Paper_-_Egyptian_Journal_of_Intenal_Medicine_f...

Document

Turnitin

Document Details

Submission ID
trn:oid:::1:3413093903

Submission Date
Nov 16, 2025, 2:10 PM GMT-5

Download Date
Nov 16, 2025, 2:12 PM GMT-5

File Name
tmp1rg8n5gf.docx

File Size
58.4 KB

20 Pages

4,816 Words

28,413 Characters

20% Overall Similarity

The combined total of all matches, including overlapping sources, for each database.

Filtered from the Report

- Bibliography

Match Groups

68 Not Cited or Quoted 20%
Matches with neither in-text citation nor quotation marks

0 Missing Quotations 0%
Matches that are still very similar to source material

0 Missing Citation 0%
Matches that have quotation marks, but no in-text citation

0 Cited and Quoted 0%
Matches with in-text citation present, but no quotation marks

Top Sources

12% Internet sources
18% Publications
3% Submitted works (Student Papers)

Integrity Flags

0 Integrity Flags for Review

No suspicious text manipulations found.

Our system's algorithms look deeply at a document for any inconsistencies that would set it apart from a normal submission. If we notice something strange, we flag it for you to review.

A Flag is not necessarily an indicator of a problem. However, we'd recommend you focus your attention there for further review.

Match Groups

- **68** Not Cited or Quoted 20%
  Matches with neither in-text citation nor quotation marks
- **0** Missing Quotations 0%
  Matches that are still very similar to source material
- **0** Missing Citation 0%
  Matches that have quotation marks, but no in-text citation
- **0** Cited and Quoted 0%
  Matches with in-text citation present, but no quotation marks

Top Sources

- 12% Internet sources
- 18% Publications
- 3% Submitted works (Student Papers)

Top Sources

The sources with the highest number of matches within the submission. Overlapping sources will not be displayed.

1	Publication	"2016 ACR/ARHP Annual Meeting Abstract Supplement", Arthritis & Rheumatolog... 2%
2	Publication	"2015 ACR/ARHP Annual Meeting Abstract Supplement", Arthritis & Rheumatolog... 2%
3	Internet	orbi.uliege.be 1%
4	Internet	www.frontiersin.org 1%
5	Publication	"2017 ACR/ARHP Annual Meeting Abstract Supplement", Arthritis & Rheumatolog... <1%
6	Internet	www.mdpi.com <1%
7	Publication	Sara Taha, Eman El Sehsah, Shaimaa Fouad, Hieba Ezzelregal, Aya Moussa, Shaim... <1%
8	Internet	www.researchsquare.com <1%
9	Internet	www.science.gov <1%
10	Publication	Rasha Ahmed Ghorab, Lamyaa Salem, Manar F. Mohamed, Azza Omran et al. "He... <1%

11	Internet	
slideheaven.com		<1%
12	Publication	
Lamia Ayed, Sana M'hir, Nedra Asses. "Sustainable whey processing techniques: I...		<1%
13	Student papers	
National University of Singapore		<1%
14	Publication	
Anaïs Makos, J. H. Kuiper, O. Kehoe, R. Amarasena. "Psoriatic arthritis: review of p...		<1%
15	Internet	
pdffox.com		<1%
16	Publication	
Vinod Chandran, Proton Rahman. "Predicting therapeutic response through biom...		<1%
17	Internet	
www.ncbi.nlm.nih.gov		<1%
18	Internet	
ntnuopen.ntnu.no		<1%
19	Internet	
worldwidescience.org		<1%
20	Publication	
Stephanie R. Harrison, George E. Fragoulis, Xabier Michelena, Cristina Macía-Villa ...		<1%
21	Internet	
discovery.researcher.life		<1%
22	Internet	
www.thieme-connect.com		<1%
23	Publication	
Céline La, Phu Quoc Lê, Alina Ferster, Laurence Goffin et al. "Serum Calprotectin (...		<1%
24	Internet	
ijaai.tums.ac.ir		<1%

25 Internet
lirias.kuleuven.be <1%

26 Internet
pmc.ncbi.nlm.nih.gov <1%

27 Publication
Ajesh B. Maharaj, Lihi Eder, Alexis Ogdie. "Obesity and Comorbidity Management ... <1%

28 Publication
Jiang Zhao, Mi Zhou, Chengfei Yang, Yang-Wuyue Liu et al. "S100A9 as a potential ... <1%

29 Publication
Krzysztof Bonek, Ewa Kuca-Warnawin, Anna Kornatka, Agnieszka Zielińska, Małgo... <1%

30 Publication
S G Baidya. "Helper T cells and atherosclerosis: the cytokine web", Postgraduate ... <1%

31 Publication
Sadia Tamanna, Choon-Mee Kim, You Mi Lee, Jun-Won Seo, Da Young Kim, Na Ra ... <1%

32 Internet
archive.org <1%

33 Internet
bora.uib.no <1%

34 Internet
fmed.stafpu.bu.edu.eg <1%

35 Internet
journals.lww.com <1%

36 Internet
lidsen.com <1%

37 Internet
www.biorxiv.org <1%

38 Publication
Bahman Arasteh, Mohammad Abdi, Asgarali Bouyer. "Program source code comp... <1%

39 Publication

Rubén Queiro, José Antonio Pinto-Tasende, Carlos Montilla-Morales. "Navigating ... <1%

40 Publication

Bolas, Ana Sofia Valério. "Bridging the Gap Between Innate and Adaptive Immuni... <1%

Serum Calprotectin: Could it be a Biomarker for Disease Activity and Radiological Severity in Psoriatic Arthritis Patients under Biological Therapy?

Abstract

Background: Psoriatic arthritis (PsA) is a chronic inflammatory arthropathy that gradually damages joints leading to joint deformities and long-term disability. The pathogenesis of PsA involves immune-mediated chronic inflammation caused by a combination of risk factors that trigger antigen-presenting cells (APCs), which stimulate activation of cytotoxic T lymphocytes through Toll-like receptor 2 pathways. Released cytokines by APCs activate T helper 1 and T helper 17 responses that release proinflammatory cytokines, causing tissue damage. Calprotectin (S100A8/A9) (CLP) acts as a proinflammatory factor of innate immunity, which mediates neutrophil, monocyte, and macrophage recruitment to inflamed sites, thus contributing to chronic inflammatory conditions. Musculoskeletal ultrasound (US) is a sensitive radiological technique that helps in the evaluation of both structural and inflammatory changes. Aim of the work: To evaluate whether serum CLP could reflect disease activity and pathological findings detected by musculoskeletal ultrasound in PsA patients receiving biological therapy. Patients and Methods: There were 120 participants in this cohort study: 60 patients with PsA receiving biological therapy for more than three months and 60 healthy controls. The Disease Activity in Psoriatic Arthritis (DAPSA) and the Psoriasis Area and Severity Index (PASI) were used to assess PsA patients. A human CLP ELISA kit was used to measure serum CLP. Musculoskeletal ultrasound was performed on the dominant site using the PsASon13 composite score to evaluate inflammatory and structural changes.

Results: The median age of PsA patients was 35 years, and 68.3% of them were female. The PsASon13 imaging score had a median (IQR) of 7.0 (3.0–14.0). Median serum CLP levels were significantly increased in patients compared to controls (1468.4 vs 1169.7 ng/mL, $p<0.001$). ESR levels also revealed a significant difference across groups. DAPSA and PsASon13 scores showed a strong positive correlation and both were significantly correlated with serum CLP ($p<0.001$). PASI scores were moderately correlated with DAPSA and PsASon13. ROC curve

analysis of serum CLP showed 73.3% sensitivity and 81.7% specificity in differentiating PsA patients from controls at an optimal cut-off value of 1285 ng/mL,.

Conclusions: Serum CLP is strongly associated with clinical disease activity and ultrasound findings in PsA. It may serve as a valuable biomarker for disease monitoring in patients undergoing biologic therapy.

Keywords: Psoriatic arthritis, serum calprotectin, DAPSA score, SON13 imaging score, PASI score, US

1. Introduction

Psoriatic arthritis (PsA) is a chronic immune-mediated inflammatory arthropathy combined with psoriasis. PsA's primary musculoskeletal presentations include peripheral arthritis, enthesitis, spondylitis, and dactylitis. In addition to cutaneous involvement, PsA may present systemically with nail disease, uveitis, and inflammatory bowel disease (IBD). [1]

Globally, PsA affects about 0.13% of the general population and up to 22% of adults with psoriasis. PsA causes gradual joint damage that ends with joint deformities and long-term disability. [2,3]

The pathogenesis of PsA is determined by both genetic and environmental factors. The environment, such as infections, mechanical stress, or obesity, starts the disease pathology by triggering antigen-presenting cells (APCs) like macrophages, dendritic cells, and monocytes activating cytotoxic T lymphocytes (CD8+ T cells) through Toll-like receptor 2 (TLR2) pathways. [4]

Released cytokines by APCs activate T helper 1 (Th1) response through interleukin 12 (IL-12) and interferon α (IFNα), and Th17 response through IL-23, transforming growth factor ß (TGFß), IL-6, and IL-1β. Subsequently, Th1 and Th17 responses release proinflammatory cytokines, including IFN-γ, tumor necrosis factor α (TNFα), IL17, IL22, IL26, and chemokine ligand 20 (CCL20). These cytokines recruit more immune cells, sustaining chronic inflammation and causing tissue damage in the joints, entheses, bone, and skin. [1]

The diversity in the clinical presentation of PsA often delays diagnosis and complicates disease assessment. Identifying reliable biomarkers to aid diagnosis and evaluate disease activity remains a major research focus. Calprotectin (CLP), a promising candidate, has attracted considerable attention. [5]

CLP is a heterodimeric complex that comprises two myeloid-related protein (MRP) subunits, MRP8 and MRP14, and is one of the S100 protein family members, S100A8/S100A9. [6]

CLP acts by calcium- and zinc-binding as a proinflammatory element of innate immunity secreted by activated phagocytes. CLP exerts various intracellular and extracellular biological effects. TLR4 and receptors for advanced glycation end products (RAGE) are the primary CLP receptors, which, upon binding together, trigger intracellular signaling pathways leading to nuclear translocation of Myeloid Differentiation Primary Response Gene 88 (MyD88) and nuclear factor-κB (NF-κB) into the nucleus leading to induction of IL-6, IL-8, IL-23, and TNF-α genes among other pro-inflammatory cytokines. [6,7] Additionally, CLP exerts antimicrobial activity by sequestering zinc and manganese (nutritional immunity) [8] and promotes leukocyte recruitment to inflamed tissues through chemotaxis, thereby amplifying chronic inflammation. [9]

CLP is abundant in different body fluids, including serum, synovial fluid, saliva, urine, and stool. Although fecal CLP is a well-established marker of inflammation in chronic IBD, serum calprotectin has recently gained attention. Studies have demonstrated that serum CLP levels are associated with disease activity in various autoimmune inflammatory diseases, including rheumatoid arthritis and axial spondyloarthritis. [10,11]

Musculoskeletal ultrasound (US) is a non-invasive, sensitive radiological tool that can detect synovial inflammation, enthesitis, tenosynovitis, and bone erosions. It is valuable in assessing both structural and inflammatory changes and is sensitive to treatment effects, making it a useful complement to physical evaluation and laboratory tests.[12]

The current study intended to assess serum CLP levels in PsA patients and to investigate their association with clinical disease activity and pathological abnormalities detected by musculoskeletal ultrasonography.

2.Patients and methods

Study ethics and design: A convenient sample of PSA patients from Kafrelsheikh University Hospital's rheumatology department's outpatient clinic participated in this cohort study, with ethical approval number KFSIRB 200-251. All participants received an explanation of the methods and study details, and prior to their enrollment in the study, their informed consent was obtained.

Sampling and study participants

The Sample Size Calculator (web) [13] was utilized to determine the sample size.

The criteria used for sample size calculation were as follows:

- The expected sensitivity of CLP at distinguishing PsA patients from controls is 98.0%, and the expected specificity is 86.7%.
- Precision of 10%
- Alpha error 5% (95% confidence level)
- Based on the previously mentioned criteria, a minimum sample size of 119 participants was needed.

A total of 120 participants were included in this study and divided into two groups : 60 PsA patients receiving biological therapy for longer than three months and 60 healthy controls of the same age and gender . All PsA patients were diagnosed according to CASPAR classification criteria.[14]

Exclusion criteria:

All patients with rheumatic, autoimmune, inflammatory, or other dermatological conditions were not included. Patients with infectious diseases or malignancies were also excluded. Newly diagnosed patients and those on biologics for less than 3 months were also excluded.

Study procedure

All patients were subjected to a complete medical history, including age, residence, lifestyle, special habits (e.g., smoking), disease onset, course, duration, current biological therapy, and other comorbidities.

Each patient underwent a detailed systemic and rheumatological examination. The Disease Activity Assessment in Psoriatic Arthritis (DAPSA score) was used to

assess joint disease activity [15].Patients were classified as remission (REM), low disease activity (LDA), moderate disease activity (MDA), and high disease activity (HDA), cut-off values of ≤4 for REM, >4 and ≤14 for LDA, >14 and ≤28 for MDA, and >28 for HDA.

Moreover, skin disease activity was evaluated using the Psoriasis Area and Severity Index (PASI score) [16]. Psoriasis severity was categorized into severe (PASI >12), moderate (PASI 7-12), and mild (PASI <7). [17] Clinical evaluation, blood samples for estimation of serum CLP biomarker, and Ultrasound Assessment were performed at the same time.

Biomarkers Estimation

Serum separator tubes were used to collect venous blood samples from each participant under sterile circumstances. The samples were centrifuged at 1000 x g for 20 minutes. Separated serum samples were kept at -80°C for subsequent use.

Sandwich ELISA KIT (ELK Biotech, Cat. ELK4602) was used to quantify human serum CLP (S100A8/S100A9 heterodimer) with high specificity and no cross-reactivity with analogs. The procedure was performed according to the manufacturer's protocol. In short , microtiter plates pre-coated with anti-human CLP antibody were loaded with standards and samples. Bound CLP was detected using a biotin-conjugated anti-CLP antibody, followed by avidin–HRP. After washing, the TMB substrate was added, producing a color change proportional to CLP concentration. The reaction was stopped with H_2SO_4, and the absorbance was measured at 450 ± 10 nm. The concentration of human serum CLP in the samples was then calculated by comparing the OD of the samples with the standard using the standard curve.

Ultrasound Assessment:

Sonographic evaluations were carried out by a skilled musculoskeletal radiologist who was unaware of the laboratory and clinical data of the study population to ensure objectivity. Scores were obtained after performing high-resolution musculoskeletal ultrasound (MSUS) using an ultrasound machine (Philips, EPIQ 7G US machine), equipped with a 5-18 MHZ linear probe on the dominant site. GS synovial and PD signal scores and any other findings were recorded according to

the ultrasound composite score (PsASon13) for assessing inflammatory and structural lesions in PsA [18].

Statistical analysis

SPSS v22.0 (IBM) was used to analyze data [19]. The Kolmogorov-Smirnov test assessed normality. Comparisons used the Mann-Whitney U test. Spearman's ρ assessed correlations. ROC analysis evaluated serum CLP performance.

1. RESULTS

This study included 60 patients with PsA and 60 age- and sex-matched healthy controls. Among the PsA patients, females presented 68.3%, with a median age of 35 (Table 1). The median disease duration was 66 months for skin involvement and 24 months for joint involvement. A positive family history of PsA was reported in 30% of patients, while 13.3% had a family history of other rheumatological diseases. The dominant arthritis pattern was polyarticular in 43.3%, followed by oligoarticular (31.7%), distal interphalangeal involvement (20%), axial disease (3.3%), and arthritis mutilans (1.7%). Regarding disease activity scores, the median PASI and DAPSA scores were 5.2 and 12.2, respectively. Nearly half of the patients (46.7%) had mild skin involvement, while 26.7% had moderate and severe skin involvement, as assessed by the PASI score. Based on the DAPSA score, 50% of patients had low disease activity, 33.3% had moderate activity, 11% were in remission, and only 5% had high disease activity. The median (IQR) SON13 imaging score was 7.0 (3.0–14.0), ranging from 0 to 24. Regarding treatment, 54 patients (90%) received methotrexate, 66.7% were on adalimumab, and 34.3% on secukinumab (Table 2). The median serum CLP levels were 1468.4 ng/mL in patients and 1169.7 ng/mL in controls, showing a highly significant difference ($p \leq 0.001$). A significant difference in ESR was also found between patients and controls ($p = 0.005$), while the difference in CRP levels was not statistically significant (Table 3). A strong positive correlation was observed between DAPSA score and SON13 imaging score (rho = 0.915, $p < 0.001$), and both were significantly correlated with serum CLP (rho = 0.691 and 0.800, respectively; $p < 0.001$). PASI score was moderately correlated with DAPSA (rho = 0.494) and SON13 (rho = 0.435) scores ($p < 0.001$) and showed weaker correlations with ESR and CRP. Joint disease duration was weakly but significantly correlated with ESR (rho = 0.343, $p = 0.007$). No significant

correlations were found between skin disease duration and inflammatory markers or activity scores (Table 4). The optimal cut-off value of serum CLP for distinguishing PsA patients from controls was 1285 ng/mL, with a specificity of 81.7% and sensitivity of 73.3%, as determined by ROC analysis (Figure 1, Table 5).

2. DISCUSSION

Both skin and musculoskeletal system including joints and entheses are intensity affected in psoriatic arthritis with joint manifestation tending to be polyarticular rather than oligoarticular or DIP. Axial disease and arthritis mutilans are usually the least of all to be encountered. The mentioned patterns changed widely in percentage among different publications. The disease is a collective interaction between many genetic, environmental and immune mediated inflammatory cascades which may be unexpectedly diffused to include features out side skin and musculoskeletal system [20, 21].

The majority of cases suffered skin manifestation earlier than joint manifestation making the course of disease in psoriatic arthritis patients with preceding skin manifestation prolonged than the minority of patients suffered joint manifestation as primary lesions. [21] In this study as educed from median PASI of 5.2 and median DAPSA of 12.2 most patients had mild to moderate skin affection and moderate joint activity.

The role of serum CLP is increasingly considered in case of systemic autoimmune diseases as non invasive efficient biomarker. [22] For PsA, in particular, recent reports have proposed the ability of serum CLP to discriminate active disease and predict treatment outcomes [23,24]. The current study proved that PsA patients had significantly higher serum CLP levels (PsA 1468.4 ng/ml and control 1169.7 ng/ml), which could serve as a valuable inflammatory biomarker.

ESR was significantly variable among patients and controls investigated; CRP showed no noticeable variation. This finding is mostly due to the fact that ESR is usually more sensitive in highlighting mild inflammation. [23, 24]

No association between CRP and serum CLP was reported despite both being elevated in PsA, which may suggest that serum CLP may function independently of acute-phase reactants and be more efficient reflection to local Neutrophil-driven activity than CRP. Serum CRP is documented by ***Torgutalp et al. (2021)*** to be of special benefit in CRP negative patients. [25]

Patients included in study were subjected to full clinical evaluation side by side to imaging and biochemical assessment for the highest benefit.

The SON13 scores ranged between 3.0–14.0 covering a vast range of synovitis severity. The scores were efficiently correlated to clinical scores (PASI,DAPSA) and laboratory biomarkers assessed (ESR, CRP, and serum CLP), ultrasound scores are out of doubt beneficial in spotting disease activity both in clinical and subclinical inflammation. The same assumption was also documented by ***Sakellariou et al. (2019)*** and ***Wirth et al. (2022).*** [24,26].

The correlation between ultrasonographic evaluation and DAPSA with stressing on its role in disease follow up and predicting diagnosis was also obtained by ***Ruta et al. (2017) and Sakellariou et al. (2019)*** [26,27]

The collective roles of clinical, imaging and laboratory assessments without underrating of any of them are the mainstone of PsA assessment. The recent study emphasize the role of CLP which can even compete imaging in its role in evaluating synovial inflammation and joint structural distortion.

Serum CLP levels scored 73.3% sensitivity and 81.7% specificity in characterizing PsA patients, The cut-off value of discrimination between patients and healthy controls was 1285 ng/ml. When stressing on subclinical synovitis including low and uncertain joint activity, sCLP mirrored ultrasonographic in diagnosis. Inciarte-Mundo and colleagues demonstrated that Elevated calprotectin levels (≥3.7 µg/ml) may indicate relapse in RA and PsA patients. This degree of sensitivity makes serum CLP of special benefit when deciding early treatment is questionable, as in the case of mild/minimal skin manifestation and denovo joint complaints. [13,28,29]

The usefulness of serum CLP in PsA is further supported by a few previous studies. For instance, **Inciarte-Mundo et al. (2018)** [29] reported that levels of serum CLP markedly reduced in anti-TNF responder patients with PsA. In

addition, a systematic review of **Jarlborg et al. (2020)** [30] found serum CLP to be a promising biomarker throughout the course of spondyloarthritis continuum, particularly if combined with imaging techniques.

Unfortunately, CRP and ESR are misleading in many cases, especially CRP, which can be even negative in some cases. Serum CLP, on the other hand, shows perfect correlation with all PASI, DAPSA, ESR, and SON13, reflecting its marvelous ability to detect the level of inflammatory activity both in the skin and joints.

Torgutalp et al. (2021) [25] also proposed that serum CLP was superior to CRP in coping with ultrasonographic synovitis in PsA. This makes it more valuable than CRP, especially when predicting subclinical and moderate disease activity.

While previous longitudinal studies have highlighted the efficacy of sCLP in management outcomes prediction whether satisfying response or possible relapse, particularly with methotrexate and adalimumab. [29,5] Our study adds a novel dimension by identifying a specific cut-off value for serum CLP, supporting its utility as a practical diagnostic and monitoring tool.

Despite moderate sensitivity and moderate to low specificity regarding CRP and ESR respectively in follow up of disease management with misleading even normal levels in some active cases, those markers are still unfortunately trusted. Serum CLP has better sensitivity and specificity and can serve as a predictor of subclinical synovial activity, a better indicator for disease suppression on management and a better early predictor of relapse. [29,31]

Despite the aggressive therapy using methotrexate (90%), adalimumab (66.7%), and secukinumab (34.3%), residual disease activity persisted. Reflect an assertive strategy in disease-modifying therapy. Patients exhibiting subclinical inflammation, undetected by conventional markers, may gain from early therapeutic intervention, optimization of anti-TNF dosage, or a transition to a different biologic when biomarkers such as serum CLP are incorporated into standard monitoring.

Conclusion

According to study results, Serum CLP was truthful reflection to disease activity obtained by ultrasonographic findings in PsA. It can be used in following up patients receiving biologic therapy.

Limitations and Recommendations

Some restrictions were met in the recent study need to be avoided when designing similar studies.

First, due to the study's cross-sectional design, it isn't yet known whether the serum CLP precedes other manifestations of the disease or only occurs concurrently with the ongoing inflammation. Therefore, longitudinal studies are recommended to better understand its role in predicting disease flare.

Second, although the sample was statistically sufficient, it was relatively small and from a single-centre cohort. Larger multi-centric trials are recommended to emphasize the generalizability of the results among wider groups of patients.

Lastly, different types of medication introduced to patients may not intentionally affect the biomarker level, so grouping patients based on disease phenotype and treatment is recommended in future studies for better judgment of the biomarker's role in disease.

3. Statements & Declarations

12

Funding

The authors affirm that they did not receive any funding, grants, or other forms of assistance while working on this manuscript.

Competing Interests

38

No pertinent financial or non-financial interests are disclosed by the authors.

.

10

Data Availability

Upon reasonable request, the corresponding author will provide the datasets created and/or analyzed during the current work.

Ethics Approval

7

The Institutional Review Board of Kafrelsheikh University Hospital accepted this study (Approval No. KFSIRB 200-251), and it was carried out in compliance with the Declaration of Helsinki's principles.

4

Consent to Participate

Every participant in the study submitted written informed consent.

39

Consent to Publish

Not applicable. This manuscript does not contain any personal information in any way, including pictures, videos, or personal details.

Clinical trial number

Not applicable.

References

1. Azuaga AB, Ramírez J, Cañete JD. Psoriatic arthritis: pathogenesis and targeted therapies. International journal of molecular sciences. 2023 Mar 3;24(5):4901.
2. Scotti L, Franchi M, Marchesoni A, Corrao G. Prevalence and incidence of psoriatic arthritis: a systematic review and meta-analysis. InSeminars in Arthritis and Rheumatism 2018 Aug 1 (Vol. 48, No. 1, pp. 28-34). WB Saunders.
3. Alinaghi F, Calov M, Kristensen LE, Gladman DD, Coates LC, Jullien D, Gottlieb AB, Gisondi P, Wu JJ, Thyssen JP, Egeberg A. Prevalence of psoriatic arthritis in patients with psoriasis: a systematic review and meta-analysis of observational and clinical studies. Journal of the American Academy of Dermatology. 2019 Jan 1;80(1):251-65.
4. Zalesak M, Danisovic L, Harsanyi S. Psoriasis and psoriatic arthritis—associated genes, cytokines, and human leukocyte antigens. Medicina. 2024 May 16;60(5):815.
5. Li B, Li G, Song Z, Zhang Z. Serum calprotectin as a promising inflammatory biomarker in psoriatic arthritis: a 1-year longitudinal study. Rheumatology and Therapy. 2023 Feb;10(1):149-60.
6. Carnazzo V, Redi S, Basile V, Natali P, Gulli F, Equitani F, Marino M, Basile U. Calprotectin: two sides of the same coin. Rheumatology. 2024 Jan 1;63(1):26-33
7. Sejersen K, Eriksson MB, Larsson AO. Calprotectin as a Biomarker for Infectious Diseases: A Comparative Review with Conventional Inflammatory Markers. International Journal of Molecular Sciences. 2025 Jul 4;26(13):6476.
8. Vignesh KS, Deepe Jr GS. Immunological orchestration of zinc homeostasis: the battle between host mechanisms and pathogen defenses. Archives of biochemistry and biophysics. 2016 Dec 1;611:66-78.

9. Inciarte-Mundo J, Frade-Sosa B, Sanmartí R. From bench to bedside: Calprotectin (S100A8/S100A9) as a biomarker in rheumatoid arthritis. Frontiers in Immunology. 2022 Nov 3;13:1001025.

10. Zollner A, Schmiderer A, Reider SJ, Oberhuber G, Pfister A, Texler B, Watschinger C, Koch R, Effenberger M, Raine T, Tilg H. Faecal biomarkers in inflammatory bowel diseases: calprotectin versus lipocalin-2—a comparative study. Journal of Crohn's and Colitis. 2021 Jan 1;15(1):43-54.

11. Abd Elsamea MH, Mahran SA, Badr AN, Kamal DT, Khidre TM. Evaluation of serum calprotectin level as a biomarker of disease activity in rheumatoid arthritis and osteoarthritis patients. The Egyptian Rheumatologist. 2022 Jun 1;44(3):185-90.

12. Agache M, Popescu CC, Enache L, Mogoșan C, Filippucci E, Codreanu C. Additional Value of Ultrasound in Patients with Psoriatic Arthritis within Treatment Target. Journal of Clinical Medicine. 2024 Aug 5;13(15):4567.

13. Badr FM, Farouk HM, Habeeb RA, Teama MA, Hamada MN, ElSherbiny DA. Serum calprotectin as an inflammatory marker in psoriatic arthritis patients: relation to disease activity and musculoskeletal ultrasound findings. Egypt J Immunol. 2024 Jul;31(3):140-9.

14. Tillett W, Costa L, Jadon D, Wallis D, Cavill C, McHUGH JE, Korendowych E, McHUGH NE. The ClASsification for Psoriatic ARthritis (CASPAR) criteria–a retrospective feasibility, sensitivity, and specificity study. The Journal of rheumatology. 2012 Jan 1;39(1):154-6.

15. Schoels MM, Aletaha D, Alasti F, Smolen JS. Disease activity in psoriatic arthritis (PsA): defining remission and treatment success using the DAPSA score. Annals of the rheumatic diseases. 2016 May 1;75(5):811-8.

16. 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. Journal of the American Academy of Dermatology. 2004 Jun 1;50(6):859-66.

17. Goel S, Bansal S, Chopra D, Batra J. Metabolic Derangements in Patients of Psoriasis and Their Association with Psoriasis Area Severity Index Score: A Cross-Sectional Study. Natl. J. Lab. Med. 2021;10.

18. Ficjan A, Husic R, Gretler J, Lackner A, Graninger WB, Gutierrez M, Duftner C, Hermann J, Dejaco C. Ultrasound composite scores for the assessment of inflammatory and structural pathologies in Psoriatic Arthritis (PsASon-Score). Arthritis Research & Therapy. 2014 Oct 31;16(5):476.

19. https://www.ibm.com/support/pages/spss-statistics-220-available-download

20. Veale DJ, Fearon U. The pathogenesis of psoriatic arthritis. The Lancet. 2018 Jun 2;391(10136):2273-84.

21. Gladman DD, Antoni C, Mease P, Clegg DO, Nash P. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. Annals of the rheumatic diseases. 2005 Mar 1;64:ii14-7.

22. Abildtrup M, Kingsley GH, Scott DL. Calprotectin as a biomarker for rheumatoid arthritis: a systematic review. The Journal of rheumatology. 2015 May 1;42(5):760-70.

23. Adarsh MB, Dogra S, Vaiphei K, Vaishnavi C, Sinha SK, Sharma A. Evaluation of subclinical gut inflammation using faecal calprotectin levels and colonic mucosal biopsy in patients with psoriasis and psoriatic arthritis. British Journal of Dermatology. 2019 Aug 1;181(2):401-2.

24. Wirth T, Balandraud N, Boyer L, Lafforgue P, Pham T. Biomarkers in psoriatic arthritis: A meta-analysis and systematic review. Frontiers in Immunology. 2022 Nov 30;13:1054539.

25. Torgutalp M, Yayla ME, Eroglu DS, Dincer AB, Yurteri EU, Okatan IE, Sezer S, Guloksuz EG, Us E, Turgay TM, Kinikli G. Serum calprotectin is indicating clinical and ultrasonographic disease activity in rheumatoid arthritis, even with normal C-reactive protein levels. Mediterranean Journal of Rheumatology. 2021;32(1):56-65.

26. Sakellariou G, Lombardi G, Vitolo B, Gomarasca M, Faraldi M, Caporali R, Banfi G, Montecucco C. Serum calprotectin as a marker of ultrasound-detected synovitis in early psoriatic and rheumatoid arthritis: results from a cross-sectional retrospective study. Clin Exp Rheumatol. 2019 May 1;37(3):429-36.

27. Ruta S, Marin J, Felquer ML, Ferreyra-Garrot L, Rosa J, García-Monaco R, Soriano ER. Utility of Power Doppler Ultrasound–detected synovitis for the prediction of short-term flare in psoriatic patients with arthritis in clinical remission. The Journal of Rheumatology. 2017 Jul 1;44(7):1018-23.

28. Alenius GM, Eriksson C, Rantapaa Dahlqvist S. Interleukin-6 and soluble interleukin-2 receptor alpha--markers of inflammation in patients with psoriatic arthritis?. Clinical & Experimental Rheumatology. 2009 Jan 1;27(1):120.

29. Inciarte-Mundo J, Ramirez J, Hernández MV, Ruiz-Esquide V, Cuervo A, Cabrera-Villalba SR, Pascal M, Yagüe J, Cañete JD, Sanmarti R. Calprotectin strongly and independently predicts relapse in rheumatoid arthritis and polyarticular psoriatic arthritis patients treated with tumor necrosis factor inhibitors: a 1-year prospective cohort study. Arthritis research & therapy. 2018 Dec 13;20(1):275.

30. Jarlborg M, Courvoisier DS, Lamacchia C, Martinez Prat L, Mahler M, Bentow C, Finckh A, Gabay C, Nissen MJ, Physicians of the Swiss Clinical Quality Management (SCQM) Registry. Serum calprotectin: a promising biomarker in rheumatoid arthritis and axial spondyloarthritis. Arthritis research & therapy. 2020 May 6;22(1):105.

31. Sokolova MV, Simon D, Nas K, Zaiss MM, Luo Y, Zhao Y, Rech J, Schett G. A set of serum markers detecting systemic inflammation in psoriatic skin, entheseal, and joint disease in the absence of C-reactive protein and its link to clinical disease manifestations. Arthritis research & therapy. 2020 Feb 12;22(1):26.

Table 1. Comparison of sociodemographic variables between PsA patients and the control group

Studied variables		**PsA Cases (N=60)**		**Controls (N=60)**	
		N	**%**	**N**	**%**
Gender	**Male**	19.0	31.7%	20.0	33.30%
	Female	41.0	68.3%	40.0	66.70%

Age (years):), *Median (IQR)*		35.0(25.0-44.0)		35.0(27.0-45.0)	
BMI (Kg/m²):), *Median (IQR)*		24.0(20.0-27.0)		24.1 (20.2–27.3)	
Marital status	**Ever Married**	47.0	78.3%	44.0	73.3%
	Single	13.0	21.7%	16.0	26.7%
Residence	**Urban**	29.0	48.3%	24.0	40.0%
	Rural	31.0	51.7%	36.0	60.0%
Occupation	**Student**	29.0	48.3%	24.0	40.0%
	Governmental	32.0	53.3%	34.0	56.7%
	Private	10.0	16.7%	11.0	18.3%
	Retired	7.0	11.7%	6.0	10.0%
Smoking	**Active**	5.0	8.3%	8.0	13.3%
	Passive	4.0	6.7%	3.0	5.0%
	Non-smoking	51.0	85.0%	49.0	81.7%

N.B. BMI body mass index, PsA: Psoriatic Arthritis

Table 2. Clinical Characteristics and Treatment History of PsA Patients

Studied variables		N= 60	%
Disease duration (years), *Median (IQR)*	**Skin affection**	66.0(42.0-168.0)	
	Joint affection	24.0(12.0-48.0)	
Main dominant classifications	**Oligoarticular**	19.0	31.7%
	Polyarticular	26.0	43.3%
	DIP	12.0	20.0%
	Arthritis Mutilans	1.0	1.7%
	Axial	2.0	3.3%
Family history	**Psoriatic Arthritis**	18.0	30.0%
	Other rheumatic diseases	8.0	13.3%
MTX drug intake	**Yes**	54.0	90.0%
	Median Duration (months, IQR)	12.0(6.0-30.0)	
Humira drug intake	**Yes**	40.0	66.7%
	Median Duration (months, IQR)	8.0(6.0-15.0)	
Cosyntyx drug intake	**Yes**	20.0	33.3%
	Median Duration (months, IQR)	18.0(9.0-36.0)	
PASI score	**Mild**	28.0	46.7%
	Moderate	16.0	26.7%
	Severe	16.0	26.7%
	Median (IQR)	5.2(3.4-10.0)	
DAPSA score	**REM**	7.0	11.7%
	LDA	30.0	50.0%
	MDA	20.0	33.3%
	HDA	3.0	5.0%
	Median (IQR)	12.2(8.3-17.8)	
SON13 Imaging Score	***Median (IQR)***	7.0(3.0-14.0)	

N.B. IQR: Interquartile range, DIP: Distal Interphalangeal Predominant Psoriatic Arthritis, MTX: Methotrexate, PASI: Psoriasis Area and Severity Index, DAPSA: Disease Activity in Psoriatic Arthritis, , SON13: Sonographic Score of 13 Joints, PsA: Psoriatic Arthritis, REM: remission, LDA: low disease activity, MDA: moderate disease activity, HAD: high disease activity

Table 3. Comparison of inflammatory biomarkers among PsA patients and controls

Biomarker		Median	25th Percentile	75th Percentile	Minimum	Maximum
Serum Calprotectin (ng/mL)	**PsA patients**	1468.4	1247.9	1796.2	843.5	2557.2
	Controls	1169.7	990.2	1276.8	705.0	1398.5
	P-value	**≤0.001***				
CRP (mg/L)	**PsA patients**	5.1	2.5	12	0.3	117.6
	Controls	4.8	2.9	6.9	1.0	8.9
	P-value	**0.108**				
ESR (mm/hr)	**PsA patients**	15.0	10.0	22.5	2.0	90.0
	Controls	11.7	8.4	15.3	5.4	24.3
	P-value	**0.005***				

N.B. PA: Psoriatic Arthritis, CRP: C-Reactive Protein, ESR: Erythrocyte Sedimentation Rate, PsA: Psoriatic Arthritis, *Percentiles 25 and 75 represent the interquartile range (IQR).*

****Significant.***

Table 4. Spearman's Correlation Matrix Between Clinical and Laboratory Variables Among Psoriatic Arthritis Patients

		Skin disease duration (months)	Joint disease duration (months)	PASI score	DAPSA score	SON13 Imaging Score	ESR	CRP	Serum CLP
Skin disease duration (months)	***Rho***	1	0.481	-0.020	0.191	0.226	0.039	-0.092	0.090
	P value		<0.001*	0.877	0.143	0.083	0.764	0.485	0.495
Joint disease duration (months)	***Rho***	0.481	1	0.041	0.230	0.140	0.343	0.212	-0.037
	P value	<0.001*		0.754	0.078	0.287	0.007*	0.104	0.782
PASI score	***Rho***	-0.020	0.041	1	0.494	0.435	0.391	0.230	0.222
	P value	0.877	0.754		<0.001*	0.001*	0.002*	0.077	0.088
DAPSA score	***Rho***	0.191	0.230	0.494	1	0.915	0.376	0.360	0.691
	P value	0.143	0.078	<0.001*		<0.001*	0.003*	0.005*	<0.001*
SON13 Imaging Score	***Rho***	0.226	0.140	0.435	0.915	1	0.341	0.273	0.800
	P value	0.083	0.287	0.001*	<0.001*		0.008*	0.035*	<0.001*
ESR	***Rho***	0.039	0.343	0.391	0.376	0.341	1	0.372	0.373
	P value	0.764	0.007*	0.002*	0.003*	0.008*		<0.001*	<0.001*
CRP	***Rho***	-0.092	0.212	0.230	0.360	0.273	0.372	1	0.094
	P value	0.485	0.104	0.077	0.005*	0.035*	<0.001*		0.305
Serum CLP	***Rho***	0.090	-0.037	0.222	0.691	0.800	0.373	0.094	1
	P value	0.495	0.782	0.088	<0.001*	<0.001*	<0.001*	0.305	

PASI: Psoriasis Area and Severity Index, DAPSA: Disease Activity in Psoriatic Arthritis, , SON13: Sonographic Score of 13 Joints, PsA: Psoriatic Arthritis, CLP: calprotectin, CRP: C-Reactive Protein, ESR: Erythrocyte Sedimentation Rate

**Significant.*

Table 5. Receiver Operating Characteristic (ROC) Analysis for serum CLP in the prediction of the occurrence of PsA in the studied patients.

	AUC	95% CI	Cut-off Score	Sensitivity	Specificity
Serum CLP	0.839	0.766-0.913	≥1285.0	73.3%	81.7%

CLP: calprotectin, , PsA: Psoriatic Arthritis

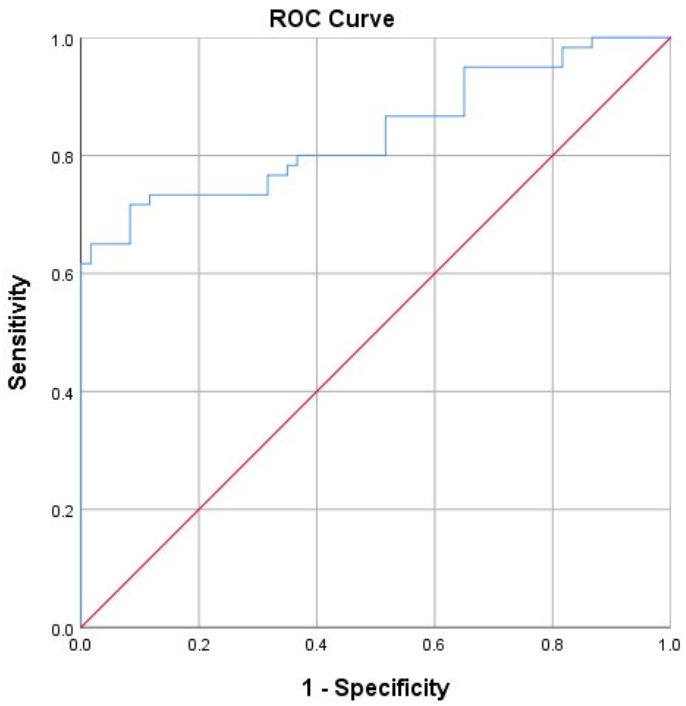

Figure 1. ROC curve showing the performance of serum CLP in the prediction of occurrence of PsA in the studied patients.