis. *Lancet* 2015; 386: 983–94.

5- Leuner K, Kraus M, Woelfle U, et al. Reduced TRPC channel expression in psoriatic keratinocytes is associated with impaired differentiation and enhanced proliferation. *PLoS One*. 2011;6 (2):e14716.

6- Menon GK, Elias PM. Ultrastructural localization of calcium in psoriatic and normal human epidermis. *Arch Dermatol*. 1991;127 (1):57- 63.

7- Plavina T, Hincapie M, et al. Increased plasma concentration of cytoskeletal and Ca2+- binding proteins and their peptides in psoriasis patients. *Clin Chem*. 2008;54:1805- 14.

8- Braun GS, Witt M, et al. Hypercalcemia caused by vitamin D3 analogue in psoriasis treatment. *Int J Dermatol*. 2007;46:1315- 7.

9- Brown AJ, Slatopolsky E. Vitamin D analogs: therapeutic applications and mechanisms for selectivity. *Mol Aspects Med*. 2008;29 (6):433- 452.

10- Cook J, Thiers B. Serum calcium and phosphorus measurements in patients with psoriasis: a retrospective review. *J Eur Acad Dermatol Venereol*. 1993;2 (1):18–21.

11- Praful Rameteke, Rahul Gadpal, et al. A STUDY OF SERUM CALCIUM AND PHOSPHORUS IN PSORIASIS. *International Journal of Scientific Research (IJSR)*. 2019;8 (10):15- 16.

12- Helena Gleeson, Narendra Reddy and Miles J. Levy. Endocrinology, Kumar & Clarck's Clinical Medicine 10th Edition (2021), Chapter 21; 644- 647.

13- Chaudhari S, Rathi S. India. Correlation of serum calcium levels with severity of psoriasis. *International Journal of Research in Dermatology*. 2018; 4 (4):591- 594.

14- Duweb G, Alhaddar J, Abuhamida M. Psoriasis vulgaris: once- versus twice- daily application of calcipotriol cream. *Int J Tissue React*. 2005;27 (4):155- 158.

15- Shahriari M, Kerr PE, Slade K, Grant- Kels JE. Vitamin D and the skin. *Clin Dermatol*. 2010;28 (6):663- 668.

16- H.H Qadim, F. Goforoushan, S.B. Nejad and M Goldust. Tabriz, Iran. Studying the calcium serum level in patients suffering from psoriasis. *Pakistan Journal of Biological Sciences*. 2013; 16 (6):291- 294.

17- Bijina KD, Raghavendra BN, Muneer Mohamed. Karnataka, India. A study of serum calcium and uric acid levels in Psoriasis. *Indian Journal of Clinical and Experimental Dermatology*. 2018;4 (4):342- 345.

18- Mohamed A. Basha, et al. Egypt. The value of calcium and high- sensitivity C- reactive protein serum levels in psoriatic patients. *Menoufia medical journal*. 2021; 34 (1):56- 60.

19- Morimoto, et al. Inverse relation between severity of psoriasis and serum 1,25- dihydroxy- vitamin D level. *J Dermatol Sci*. 1990;1 (4):277- 282.

20- Zhai Z, Chen L, Yang H, Yan J, Wang C, Yang J, et al. Can pretreatment serum calcium level predict the efficacy of methotrexate in the treatment of severe plaque psoriasis? *J Am Acad Dermatol*. 2015;73 (6):991–7.