

SERUM LEVELS OF CALCIUM, CORTISOL AND VITAMIN D3 OF PLAQUE PSORIASIS PATIENTS IN ANBAR PROVINCE, IRAQ

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ABSTRACT : Psoriasis is a chronic inflammatory skin disease with a genetic and autoimmune background and the prevalence of it vary between countries. Psoriasis lesions are characterized by hyper-proliferation of epidermal keratinocytes associated with inflammatory cellular infiltrate in both dermis and epidermis. This study aimed to determine the serum levels of cortisol, vitamin D3 and Calcium in Iraqi patients with plaque psoriasis. Results of this study indicated that the frequencies disease were more frequent in male (70%) than female (30%) and in age < 40 years old. On other hand, among the 50 patients with psoriasis, 28 (56%) had blood group O, 13 (26%) blood group A, 7 (14%) blood group B and 2 (4%) had blood group AB. In addition, there is a statistical significance increased the serum levels of cortisol and vitamin D3 and a significant decreased in serum levels of calcium between plaque psoriasis patients than apparently healthy control.

Key words : Psoriasis, ABO blood group system, cortisol, vitamin D3, calcium.

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INTRODUCTION

Psoriasis happens all over the world. It affects men and women of all ages and ethnic backgrounds in every country (WHO, 2016). There is evidence that psoriasis is becoming more prevalent. Many studies about the prevalence of psoriasis in countries vary between 0.09% (Gibbs, 1996) and 11.4% (Danielsen *et al*, 2013). In Iraq, the psoriasis prevalence was 2.3% (Al Samarai, 2009).

Psoriasis is a chronic inflammatory disease that speeds up the growth cycle of skin cells. Psoriasis is classified into five distinct types: plaque, guttate, inverse, pustular, and erythrodermic. Plaque psoriasis, also called psoriasis vulgaris, accounts for about 90% of cases. It is most often manifested as red patches with white scales on top (Kim *et al*, 2019). While the majority of cases are mild and include only localized skin lesions, extreme cases include substantial skin lesions, joint involvement, and significantly impair life quality. Additionally, patients with psoriasis have a higher prevalence of psychiatric illnesses, such as severe depression (Akarsu, 2020). Additionally, psoriasis exacerbations are often preceded by traumatic life events. (Kamiya *et al*, 2019; Mohsen and AlJoofy, 2019). Stress triggers increased sympathetic activity, hypothalamic pituitary adrenal (HPA) hyperactivity and

the release of proinflammatory cytokines that can perpetuate and aggravate the psoriasis because the disease is associated to increased activity of many pro-inflammatory cytokines (Estelius, 2018).

Psychological stress therefore seems to be a vital bidirectional link between psoriasis, reduced quality of living and mental illnesses, and hyperactivity of the HPA axis is thus one of the physiological factors linked to the stress and stress response. The Cortisol levels can be used in the evaluation of HPA activity, although only a few studies have investigated the role of cortisol in psoriasis (Sinagar, 2017). Its pathogenesis is not clear, but it is a known fact that there is activation of innate and adaptive immune responses sectors. Vitamin D regulates both innate and adaptive immunity and it is an established fact that lower levels of vitamin D are associated with the initial development of some autoimmune diseases and premature mortality (Zuchi *et al*, 2015). Vitamin D also plays a vital role in the metabolism of calcium. Hypocalcemia is a known risk factor in precipitating pustular psoriasis (Plavina *et al*, 2008). Therefore, the current study aimed to determine the serum levels of cortisol, vitamin D3 and Calcium in Iraqi patients with plaque psoriasis and compare their levels with controls group.

MATERIALS AND METHODS

A total of 100 individuals were included in this study. 50 individuals of them had psoriasis (patients group); their age range was 18-60 years. They were referred for diagnosis and treatment to the Al-Ramadi and Al-fallujiah Hospitals for dermatologist in Anbar province during the period from August 2020 to November 2020. The investigation and the diagnosis were done by the advisor medical staff in the previous hospitals. While, the other 50 individuals were apparently healthy subjects (control group). Their age range was similar to patients group. Information was collected for each patient by using a special form; all participants gave informed consent before enrolling in the research, which was approved by the Scientific Research Ethics Committee in University of Anbar in accordance with the Helsinki Declaration.

Both of cortisol and vitamin D3 level were evaluated using automated cobas® E411 analyser system (Roche, Germany) while calcium levels by using automated cobas® C111 (Roche, Germany).

Statistical analysis

All statistical analysis were performed using statistical package for social science (SPSS) program version 23 for windows (SPSS IINC., Chicago IL, USA). Results were expressed as numbers and percentage or mean \pm SD. Comparisons between two groups were performed using t- test for categorical data. P values of < 0.05 or < 0.01 were considered to indicate statistical significance.

RESULTS AND DISCUSSION

Distribution of patients group according to sex

According to sex of patients group, the present study showed that the frequencies of plaque psoriasis disease were more frequent in male (70%) than female (30%) and the difference between them was significant ($P < 0.05$) as shown in Fig. 1.

Clear gender disparities in incidence and prevalence of psoriasis were not agreed. Psoriasis is similarly prevalent in both sexes in some studies (Boehncke, 2018). No differences in the frequency of psoriasis between genders were found in Taiwanese children (Tsai *et al*, 2011) and combined individuals of all ages in the United States, Norway, Spain, Scotland and Taiwan (Parisi *et al*, 2013). However, other psoriasis prevalence by sex studies reported that psoriasis is more common in men although quoted values are not statistically significant (Pezzolo *et al*, 2019; Kjersti Danielsen *et al*, 2019 and DiBonaventura *et al*, 2018). In contrast, several studies have shown that psoriasis is more common in women (Radtke *et al*, 2017; Ba° *et al*, 2016 and Svensson *et al*,

2018). This issue requires further research, particularly into the differentiation of genetic and behavioral factors.

In Iraq, some psoriasis studies reported that a slightly female predominance in AL-Najaf and AL-Hilla city (Mohammed *et al*, 2015) and in Thi-Qar Province (Mousa and Hassan, 2020), which may reflect a sex related preference in psoriatic patients. While, in Anbar province, Mohammed *et al* (2013) and Al-Hasan (2021) reported that psoriasis was more frequent in male than female, this results were correspondent with results of this study. In the results of this study, the number of men with plaque psoriatic patients was significantly increased than women may be due to the men patients went to doctors and hospitals to be treated, which facilitates the process of obtaining clinical samples for studies and research from women who prefer to be treated at home.

Distribution of patients group according to age

The distributing of patients in two age groups (< 40 years and ≥ 40 years) clarified that the plague psoriatic patients were more frequent in < 40 years group than other group and the difference between them were highly significant ($P < 0.01$) as shown in Fig. 2.

Psoriasis has been graded according to the age at which it manifests. Early onset psoriasis (also known as type I) manifests before the age of 40 years, with a peak onset between the ages of 16–22 years and accounts for 70% of all psoriatic cases. Late-onset psoriasis, also known as type II psoriasis, manifests itself at or after the age of 40 years, peaking between the ages of 57 and 60 years (Queiro *et al*, 2014). According to previous information the patients in this study divided in two age groups (< 40 years and ≥ 40 years).

Armstrong (Takeshita *et al*, 2017) reported that most people develop psoriasis between the ages of 15 and 35. Although psoriasis could get better or worse, it doesn't get worse with age depending on various environmental factors. Obesity and stress are two potential components of psoriasis. Some patients are predisposed to developing psoriasis, especially if a family member has psoriasis..

Psoriasis may take place at any age. Although, some research showed that the average age of psoriasis was 33 years and 75% of cases were prior to 46 years (26), Psoriasis age-specific prevalence showed a growing pattern with age until about the age of 60 or 70, after which it declines (Iskandar *et al*, 2021).

A local study by Mohammed *et al* (2015) found that 53 % of patients with psoriasis were 20–39 years old and 47 % were 40–60 years old in the city of Najaf and AL-Hilla. Ishaq *et al* (n.d.) reported that in Erbil city, the majority of psoriatic cases, 72% present before the age

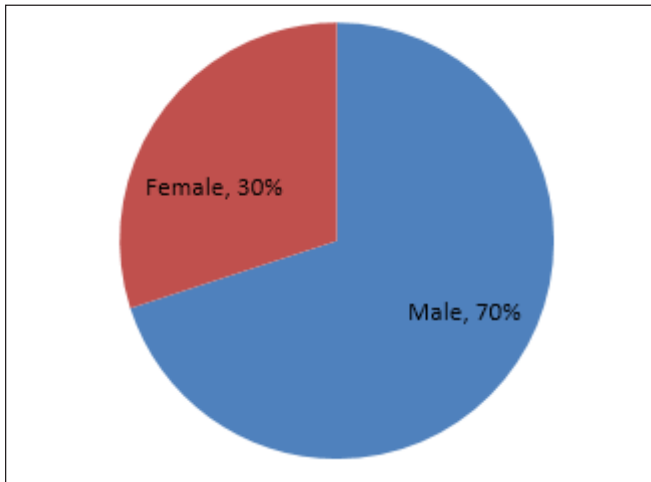


Fig 1 : The distribution of patients group according to the sex.

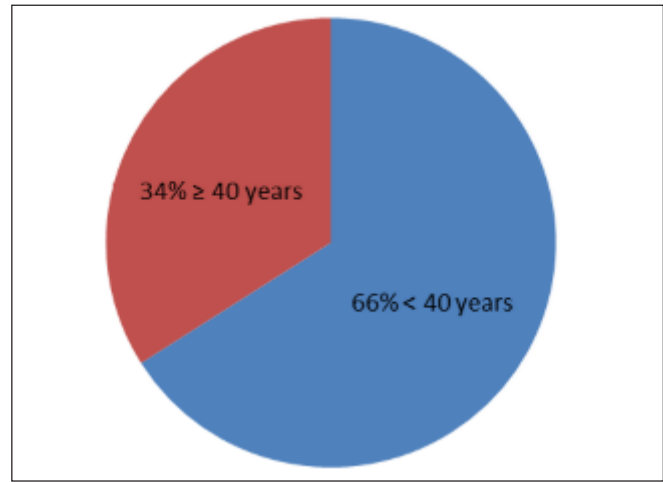


Fig. 2 : Distribution of plague psoriatic patients according to age.

of 40 years. The remaining cases, 28 % present after the age of 40 years.

ABO blood group Antigens in patients group

The ABO blood groups frequencies for plague psoriasis patients as follows; the blood group O was more frequent in patients followed by blood group A, B then AB. The differences between ABO blood groups frequencies were significant, as shown in Table 1.

The ABO blood group antigens play a role in the pathophysiology of some diseases and several researches have investigated this relationship in the field of dermatology like psoriasis. Mohammad Shahidi *et al* (2015) reported in Iran, among patients with psoriasis, 42%(O), 30% (A), 20% (B) and 4% (AB). This is accordance with the results of this study. Rather *et al* (2014) also found that in Indian psoriasis patients, blood group O was the most common, followed by blood type B and blood group A. Harris *et al* (2020) reported in US, blood group O was the most common, followed by blood type A and blood group B then AB. The distributions of blood groups in patients with psoriatic diseases in previous studies were not significantly different from the control group and those studies did not find any relationship between the disease and blood group Antigens. However, other researches, found associations between ABO blood group antigens and psoriasis, such as Qamar (Mohammad Shahidi *et al*, 2015) reported that persons with blood group B Positive are more at risk of developing psoriasis than those of other blood groups.

Body mass index in study groups

There is no significant difference between the mean ± SD of BMI in plague psoriatic patients (26.09 ± 5.0) than control group (26.05 ± 4.3) as shown in Table 2.

Epidemiological data demonstrates unequivocally that

Table 1 : The distribution of plague psoriatic patients according to ABO Blood group system.

ABO Blood groups	Patients	
	No.	%
O	28	56
A	13	26
B	7	14
AB	2	4
Total	50	100
P value		< 0.01

Table 2 : Body Mass index for plague psoriatic patients and control.

Subject	Body Mass index
Patients	26.09 ± 5.0
Controls	26.05 ± 4.3
P value	> 0.05

Obesity increases the risk of developing psoriasis and exacerbates psoriatic inflammation in patients (Setty *et al*, 2007). In obese individuals, adipose tissue produces increased levels of pro-inflammatory cytokines such as tumor necrosis factor, interleukin-1, interleukin-6, and interleukin-8, 9, 10 and the resulting abnormal inflammatory milieu can contribute to the pathophysiology of psoriatic diseases (Hamminga *et al*, 2006) that explains the relationship between BMI and psoriasis.

Patients with a BMI of 35 or greater have a significantly increased risk of developing psoriasis. The Body Mass Index (BMI) is a straightforward measure of weight in relation to height that is often used to identify individuals as underweight, overweight, or obese. A prospective study indicated that obesity and high abdominal fat mass doubled the risk of psoriasis (Snekvik *et al*, 2017). Therefore, preventing weight gain, promoting maintenance of a normal body weight, and reduction of body mass may reduce incidence of psoriasis (Alotaibi,

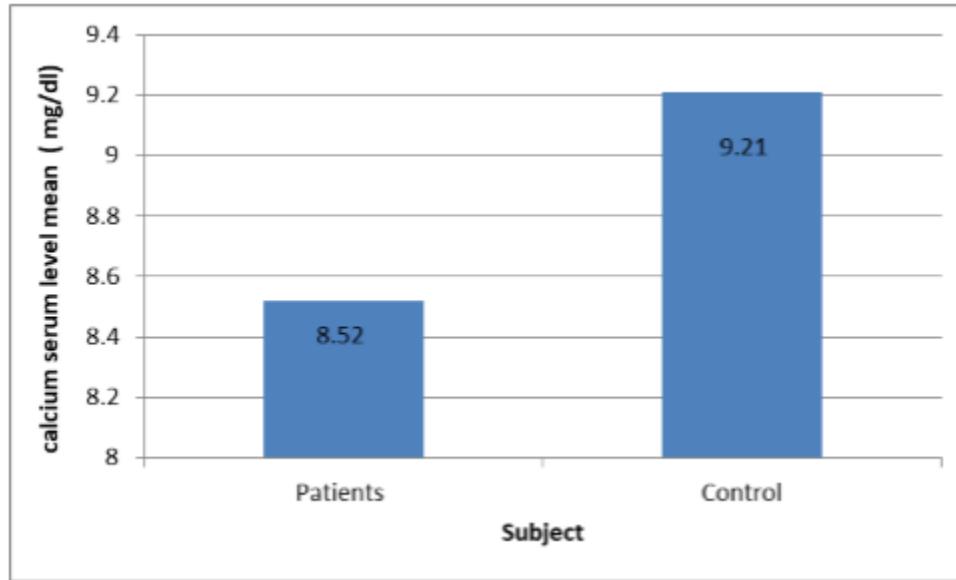


Fig. 3 : Calcium serum level in plaque psoriatic patients and control.

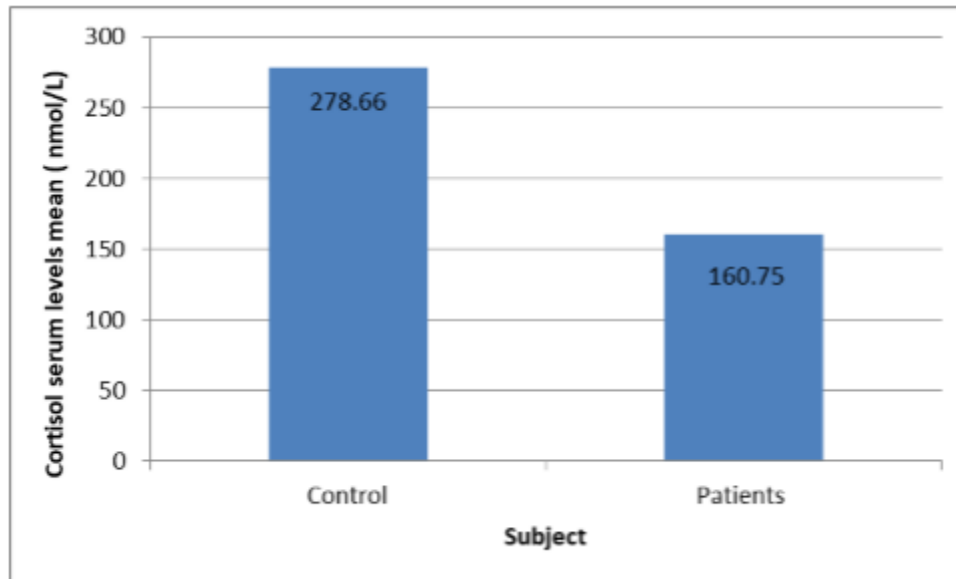


Fig. 4 : Cortisol serum levels in plaque psoriatic patients and control.

2018).

The result of this study was not agreed with Farshchian *et al* (2015) results, which highlighting in their study that BMI of psoriasis cases (26.36 ± 4.71 kg/m²) was significantly ($P=0.02$) higher than that of controls (24.6 ± 3 kg/m²) and Felming *et al* (2015) conducted a literature review that indicated a strong association of increased psoriasis incidence with higher BMI in seven out of nine articles.

Serum levels of calcium in study groups

Mean serum levels of calcium was significantly ($P < 0.01$) decreased in plaque psoriatic patients (8.52 ± 0.74 mg/dl) compared to control (9.21 ± 0.69 mg/dl) as shown in Fig. 3.

The skin hyper proliferation and keratinocytes differentiation in psoriasis is controlled by calcium inside the cells (Cook and Thiers, 1993). It has been observed that there is disturbance in the metabolism of calcium in few cases with psoriasis. Pustular psoriasis has been found to be associated with mild hypocalcemia (Plavina *et al*, 2008). Psoriasis has been found to be aggravated with the decrease in the serum calcium levels. This is because the calcium has an important role in the regulation of keratinocytes. Cell adhesion molecules can be damaged by hypocalcemia (Basha *et al*, 2021).

The results of this study was agreed with Chaudhari and Rathi (2018) result, they found that the mean serum calcium levels were significantly lower in psoriasis patients compared to the control in the present study.

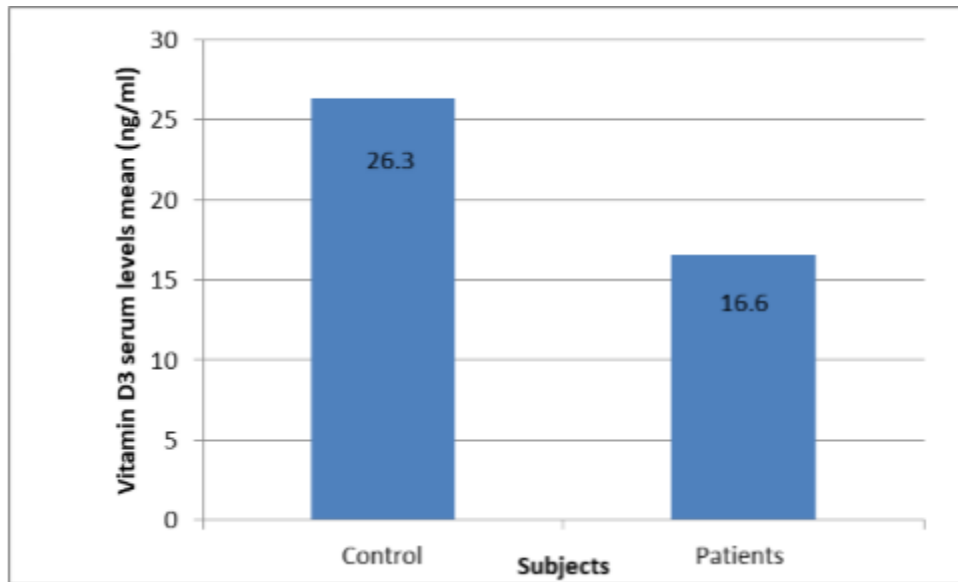


Fig. 5 : Vitamin D3 serum levels in plaque psoriatic patients and control.

Serum calcium level was compared across severity of psoriasis and with Qadim *et al* (2013) result, they compared the 98 psoriasis cases with 100 cases without psoriasis. The prevalence of hypocalcemia was 37.2% in the cases compared to only 9% among the controls. The authors concluded that for psoriasis patients, hypocalcemia was a significant risk factor and they recommended to include calcium rich foods for psoriasis patients.

Serum level of cortisol in study groups

Mean serum levels of cortisol was highly decreased significantly ($P < 0.01$) in plaque psoriatic patients (160.75 ± 102.8 nmol/L) compared to control (278.66 ± 103.9 nmol/L) as shown in Fig. 4.

Certain hormones, such as prolactin, may play a role in the pathogenesis of psoriasis through their effect on keratinocyte proliferation. Additionally, stress hormones such as cortisol, thyroid hormones, and thyroid stimulating hormone play a role in the pathogenesis of psoriasis; cortisol mediates psychoemotional stress, and it has been shown that psoriasis patients have a reduced cortisol response to stress (Evers *et al*, 2010). As a result, it can be hypothesized that changes in the function of the hypothalamus-pituitary-adrenal (HPA) axis, as measured by cortisol levels, can play a role in the pathogenesis of psoriasis (ZANGANEH and Fazeli, 2008).

Cortisol levels are low in patients with psoriasis, predisposing them to exacerbations caused by psychoemotional stress. Changes in the hypothalamus-pituitary-adrenal (HPA) axis' function may contribute to the pathogenesis of psoriasis. Additionally, cortisol's impact on the balance of T-helper type 1 (TH1) and type

2 (TH2) lymphocytes offers evidence for cortisol's involvement in the pathogenesis of this disease by dysregulation of the TH1/TH2 balance (Elenkov *et al*, 2000). Cortisol's immunomodulatory impact on psoriasis pathogenesis are illustrated by the fact that the first immunologic occurrence in new psoriasis lesions is CD4+ and CD8+ cell aggregation. T-helper lymphocytes and their extravasation (Robati *et al*, 2013).

Zangeneh and Fazeli (2008) reported that psoriatic patients showed markedly low cortisol values than control and other study reported Psoriatic patients, for whatever reason have lower base levels of cortisol and don't produce as much as a result of stress (Berg *et al*, 2008). While, Robati *et al* (2013) reported that there was no significant difference in the level of cortisol between psoriatic patients and control.

Serum level of vitamin D3 in study groups

Mean serum levels of vitamin D3 was highly significantly ($P < 0.01$) decreased in plaque psoriatic patients (16.6 ± 6.69 ng/mL) compared to control (26.3 ± 8.55 ng/mL) as shown in Fig. 5.

Vitamin D deficiencies have been linked to psoriasis. While a deficiency doesn't seem to cause psoriasis immediately, it may impair the body's ability to keep the skin healthy. This may increase flares. Controversial data was discussed on the relationship of psoriasis with vitamin D. Initial findings showed substantially lower levels of vitamin D relative to stable controls in psoriatic patients (Gisoni *et al*, 2012; Orgaz-Molina *et al*, 2012; Ricceri *et al*, 2013). Later studies did not confirm these results (Maleki *et al*, 2016; Zuchi *et al*, 2015). However, many factors can affect vitamin D deficiency and insufficiency

prevalence, such as race, ultraviolet radiation exposure, and vitamin D dietary intake (Bertrand *et al*, 2012).

CONCLUSION

This study clarified that Iraqi patients with plaque psoriasis have significantly different serum levels of calcium, cortisol and vitamin, D3 when compared with apparently healthy individuals.

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