Assessment of CCL20 Serum Level as Biomarker for Psoriasis Severity and Disease Related Comorbidities.

Abstract
Background: Psoriasis is a long-lasting inflammatory skin disease associated with immune system dysregulation and systemic complications. Chemokine plays a crucial role in monocyte recruitment and has been linked to the development of various autoimmune conditions.. However, its relationship with psoriasis severity and associated with disease complications remains obscure.
Aim: This study aims to propose that monitoring serum CCL20 levels in patients with psoriasis may provide valuable insights into disease severity as well as its associated complications.
Methods: A cross sectional study was conducted involving psoriasis patients. Serum CCL20 levels were measured using enzyme-linked immunosorbent assay (ELISA). Psoriasis Area and Severity Index (PASI used to assess disease severity, and information on comorbidities were collected. Statistical analyses were performed to determine associations between CCL20 levels, PASI scores, and complications.
Findings: The mean serum CCL20 levels in psoriasis patients were 112.14 ng/L ± 8.72 SE, with range values from 42.89 to 293.50. The mean CCL20 level was higher in mild disease 207.96 ± 13.88 in comparison to 132.68±15.76 for the moderate and 78.31 ± 6.48 for the severe group, (p = 0.0001). The mean serum CCL20 levels was higher significantly in patients with metabolic syndrome p=0.001, while the mean serum CCL20 levels was inversely lower in psoriatic patients with psoriatic arthritis in comparison to those did not (57.63 ±8.05 versus 123.82± 9.8, p=0.003)

Conclusion: The findings revealed an unexpected inverse relationship between serum CCL20 levels and the severity of psoriasis and serum CCL20 levels were associated significantly with metabolic syndrome among psoriatic patients.
Keywords: Serum CCL20, psoriasis, severity, metabolic syndrome.

Introduction

Psoriasis is a chronic persistent, immune-mediated inflammatory skin disease affecting approximately 2–3% of the global population [1]. Psoriasis typically presents as well-defined, red plaques covered with silvery-white scales, most frequently affecting the elbows, knees, scalp, and lower back. The pathogenesis of psoriasis is multifactorial and involves a dynamic interplay between genetic predisposition, environmental triggers, and immune system dysregulation [2,3].
The immunopathogenesis of psoriasis involves a complex network of cellular and molecular interactions. Central to this process is the dysregulation of adaptive immune responses, particularly the activation of specific T cell subsets. At the core of this immune dysregulation is the aberrant activation of T lymphocytes—especially Th1, Th17, and Th22 subsets—which secrete pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-17 (IL-17), and interleukin-23 (IL-23). These cytokines create a self-sustaining inflammatory loop that promotes keratinocyte hyperproliferation, epidermal thickening, and recruitment of additional immune cells, culminating in the formation of psoriatic plaques.
Dendritic cells play a pivotal role in initiating the inflammatory cascade by producing cytokines like IL-23 and TNF-α, which drive the differentiation and maintenance of Th17 cells. These Th17 cells, in turn, release IL-17A, IL-17F, and IL-22, which act directly on keratinocytes to enhance their proliferation and trigger the production of antimicrobial peptides and further inflammatory mediators. Keratinocytes are not merely passive targets, but actively contribute to the inflammatory milieu by releasing cytokines such as IL-1β, IL-6, and chemokines like CCL20. These molecules amplify the immune response by recruiting additional immune cells, especially CCR6-expressing Th17 cells, into the dermis and epidermis [4,5].
Chemokines, represent a class of small signaling proteins, are critical mediators of leukocyte movement and tissue-specific immune responses [6–8]. In psoriasis, several chemokines and their receptors are upregulated in lesional skin, promoting and driving the infiltration of Th17 cells, neutrophils, and monocytes. Key examples include the CCL20-CCR6 axis, as well as CXCL1, CXCL8, CXCL9, CXCL10, and CXCL11, all of which work in concert with pro-inflammatory cytokines such as IL-17, IL-23, IFN-γ, and TNF-α to amplify local inflammation and tissue damage [9–11]. Additionally, certain chemokines like CXCL12 and its receptor CXCR4 contribute to angiogenesis and vascular inflammation, further supporting their role in disease progression [12,13].

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Among these, chemokine (C-C motif) ligand 20 (CCL20), also known as macrophage inflammatory protein-3 alpha (MIP-3α), plays a pivotal role in the development and progression of psoriasis by recruitment of CCR6-expressing immune cells, particularly Th17 cells, regulatory T cells (Tregs) and dendritic cells (DCs), into psoriatic lesions [14]. Elevated CCL20 expression has been observed in lesional skin and appears to contribute to both local and systemic immune activation. The CCL20-CCR6 axis is now recognized as a major component of the psoriatic inflammatory cascade [15].

Recent research suggests that serum levels of CCL20 may reflect disease activity and systemic immune involvement in psoriasis. Elevated circulating levels of CCL20 have been associated not only with skin inflammation but also with psoriatic comorbidities, including psoriatic arthritis, metabolic syndrome, and cardiovascular disease [16–18]. This highlights the potential of CCL20 as a biomarker for disease severity and for stratifying the risk of systemic complications.

Therefore, the present study aimed to assess serum CCL20 levels in patients with psoriasis and evaluate their association with disease severity and the presence of comorbid conditions.

Materials and methods

This cross- section study was conducted at Merjan Teaching Hospital in Hilla City, Babylon Province during the period between October 2024 and January 2025. It comprised 68 patients with psoriasis (24 females and 44 males), with age ranged from (18 -65) years.

Consents were obtained from each participant after clear description of study purpose, and then demographic and clinical data of patients were collected as (duration of disease, family history, weight, treatment of psoriasis, disease comorbidities, aggravating factors and complication). All patients were evaluated for obesity using body mass index (BMI) according to WHO classification [19].

Patients were clinically diagnosed by dermatologist. Disease severity was evaluated by using the Psoriasis Area and Severity Index (PASI) and categorized into mild, moderate, and severe psoriasis groups [20]. The study excluded criteria of these subjects (Pregnant women, person with disease other than psoriasis such as skin and inflammatory diseases and the patient who has not received Biologics therapy at last three months. The study was approved by the ethical committee in the Faculty of Medicine, University of Kufa (ethical approval. No. 33 in 23/10/2024).

Blood Sample collection

Five ml of venous blood were collected from patients with psoriasis. Blood samples were allowed to clots then serum was separated by using centrifugation after that was stored at -24 until used. Serum levels of CCL20 were measured using an enzyme-linked immunosorbent assay (ELISA) kit (BT. LAB, China; Cat. No. E6513Hu), following the manufacturer's instructions.

Statistical analysis

For statistical analysis, SPSS software (version 26) was used. Descriptive statistics were used to summarize the information, calculating averages and standard deviations (or standard errors) for continuous data and reporting counts and percentages for categorical data. To compare two separate groups, independent samples t-tests were used. For comparisons of three or more groups, a one-way ANOVA test was performed. Pearson's correlation coefficient was used to examine the relationships between numerical measurements. Statistical significance was determined if the p-value was less than or equal to 0.001 or less than or equal to 0.05.

Results

The study consists of 68 patients with psoriasis; 24 (35.3%) females and 44 (64.7%) males, the mean age is 38.15±14.4 years old with a minimum of 18 years and maximum age of 65 years. Mean years of disease duration was 38.15± 14.4 Y. obese patients constitute 38.2% in comparison to 61.8% of non-obese, with mean BMI about 30 for all study participants, half of patients suffer from sever disease and 61.8% of them suffer from disease complications. Several complications had been demonstrated among patients included metabolic syndrome (14 patients, 20.6%), ischemic heart disease (IHD) (28 patients, 41.2%), and psoriatic arthritis (12 patients, 17.6%) table 1.

Table 1: Some Demographic and Clinical Characteristics of Psoriasis Patients

Characteristic	**Patients**
sex	
Male n (%)	44(64.7%)

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Female n (%)	24 (35.3%)
Age	
mean± SD	38.15± 14.4 Y
Range	47 Y
Duration	
mean± SD	14.06 ± 11.930
Range	42
Smoking	
Smoker n (%)	42(61.8%)
Non-smoker n (%)	26(38.2%)
Obesity	
BMI	29.474± 6.2
Obese , *n* (%)	26(38.2%)
Non obese, *n* (%)	42(61.8%)
Severity	
PASI	29.37± 6.2
Mild	6(8.8%)
Moderate	24(41.2%)
Sever	34(50%)
Complications	
Present, *n* (%)	42(61.8%
Absent, *n* (%)	26(38.2%
Comorbidities	
Metabolic syndrome, *n* (%)	14(20.6%)
IHD, *n* (%)	28(41.2%)
Psoriatic arthritis, *n* (%)	12(17.6%)
Obesity, *n* (%)	26(38.2%)

The mean serum CCL20 levels in psoriasis patients were 112.14 ng/L ± 8.72 SE, with range values from 42.89 to 293.50. The mean CCL20 level was higher in mild disease 207.96 ± 13.88 in comparison to 132.68±15.76 for the moderate and 78.31 ± 6.48 for the severe group with a p-value

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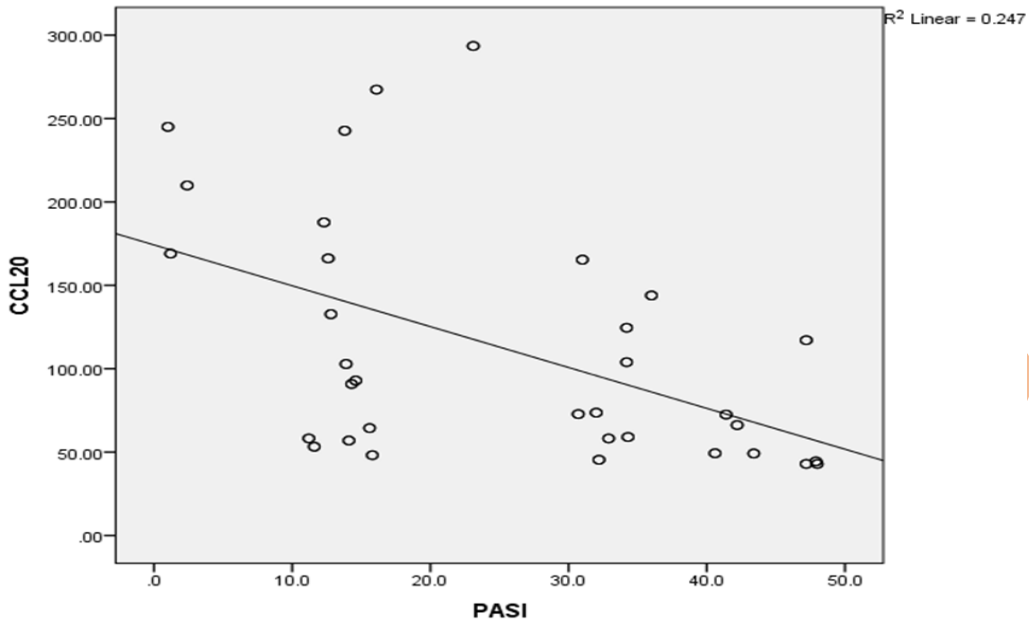
of 0.0001; the difference observed in CCL20 levels was statistically significant across the severity groups, the result shows a negative and significant correlation between PASI (the index of severity) and CCL20 levels (figure1).



p=0.0001

Figure 1: Correlation between Psoriasis Area and Severity Index (PASI) and Serum CCL20 Levels.

Table 2 also appeared the association of CCL20 levels with complications and the results demonstrated that there was no significant difference in CCL20 levels between patients who were obese and those who were not, as well as between patients with and without ischemic heart disease (IHD), p=0.24, 0.84 respectively, while patients with metabolic syndrome had significantly higher CCL20 levels (168.77±25.07) compared to those without (97.45± 7.83), with a p-value of 0.001. Remarkably patients with psoriatic arthritis had significantly lower CCL20 levels (57.63± 8.05) compared to those without (123.82±9.8), with a p-value of 0.003.

Table 2: Association of Serum CCL20 Levels with Complications in Psoriasis Patients:

Characteristics		***N***	**Mean ± SE(ng/L)**	***P***
Obesity	**Obese**	26	125.22±18.7	**0.24 NS**
	Non-Obese	42	104.03±8.04	
Metabolic syndrome	**Present**	14	168.77±25.07	**0.001 S**
	Absent	54	97.45±7.83	
IHD	**Present**	28	114.26±16.3	**0.84 NS**
	Absent	40	110.65±9.6	

Psoriatic Arthritis	**Present**	12	57.63 ±8.05	**0.003 S**
	Absent	56	123.82± 9.8	

Discussion

Psoriasis is a multifaceted, chronic immune-mediated disorder that primarily affects the skin and nails. However, growing research highlights its strong link to systemic inflammation, which extends beyond dermatological manifestations. Studies suggest that persistent inflammation in psoriasis patients contributes to the development of complication, including cardiovascular diseases, and insulin resistance. This association underscores the need for a comprehensive approach to managing psoriasis, not only to control skin symptoms but also to mitigate the risk of serious systemic complications.

This study presented a demographic and clinical profile of psoriasis patients, offering insights into potential factors associated with disease severity and complications. The patients were predominantly male. And with long disease duration reflect the chronic nature of psoriasis.

A notable proportion of patients were smokers and/or obese. Both smoking and obesity were recognized aggravating factors for psoriasis, contributing to chronic systemic inflammation and potentially influencing disease severity. The mean BMI fell within the overweight to obese range, which supports the notion of metabolic involvement in the pathogenesis of psoriasis [21].

In terms of disease severity, a majority of patients had moderate and severe psoriasis based on the PASI score, suggested that more than 90% of the study population had significant disease activity, possibly reflected referral bias or a focus on moderate-to-severe cases in the study design.

The presence of complications was common in this current study, the most frequent comorbid conditions were ischemic heart disease, obesity, metabolic syndrome, and psoriatic arthritis These findings were consistent with current literature, which emphasizes the systemic nature of psoriasis and its association with increased cardiovascular and metabolic risks [22,23].

It has been established that chemokines (CCL20) plays essential starring role in the development of psoriasis, also participate in the progression of disease by influencing disease severity and contributing to many complications. In this study result reveals a statistically significant inverse relationship between psoriasis severity and serum CCL20 levels. Patients with mild psoriasis exhibited the highest mean CCL20 levels, which progressively declined in moderate and severe cases. Brunner *et.al* research recorded elevation in serum level of this type of chemokines of psoriasis patients [24]. This trend contrasts with much of the existing literature, which typically reported positive correlations between CCL20 levels and disease severity due to CCL20 chemokine was established role in Th17 recruitment and chronic inflammation in psoriatic lesions [13,14].

One possible explanation for this unexpected pattern could be related to dynamic nature or the complexity relationship of cytokine and chemokine expression throughout disease progression. In early or moderate stages, CCL20 may be a primary driver of inflammation, particularly by attracting CCR6+ immune cells, particularly Th17 cells, to the skin. However, in severe psoriasis, the inflammatory profile becomes more complex, potentially dominated by other mediators such as TNF-α, IL-17A, and IL-22, and mediators may become more dominant, potentially affecting CCL20 levels and reduce or alter the role of CCL20 pathway in progression and expression or distribution. Therefore, CCL20 plays a significant role in recruiting inflammatory cells to psoriatic lesions at beginning, exacerbating the inflammatory process [25].

Individual variability in immune response and comorbid conditions such as obesity and smoking status may also affect CCL20 expression. Given that these factors influence systemic inflammation; they could modulate chemokine profiles differently across patient subgroups.

Our study was differ with research of Harper E.G. *et al.* Which indicates that Th17 cytokines, such as IL-17A and IL-22, significantly upregulate CCL20 expression in human keratinocytes, this upregulation facilitates the recruitment of CCR6+ Th17 cells into psoriatic lesions, contributing to the disease's progression[8]. And study of Furue K., *at al.* that showed (CCL20 is constitutively expressed in cultured keratinocytes) [26].

Also this results may be attributed to the body's regulatory mechanisms in severe psoriasis, where negative feedback loops were likely activated to mitigate excessive inflammation, potentially leading to reduced systemic production or released of CCL20. Moreover, in advanced disease stages, a substantial portion of CCL20 may be sequestered within the psoriatic skin lesions, resulting in lower measurable levels in the serum despite ongoing local inflammation[14].

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Based on these studies, it appeared that CCL20 levels in the skin increased with the progression of psoriasis, which might differ from its serum levels due to the influence of multiple factors most notably, its abundant production by keratinocytes. This discrepancy might explained the findings in our study, where higher levels of CCL20 in the blood were linked to less severe psoriasis and vice versa.

The severity of psoriasis is influenced by a range of factors, including genetic predisposition, environmental triggers, and associated comorbidities. Variability in cytokine and chemokine profiles among individuals may impact study findings, as differences in patient composition across severity groups can contribute to variations in observed outcomes [27,28].

This inverse correlation challenges some conventional assumptions and underscores the need for further research to explore the temporal and contextual roles of CCL20 in psoriasis progression. Longitudinal studies and stratification based on treatment status may help clarify these findings.

In addition to its role in cutaneous inflammation, CCL20 is implicated in the development of systemic comorbidities in psoriasis patients, such as psoriatic arthritis, metabolic dysfunction, and cardiovascular complications, through its involvement in chronic immune activation and Th17 cell recruitment [28].

This study examined the association between serum chemokines CCL20 levels and several selected comorbid conditions in patients with psoriasis (obesity, metabolic syndrome, ischemic heart disease and psoriatic arthritis), and obtained to that a strong association and significantly findings in data of serum levels CCL20 with metabolic syndrome and psoriatic arthritis, While the mean chemokine level was numerically higher in the obese group than non-obese but with $p>0.05$. Several factors may explain this finding, such as the relatively small sample size, which could limit statistical power and make it difficult to detect moderate associations. And chemokine expression may be more pronounced locally in adipose tissue rather than in systemic circulation. Additionally, inconsistent chemokine levels across individuals may also result from variability in assay methods and differences in regulatory pathways such as NF-κB [29,30]. These considerations suggested that while chemokines play a role in inflammation, their relationship with obesity was complex and might not be adequately captured in small or unstratified cohorts.

The results about IHD showed no significant difference association with chemokines. This result could be attributed to chemokine levels in circulation might vary depending on whether the individual was experienced acute coronary syndrome or stable chronic IHD. Since the study likely included patients with stable disease, which often shows less systemic chemokine elevation [31].

Regarding to the relation with metabolic syndrome, this result aligned with current evidence of Rocha VZ and Libby P.2009, Francesco B. et al. 2024. and Zhang P and Wu M. (2021) [13,32-34]. One study suggested that metabolic deregulation enhances systemic inflammation and chemokine expression. These studies showed that adipose tissue dysfunction in metabolic syndrome that increased release of pro-inflammatory cytokines, such as IL-6 and TNF-α, which might stimulate increased production of chemokine CCL20 in the keratinocytes and cells of immune system [35].

The present results appeared relationship between CCL20 serum levels with psoriatic arthritis, and appeared a significantly lower in patients with PsA compared to those without joint involvement. Although CCL20 is a key chemokine in Th17 cell trafficking and synovial inflammation, this inverse association may reflect local tissue sequestration of CCL20 in joint compartments, or immune exhaustion/adaptation in chronic disease. Additionally, many PsA patients may be undergoing systemic immunosuppressive therapy, potentially lowering serum CCL20 levels [36,37] .

These observations highlighted the need for further investigation into the site-specific expression of CCL20 and its regulatory mechanisms in the pathophysiology of psoriatic arthritis (PsA).

The study has limitation that is; the snapshot observational study couldn't establish a clear timeline or prove cause and effect between CCL20 levels, psoriasis severity, and comorbidities.

We recommend further research to explore the temporal and contextual roles of CCL20 in psoriasis progression by conducting longitudinal studies with continuous measurement and follow-up.

Conclusions: the relationship between CCL20 levels and psoriasis severity is complex, with the study finding an inverse relationship, contrary to some existing literature. The study also found significant associations between CCL20 levels and certain comorbidities, specifically metabolic syndrome and psoriatic arthritis.

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