Suez Canal University Medical Journal Vol. 28 (8), 2025
Pages 9-16

Assessment of Serum CCL20 Level in Patients with Psoriasis and Its Correlation with Disease Severity

Yomna F.M. Hassan [1] Nader A. Ismail [2] Hanan H. Omar [3] Hesham A. Nada [2]

[1] *Dermatology, Venereology, and Andrology Department, Mit Ghamr General Hospital, Dakahlia, Egypt.*
[2] *Dermatology, Venereology, and Andrology Department, Faculty of Medicine, Suez Canal University, Ismailia, Egypt.*
[3] *Clinical Pathology Department, Faculty of Medicine, Suez Canal University, Ismailia, Egypt.*

Abstract:

Background: **Epidermal CCL20 expression is prevalent in human psoriatic lesions. CCL20 expression is mostly limited to the psoriatic epidermis, despite the fact that dermal dendritic cells and T cells also express it in the psoriatic dermis. This suggests that epidermal keratinocytes are the primary source of CCL20 synthesis in psoriatic lesions. Additionally, psoriasis is associated with elevated serum levels of CCL20.** ***Aim:*** **To assess serum level of CCL20 among patients with psoriasis to help to understand the pathogenesis of psoriasis and it`s management to improve quality of life of patients with psoriasis.** ***Materials and Methods:*** **A case control study was conducted, and patients were recruited from the Dermatology Outpatient Clinic of the Suez Canal University Hospitals, Ismailia. Subjects were divided into two groups: patients' group: patients with psoriasis and controls group: age and sex matched healthy controls. Serum CCL20 was measured in all subjects.** ***Results:*** **CCL20 levels were significantly higher in patients with psoriasis than controls (P value < 0.001). There was a significant positive correlation between CCL20 and PASI score.** ***Conclusions:*** **Serum CCL20 was significantly increased in psoriasis than controls. Moreover, its level was significantly correlated with disease severity.**

Keywords: Serum CCL20, Psoriasis, PASI score, Keratinocytes

Introduction

Psoriasis is characterized by epidermal hyperproliferation and dermal inflammatory cell infiltrates composed of T-cells and dendritic cells, an immune-mediated skin condition. Psoriasis prevalence varies by demographic globally, with Europeans having a prevalence of 2.5%, Africans having a prevalence of 0.05%–3%, and Asians having a prevalence of 0.1%–0.5% [(1)]. It is thought to start between the ages of 20 and 35 and can affect both men and women equally [(2)].

Many dermatologic and non-dermatologic comorbidities can result from this chronic, systemic inflammatory condition, which lowers a patient's quality of life [(3)]. However, a number of comorbidities, such as Crohn's disease, atherosclerosis, myocardial infarction, psoriatic arthritis, anxiety, depression, and many more, are linked to psoriasis and exacerbate the overall state of the disease [(4)].

The knees, buttocks, elbows, nails, scalp and shins are frequently affected by psoriasis, which can develop anywhere on the body. It also demonstrates the trait of having a symmetrical appearance [(5)].

**Corresponding author: yomna.fawzy1234@gmail.com*

It is still unclear what specifically causes psoriasis to occur. Nonetheless, it has been hypothesized that psoriasis development may be promoted by immune system damage caused by a number of environmental and genetic variables, including infections, drugs, weight, stress, alcohol, tobacco, genetic predisposition, and family background [2].

Large levels of TNF-α and IL-23 are produced by the invading dermal dendritic cells, which also stimulate the development of helper T (Th17) cells that produce IL-17A [6]. Keratinocytes' differentiation is downregulated, and their proliferation is upregulated by IL-17A [7].

Furthermore, the neutrophil-attracting cytokines CXCL1, CXCL2, CXCL8, and IL-36 are produced in greater amounts by keratinocytes when exposed to IL-17A [8]. Additionally, CCL20, a crucial chemoattractant for CCR6 + Th17 cells, is produced by keratinocytes in response to IL-17A (9). CCL20 can also be produced by Th17 cells [7].

Furthermore, Th17 cells generate a lot of TNF-α [9]. As a result, the TNF-α/IL-23/IL-17A axis creates a positive feedback loop that ultimately leads to the onset of psoriasis. Furthermore, the TNF-α/IL-23/IL-17A axis depends critically on the CCL20/CCR6 chemotactic system [10].

Anti-TNF-α/IL-23/IL-17A biologics are very effective because the TNF-α/IL-23/IL-17A axis is essential to the pathophysiology of psoriasis [11].

The gene for the 8-kDa protein CCL20, often referred to LARC, also known as MIP-3α, is situated on 2q33-37. In peripheral tissues like the skin, CCL20 is expressed at the tissue and organ level. liver, thymus, and mucosal sites (intestines and lungs). CCL20 has only one recognized receptor, although the majority of chemokines bind to several [12].

Cultured keratinocytes constitutively express CCL20, and TNF-α and IL-17A upregulate its synthesis, while IL-22 has a less significant effect [7].

Epidermal CCL20 expression is prevalent in human psoriatic lesions. CCL20 expression is mostly restricted to the psoriatic epidermis, even though T cells and cutaneous dendritic cells also generate it. This implies that the main source of CCL20 production in psoriatic lesions is epidermal keratinocytes. Furthermore, psoriasis is associated with elevated serum levels of CCL20 [13].

In order to determine the blood level of CCL20 in psoriasis and the relationship between it and the severity of the disease, this study was carried out.

Our goal was to measure the blood level of CCL20 in psoriasis patients in order to better understand the disease's pathophysiology and how to treat it to enhance the patients' quality of life.

Subjects and Methods

Patients were gathered from the Dermatology Outpatient Clinic for a case control study at the Suez Canal University Hospitals in Ismailia. The participants were split up into two groups: patients group: psoriasis sufferers and controls group: healthy controls who were matched by age and sex.

Inclusion Criteria: Age: older than eighteen. There were people of both sexes. Prior to being included in the trial, none of the patients had been receiving topical medicine for at least two weeks or systemic treatment for psoriasis for at least four to six weeks.

Exclusion criteria: Patients with immune-mediated comorbidities, such as vitiligo,

atopic dermatitis, or insulin-dependent diabetes. Individuals on immunosuppressive medications, such as methotrexate, or those with a history of skin cancer or premalignant skin lesions. Lactation or pregnancy. Immunotherapy, such as the Mumps, Measles, and Rubella Vaccine (MMR vaccine), had been used to treat the patients in the past.

Study variables:

Independent variables: Features of psoriasis lesions on the skin. Dependent variables: The disease's duration, progression, and severity. Background factors: sex and age. Confounding factors: medications that may impact psoriasis and systemic skin conditions. Each patient's personal information was gathered as follows: name and age, sex, address, occupation, marital status, number of children, and special medical habits; the current illness's onset, course, and duration; any allergies that have occurred in the past; the type and timing of any treatments for the current lesion; past medical history, including previous surgeries; diabetes mellitus; hypertension; hemolytic blood disorders or blood transfusions; drug history; systemic treatment history (type, duration, response, and the date of the last treatment); and family history of conditions similar to the patient.

To rule out systemic diseases, a general examination was performed to look for indications of other illnesses. To rule out further skin conditions, a total body skin examination (TBSE) was performed (e.g Vitiligo).

The PASI score was calculated as part of a blind clinical evaluation. Three parameters—E, erythema; I, infiltration; and D, desquamation— are employed by the PASI score to evaluate psoriasis severity [14].

A person's head (H) makes up 10% of their body, followed by their arms (20%), trunk (30%), and legs (40%). The four separate scores from each of these categories are added to determine the final PASI. A grade between 0 and 6 is then created from the expected proportion of skin area affected for each segment: 0% of the involved area, less than 10% of the involved area, 5–69% of the involved area, 70–89% of the involved area, 30–49% of the involved area, and 90–100% of the involved area.

The severity within each region is assessed using three clinical signs: desquamation (scaling), induration (thickness), and erythema (redness). Severity characteristics were measured on a scale from zero to four, or from zero to maximum. The area score for each skin region was then multiplied by the sum of the three severity factors, and the weight of each skin section (0.1 for the head, 0.2 for the arms, 0.3 for the body, and 0.4 for the legs) was the result.

Following the guidelines provided by the manufacturer, the enzyme-linked immunosorbent test (ELISA) kits (Cloud-Clone Corp., USA; Catalog No.: E-00982hu) were used to determine the amount of serum CCL20.

Ethical considerations:

The Suez Canal University Research Ethics Committee gave its approval to the study protocol. Medical Faculty (Approval No. 4817). Before collecting any data or doing any physical examinations, each participant gave their signed, informed consent.

Statistical analysis:

The data that was entered into the computer was analyzed using IBM SPSS software package version 20.0 (Armonk, NY: IBM Corp). The tests that were employed included the chi-square test, Fisher's exact or Monte Carlo correction, the Pearson coefficient, the student t-test, and the receiver operating characteristic curve.

Results:

Psoriasis patients and controls did not differ substantially in terms of age or sex (P value > 0.05) (Table 1).

According to PASI scores, which varied from 1.60 to 21.20 with a mean ± standard deviation of 9.20 ± 4.97, 24% of patients had mild disease severity and 76% had moderate to severe disease (Table 2).

Table 1: Comparison between patients with psoriasis and controls according to demographic data

	Patients with psoriasis (n = 25)		Controls (n = 25)		Test of Sig.	P
	No.	%	No.	%		
Sex						
Male	12	48.0	12	48.0	χ^2=0.0	1.000
Female	13	52.0	13	52.0		
Age (years)						
Min. – Max.	19.0 – 67.0		19.0 – 70.0		t=0.948	0.348
Mean ± SD.	39.72 ± 14.86		35.60 ± 15.85			
Median (IQR)	37.0 (28.0 – 53.0)		32.0 (25.0 – 38.0)			

*Interquartile range (IQR), standard deviation (SD), student t-test (t), chi square test (α2), and Fisher's error (FE) The exact p-value for comparing the two groups under study is *: p < 0.05 indicates statistical significance.*

Table 2: Distribution of the patients according to grade of severity and PASI score (n = 25)

	No.	%
Grade of Severity		
Mild	6	24.0
Moderate, Severe	19	76.0
PASI score		
Min. – Max.	1.60 – 21.20	
Mean ± SD.	9.20 ± 4.97	
Median (IQR)	9.60 (6.40 – 11.20)	

IQR: Inter quartile range, SD: Standard deviation, PASI: Psoriasis Area and Severity Index

Psoriasis patients had considerably greater levels of CCL20 than controls (P value < 0.001). While their levels in controls ranged from 17.20 to 24.10 with 20.54 ± 2.08 as Mean ± SD, their levels in psoriasis patients ranged from 23.30 to 35.30 with 27.58 ± 2.99as Mean ± SD (Table 3).

There was a significant positive correlation between CCL20 and PASI score (P value <0.001) (Table 4, Figure 1).

CCL20 significantly increased with increased disease severity (P value <0.001). (Table 5).

Table 3: Comparison between patients with psoriasis and controls according to CCL20				
CCL20	Patients with psoriasis (n = 25)	Controls (n = 25)	T	P
Min. – Max.	23.30 – 35.30	17.20 – 24.10	9.665*	<0.001*
Mean ± SD.	27.58 ± 2.99	20.54 ± 2.08		
Median (IQR)	27.40(25.10 – 29.10)	20.30(19.30 – 22.40)		
*IQR: Inter quartile range, SD: Standard deviation, t: Student t-test, p: p value for comparing between the two studied groups, *: Statistically significant at p ≤ 0.05*				

Table 4: Correlation between CCL20 and PASI score in patients with psoriasis (n = 25)		
	CCL20	
	R	P
PASI score	0.903	<0.001*
*r: Pearson coefficient , *: Statistically significant at p ≤ 0.05, PASI:Psoriasis Area and Severity Index*		

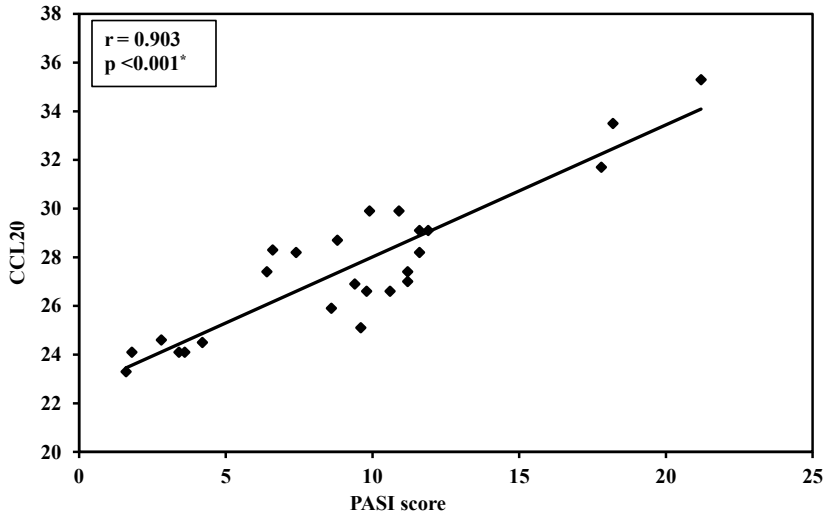

Figure 1: Correlation between CCL20 and PASI score in patients with psoriasis (n = 25)

Table 5: Relation between Grade of Severity and CCL20 level in patients with psoriasis				
CCL20	Grade of Severity		t	P
	Mild (n = 6)	Moderate, severe (n = 19)		
Min. – Max.	23.30 – 24.60	25.10 – 35.30	7.376*	<0.001*
Mean ± SD.	24.12 ± 0.46	28.67 ± 2.57		
Median	24.10	28.20		
*SD: Standard deviation, t: Student t-test, p: p value for comparing between the two studied groups, *: Statistically significant at p ≤ 0.05*				

Discussion

Psoriasis is a polygenic, inflammatory, immunomodulated, and chronic dermatosis [15]. These days, the shape, extent, and distribution of skin lesions are used to diagnose psoriasis. Even while skin biopsy histopathological analysis aids in effective clinical identification, psoriasis caused by subtle pathologic alterations is challenging to diagnose [16].

Early research revealed that psoriasis patients' serum numerous pro-inflammatory cytokine levels increased [17]. TNF-α and IL-17A upregulate the synthesis of CCL20, which is constitutively produced in cultured keratinocytes. IL-22 has a less significant effect [1]. Psoriasis is said to be associated with elevated serum levels of CCL20 [13].

In order to better understand the pathophysiology of psoriasis and how to manage it to enhance the quality of life for those who suffer from it, we therefore carried out this case control study to evaluate the blood level of CCL20 among individuals with psoriasis and relate their intensity to the illness.

To the best of our knowledge, relatively few researchers have examined the function of CCL20 in individuals with psoriasis. Most research has focused on other biomarkers, such as IL23, TNFα, and IL17.

According to the demographic characteristics of the study, the average age of psoriasis patients varied from 39.72 ± 14.86 years, whereas the average age of controls was 35.60 ± 15.85 years. The study's overall outcome was unaffected because between the two groups, there was no statistically significant difference. One hundred psoriatic patients participated in the study. Özkesici et al. [18] showed somewhat better results; the mean age at which psoriasis first appeared was 42.07±16.12 years.

The mean ± SD of CCL20 levels in psoriasis patients in our study was 27.58 ± 2.99, with a range of 23.30 to 35.30. Compared to controls, these levels were significantly greater in psoriasis patients. Getschman et al. [19] published similar results [19], who claimed that psoriasis patients have higher serum levels of CCL20.

According to reports, human psoriatic lesions are linked to high levels of T lymphocytes that target the skin, dermal CCR6-expressing dendritic cells, and epidermal CCL20 expression. In the psoriatic dermis, T cells and dermal dendritic cells both express CCL20 [20].

Keratinocytes in a mouse model express CCL20 soon after being injected with IL-23 [21]. Although CCL20 is typically expressed at a modest baseline level, proinflammatory signals like main cytokines can greatly increase its expression [22].

According to the PASI scores ($p < 0.001$), 24% of patients had mild disease severity and 76% had moderate to severe disease. The PASI scores in this study varied from 1.60 to 21.20, with a mean ± SD of 9.20 ± 4.97. According to Ekman et al. [23] in the same line, there was a baseline connection ($r = 0.5$, $p < 0.01$) between the severity of psoriasis as assessed by the PASI and the levels of CCL20. Patients with more severe psoriasis (PASI > 7) had greater levels of CCL20. than in those with less severe psoriasis (PASI < 7; $p < 0.05$). The only chemokine that was shown to be related to the severity of the condition was CCL20,

also concurred with numerous researches. The findings of Elnabawi et al. [24] showed

a strong correlation between CCL20 and PASI score.

Conclusions:

Serum CCL20 levels in psoriasis patients were significantly greater than those in controls. Furthermore, there was a substantial correlation between its level and the severity of the condition.

References:

1. Furue K, Yamamura K, Tsuji G, et al. Highlighting Interleukin-36 Signalling in Plaque Psoriasis and Pustular Psoriasis. Acta Derm Venereol. 2018;98(1):5-13.
2. Gowda BHJ, Ahmed MG, Hani U, Kesharwani P, Wahab S, Paul K. Microneedles as a momentous platform for psoriasis therapy and diagnosis: A state-of-the-art review. Int J Pharm. 2023;632:122591.
3. Buja A, Miatton A, Cozzolino C, et al. The Prevalent Comorbidome at the Onset of Psoriasis Diagnosis. Dermatol Ther (Heidelb). 2023;13(9):2093-2105.
4. Bu J, Ding R, Zhou L, Chen X, Shen E. Epidemiology of Psoriasis and Comorbid Diseases: A Narrative Review. Front Immunol. 2022;13:880201.
5. Moon C-I, Lee J, Baek YS, Lee O. Psoriasis severity classification based on adaptive multi-scale features for multi-severity disease. Scientific Reports. 2023;13(1):17331.
6. Hu P, Wang M, Gao H, et al. The Role of Helper T Cells in Psoriasis. Front Immunol. 2021;12:788940.
7. Furue K, Ito T, Tsuji G, Nakahara T, Furue M. The CCL20 and CCR6 axis in psoriasis. Scand J Immunol. 2020;91(3):e12846.
8. Bouma G, Zamuner S, Hicks K, et al. CCL20 neutralization by a monoclonal antibody in healthy subjects selectively inhibits recruitment of CCR6(+) cells in an experimental suction blister. Br J Clin Pharmacol. 2017;83(9):1976-1990.
9. Imafuku S, Zheng M, Tada Y, et al. Asian consensus on assessment and management of mild to moderate plaque psoriasis with topical therapy. J Dermatol. 2018;45(7):805-811.
10. Meephansan J, Subpayasarn U, Ponnikorn S, et al. Methotrexate, but not narrowband ultraviolet B radiation, suppresses interleukin-33 mRNA levels in psoriatic plaques and protein levels in serum of patients with psoriasis. J Dermatol. 2018;45(3):322-325.
11. Morita A. Current developments in phototherapy for psoriasis. J Dermatol. 2018;45(3):287-292.
12. Lee AYS, Körner H. The CCR6-CCL20 axis in humoral immunity and T-B cell immunobiology. Immunobiology. 2019;224(3):449-454.
13. Furue K, Ito T, Tanaka Y, et al. Cyto/chemokine profile of in vitro scratched keratinocyte model: Implications of significant upregulation of CCL20, CXCL8 and IL36G in Koebner phenomenon. J Dermatol Sci. 2019;94(1):244-251.
14. Carlin CS, Feldman SR, Krueger JG, Menter A, Krueger GG. A 50% reduction in the Psoriasis Area and Severity Index (PASI 50) is a clinically significant endpoint in the assessment of psoriasis. J Am Acad Dermatol. 2004;50(6):859-866.
15. Michalek IM, Loring B, John SM. A systematic review of worldwide epidemiology of psoriasis. J Eur Acad Dermatol Venereol. 2017;31(2):205-212.
16. Zou C, Huang C, Yan L, et al. Serum N-glycan profiling as a diagnostic biomarker for the identification and assessment of psoriasis. J Clin Lab Anal. 2021;35(4):e23711.
17. Liu XQ, Zhou PL, Yin XY, et al. Circulating inflammatory cytokines and psoriasis risk: A systematic review and meta-analysis. PLoS One. 2023;18(10):e0293327.
18. Ozkesici-Kurt B, Dönmez L, Nazlim B, et al. Defining the natural course of psoriasis: A single-center cohort study of 100 patients. TURK DERMATOLOJI DERGISI-TURKISH JOURNAL OF DERMATOLOGY. 2018;12(1).
19. Getschman AE, Imai Y, Larsen O, et al. Protein engineering of the chemokine CCL20 prevents psoriasiform dermatitis in an IL-23-

dependent murine model. Proc Natl Acad Sci U S A. 2017;114(47):12460-12465.
20.Kim TG, Jee H, Fuentes-Duculan J, et al. Dermal clusters of mature dendritic cells and T cells are associated with the CCL20/CCR6 chemokine system in chronic psoriasis. J Invest Dermatol. 2014;134(5):1462-1465.
21.Mabuchi T, Singh TP, Takekoshi T, et al. CCR6 is required for epidermal trafficking of γδ-T cells in an IL-23-induced model of psoriasiform dermatitis. J Invest Dermatol. 2013;133(1):164-171.
22.Shi ZR, Mabuchi T, Riutta SJ, et al. The Chemokine, CCL20, and Its Receptor, CCR6, in the Pathogenesis and Treatment of Psoriasis and Psoriatic Arthritis. J Psoriasis Psoriatic Arthritis. 2023;8(3):107-117.
23.Ekman AK, Sigurdardottir G, Carlström M, Kartul N, Jenmalm MC, Enerbäck C. Systemically elevated Th1-, Th2- and Th17-associated chemokines in psoriasis vulgaris before and after ultraviolet B treatment. Acta Derm Venereol. 2013;93(5):527-531.
24.Elnabawi YA, Garshick MS, Tawil M, et al. CCL20 in psoriasis: A potential biomarker of disease severity, inflammation, and impaired vascular health. J Am Acad Dermatol. 2021;84(4):913-920.