Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 11820 - 11827
Received 05 March 2021; Accepted 01 April 2021.

High Sensitivity C - Reactive Protein in Psoriasis: A Marker of Disease Severity and Cardiovascular Risk.

Siham Taher Amedi*, Salam Naser Zangana**

*MBChB, DVD (UK). Dermatologist in Hawler Medical University-College of Medicine.
** Corresponding author .MBChB, DM, MD, FRCP (Edin), FRCP (Glasg). Consultant Physician and Assistant Professor of internal medicine, Hawler Medical University, College of Medicine. Email:dr_salam2003@yahoo.com. Telephone: 009647504972628

Abstract

Background: Psoriasis is a chronic skin disease in which many factors play a role in its initiation. Recently, psoriasis has been considered a systemic disease associated with many cardiovascular diseases (CVDs). High sensitivity C - reactive protein (Hs-CRP) is an important inflammatory marker to predict cardiovascular diseases and it has significant importance in psoriasis because of its close relation with skin inflammation. The study aimed to evaluate the role of Hs-CRP as a marker of disease severity and cardiovascular risk factor in patients with psoriasis.

Material and Methods: 110 patients were enrolled in this study and were divided into two groups, 55 patients diagnosed as having psoriasis (group I) and 55 age and sex-matched healthy controls (group II). Psoriasis patients with Psoriasis Area Severity Index (PASI) less than 10 are considered as mild psoriasis and PASI greater than 10 considered as moderate to severe psoriasis. Hs-CRP levels were detected in the studied population.

Results: A significant correlation between hs-CRP and PASI was found ($p < 0.0001$). The mean value of hs-CRP in PASI<10 (mild psoriasis) was 0.8 mg/L± 0.42while the mean value of hs-CRP with PASI >10 (moderate to severe psoriasis) was 6.96 ± 4.18 mg/L.

Conclusion: Patients with moderate to severe psoriasis have higher mean serum hs-CRP level than patients with mild psoriasis and controls. Serum hs-CRP level correlates significantly with the PASI and can be used as a marker for assessing disease severity and subsequently to predict CVDs.

Keywords: Psoriasis, hs-CRP, Psoriasis Area Severity Index (PASI), CVDs.

Introduction:

Psoriasis is a common and chronic skin disorder that affects 1 to 3% of populations [1] and causes skin cells to multiply rapidly nearly 10 times faster than normal[2]. It is characterized by sharply demarcated, erythematous, scaly plaques of different sizes [3]. The lesions are usually distributed symmetrically and can grow anywhere in the body but occur most commonly on the extensor aspects of elbows and knees, scalp, lumbosacral region, and umbilicus[4]. The disease shows

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 11820 - 11827
Received 05 March 2021; Accepted 01 April 2021.

exacerbations and remission attacks [5]. The mean age of presentation is between 15 – 20 years, with a second peak at 55 – 60 years. Men and women are equally affected [6]. Many factors may be responsible for the pathogenesis of the disease, such as immunological, environmental, genetic, and inflammatory factors[7]. There are five main types of psoriasis: plaque, guttate, inverse, pustular, and erythrodermic.[8] In the present study, all our cases were of plaque psoriasis which was considered the commonest type, accounting for 90 percent of cases.

Psoriasis is associated with many comorbid conditions like type2 diabetes mellitus, metabolic syndrome , and cardiovascular diseases (CVDs), which might decrease the quality of life.[9] Changes in plasma lipid composition in psoriatic patients were responsible for an increased risk of atherosclerosis.[10] Many current data hypothesized the role of autoimmunity and inflammation in the pathogenesis of psoriasis. The rapid growth of the epidermal layer of the skin is believed to be secondary to dermal inflammation with abnormal keratinocyte proliferation.[11] Many immune cells such as dendritic cells, macrophages, and T cells move from the dermis to the epidermis and secrete inflammatory chemical signals (cytokines) such as interleukin-36γ, interleukin-22, interleukin-1β, interleukin-6, and tumor necrosis factor- α [12]. The ongoing inflammatory process in psoriasis affects the arterial wall, promoting the atherosclerotic process and increasing the risk of cardiovascular disease. Inflammation plays a fundamental link between psoriasis and atherosclerosis.[13]

C-reactive protein plays an important role in the defense mechanism against infection and is considered a pivotal marker for acute inflammation, infection, and tissue injury.[14] Highly-sensitive' C-reactive protein is a brand of CRP and refers to the detection of small amounts in C-reactive protein concentrations that occur below the 'normal' cut-off values.[15] Hs-CRP is considered an independent risk marker of cardiovascular disease. Hs-CRP concentrations predict vascular risk even when cholesterol concentrations are low and also patients with low LDL-C and high hs-CRP are at a higher risk of future coronary events.[16] C-reactive protein has special importance for psoriasis due to its relation with cytokines which are responsible for skin inflammation. In the current study, we tried to determine the level of CRP by using a highly sensitive method and to correlate this with the severity of disease and to predict ongoing CVD. To the best of our knowledge, there was no previous study done in Erbil city regarding the same subject.

Material and methods:

This case-control study was conducted between September 2019 and March 2020 in Rizgary teaching hospital-Department of medicine and Shadi health center-Department of dermatology in Erbil city, Iraq. 110 patients were enrolled in this study and were divided into two groups; 55 patients diagnosed as having psoriasis (group I) and 55 age and sex-matched healthy as control (group II). Psoriasis patients with Psoriasis Area Severity Index (PASI) less than 10 are considered as mild Psoriasis and PASI greater than 10 considered as moderate to severe Psoriasis.[17, 18] The inclusion criteria were psoriasis patients, age ≥18 years and of both genders.

Patients with known chronic infections (i.e. tuberculosis), any apparent signs of acute or chronic inflammation (hepatitis, arthritis or autoimmune disease), Liver or renal problems, excessive alcohol consumption, statin usage, and pregnant women were excluded from the study. Patients with psoriasis were diagnosed by clinical features. A detailed history which including personal data, present complaints, past medical history, family history, personal history, and treatment history was taken followed by a physical examination. Under aseptic precautions, a blood sample was drawn from all participants to estimate serum hs-CRP levels using COBAS INTEGRA cardiac C - reactive protein (latex) High Sensitive (CRPHS test) and to be analyzed using fully automated Cobas E601 clinical chemistry analyzer. A high-sensitivity CRP test measures low levels of CRP down to 0.04 mg/L.[19] According to The American Heart Association and U.S. Centers for Disease Control and Prevention , we can define risk groups as follows: low: hs-CRP level under 1.0 mg/L, average: between 1.0 and 3.0 mg/L, and high: above 3.0 mg/L.[20]

Questionnaire and data collection:

The data were collected by designing a self-administered, close-ended questionnaire, prepared for this purpose by the researcher and was filled by direct interview.

Ethical considerations:

An ethical approval was submitted to the Ethics Committee of the College of Medicine at Hawler Medical University. This study was conducted by using informed verbal consent that was obtained from all patients before participating in the study.

Statistical analysis:

For data analysis, the statistical package for social sciences (SPSS, version 22) was used. The results were analyzed using the frequency of distribution, the Chi-square test of association was used to compare proportions, and a 95% C.I. reference range was calculated. Fisher's exact test was used when the expected count of more than 20% of the cells of the table was less than 5. Appropriate tables and graphs were used for data representation .P-value of ≤ 0.05 was considered as statistically significant.

Results:

As has been mentioned in materials and methods, the study population enrolled 110 participants and were divided into two groups, 55 psoriasis patients (group I), and 55 age and gender matched controls (group II). Table 1 shows that the mean ±SD of Hs-CRP level in psoriasis patients (3.7±4.2) was significantly higher (p= <0.001) when compared to the controls (0.47±0.21).

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 11820 - 11827
Received 05 March 2021; Accepted 01 April 2021.

Table 1: Comparison of Hs-CRP values between psoriasis patients and controls.

Variables		Group I Psoriasis Patients (n=55)	Group II Controls (n=55)	P value
Gender	Male	25	25	NS
	Female	30	30	NS
Age (years)		32.75±8.9	33.98±12.7	0.54
Hs-CRP (mg/l)		3.7±4.2	0.47±0.21	<0.001

Ns=Non specific

According to the PASI, the 55 psoriasis patients were further divided into two subgroups, 29 patients with PASI <10 had mild psoriasis and 26 patients with PASI >10 had moderate to severe psoriasis. The mean ±SD of Hs-CRP level in PASI >10 group (6.96±4.18) was significantly higher (p= <0.001) when compared to the PASI <10 group (0.82±0.43), as shown in Table2.

Table 2: Comparison of Hs-CRP values between psoriasis patients.

Variables	PASI<10 (n=29)	PASI>10 (n=26)	P value
Hs-CRP (mg/l)	0.82±0.43	6.96±4.18	<0.001
PASI	4.92±2.84	18±6.2	<0.001

Hs-CRP showed a significant strong positive correlation with PASI (r=0.66, p=<0.001), as shown in table 3.

Table 3: Correlation of Hs-CRP values with PSAI in psoriasis patients.

Pairing	Psoriasis patients	
	r value	P value
Hs-CRP vs PSAI	0.66	<0.001

Discussion:

The present study showed that the mean level of Hs-CRP was significantly high in psoriasis patients compared to controls and it was positively correlated with PASI. The high level of Hs-

CRP in this study is in concordance with many previous studies. A study was done by Yiu et al. in china [21], and another one by Lucy Piper[22] in 2009 has shown that patients with psoriasis have significantly high baseline levels of hs-CRP compared with healthy controls. Another two studies done by Agravatt et al [23] and Jagannath et al[24] showed the same results.

Although psoriasis is considered a chronic immune-mediated skin disease, many current data focus on the role of inflammation in the pathogenesis. T cells and their cytokines have been shown to trigger a serious inflammation, and lately, psoriasis was assumed as an immune-mediated inflammatory disease with subsequent systematic effects of the inflammation.[25,26] Several studies were conducted to define the inflammatory process of psoriasis by measuring multiple proinflammatory cytokines such as IL-1 and hepatic acute phase reactants as CRP.[27] CRP testing and to be more specific, hs-CRP, is especially important as it has been proved to be a risk predictor for many CVDs.[28,29] Many recent studies, like the aforementioned above, showed that psoriatic patients have increased CRP levels and it has been suggested that psoriasis is a systemic inflammatory disease and hypothesized that psoriatic patients are more liable for cardiovascular diseases and several comorbidities. , like type 2 diabetes, metabolic syndrome, hypertension, and atherogenic dyslipidemia.[30-32] In the present study, the mean hs-CRP level in psoriatic patients was 3.7 mg/l which will put them under the high-risk group category for ongoing CVDs according to The American Heart Association and U.S. Centers for Disease Control and Prevention .[20]

In the current study, there was a significant association between disease activity (represented by PASI) and elevated hs-CRP levels. Psoriatic patients with PASI more than 10 had significantly higher hs-CRP levels than those with PASI less than 10, and the correlation was statistically positive. This result supports again the inflammatory hypothesis. Several other studies have also reported a correlation between high hs-CRP and PASI.[33-35] Thus, hs-CRP can be considered as a helpful marker to detect disease severity, as well as to monitor the disease course and its treatment.[36] Hs-CRP could be used as a strong and sensitive biomarker to evaluate psoriasis disease activity, as it is not based on visual assessment of the skin lesion.

Conclusion:

Patients with moderate to severe psoriasis (PASI > 10) have higher mean serum hs-CRP level than patients with mild psoriasis (PASI <10) and controls. Serum hs-CRP level correlates significantly with Psoriasis Area Severity Index (PASI) and can be used as a marker to detect disease severity and subsequently to predict CVDs.

Recommendations:

1-According to many recent studies, psoriasis patients are more liable to get ongoing CVDs and other comorbidities. Thus, early identification should be done by using helpful biomarkers like hs-CRP. It is widely available, inexpensive, and can be easily done in outpatient clinics.

2-Early screening in psoriasis patients will help in early intervention and turn can reduce the mortality.

3-It can also be used to monitor the disease course and treatment.

4-Further studies with a large number of patients are needed to evaluate precisely the relationship between hs-CRP and psoriasis and to detect the use of hs-CRP as a monitor to disease course and treatment.

Limitation:

The main limitation of the current study is the small number of patients.

Conflict of Interest:

No conflict of interest was declared by the author.

Financial Disclosure:

The author declared that this study has received no financial support.

References:

1. Parisi R, Symmons DP, Griffiths CE. Identification and Management of Psoriasis and Associated ComorbidiTy (IMPACT) project team. "Global epidemiology of psoriasis: a systematic review of incidence and prevalence". Journal of Investigative Dermatology.2013; 133 (2): 377–85

2. "Questions and Answers about Psoriasis". National Institute of Arthritis and Musculoskeletal and Skin Diseases. October 2013. Archived from the original on 8 July 2015. Retrieved 1 July 2015.

3. Menter A, Gottlieb A, Feldman SR. "Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics". Journal of the American Academy of Dermatology. (May 2008). 58 (5): 826–50.

4. Boehncke WH, Schön MP "Psoriasis". Lancet. (September 2015). 386 (9997): 983–94.

5. Baker BS. From Arsenic to Biologicals: A 200 year History of Psoriasis. Garner Press, 2008

6. Questions and Answers About Psoriasis". www.niams.nih.gov. 12 April 2017. Archived from the original on 22 April 2017. Retrieved 22 April 2017.

7. Krueger G, Ellis CN. Psoriasis recent advances in understanding its pathogenesis and treatment. J Am Acad Dermatol 2005; 53: 94-100.

8. Jain S). Dermatology : illustrated study guide and comprehensive board review. Springer. 2012; pp. 83–87. ISBN 978-1-4419-0524-6. Archived from the original on 8 September 2017

9. Dogan S , Atakan N Psoriasis: A Disease of Systemic Inflammation with Comorbidities, Psoriasis - Types, Causes and Medication, (2013). Dr. Hermenio Lima (Ed.), ISBN: 978-953-511065-1, InTech, DOI: 10.5772/54347. Available from: http://www.intechopen.com/books/psoriasistypes-causes-and-medication/psoriasis-a-disease-of-systemic-inflammation-with-comorbidities

10. Akkara Veetil B M, Matteson E .L. , maraditt-Kremers H, McEvoy M.T. , Crowson C S.. Trends in lipid profile in patients with psoriasis a population based analysis. BMC Dermatology .2012; 12:20 .

11. Guttman-Yassky E, Krueger J.G. Psoriasis: evolution of pathogenic concepts and new therapies through phases of translational research. British Journal of Dermatology. 2007; 157 1103–1115.

12. Gaspari AA. Innate and adaptive immunity and the pathophysiology of psoriasis. Journal of the American Academy of Dermatology. 2006;54 67-80.

13. Prodanovich S, Kirsner RS, Kravetz JD, Fangchao, Martinez L, Federman DG. 2009. Association of psoriasis with coronary artery, cerebrovascular and peripheral vascular diseases and mortality. Arch Dermatol. , 145(6): 700-703.

14. Pearson TA, Mensah GA, Alexander RW, Anderson JL, Cannon RO 3rd, Criqui M, et al. Markers of inflammation and cardiovascular disease. Circulation 2003;107: 499-511.

15. Glenn Reeves .C-reactive protein. Australian Prescriber .2007 June; 30(3):74-76.

16. Ridker PM, Nader R, Lynda R, Buring JE, Nancy R. 2002. Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events. N Engl J Med., 347: 1557-65.

17.Louden BA, Pearce DJ, Lang W, Feldman SR .A Simplified Psoriasis Area Severity Index (SPASI) for rating psoriasis severity in clinic patients . J Dermatol. 10 (2):2004.

18. Langley RG, Ellis CN .Evaluating psoriasis with Psoriasis Area and Severity Index, Psoriasis Global Assessment, and Lattice System Physician's Global Assessment. J Am Acad Dermatol. 2004;51:563- 569

19. Normal results". C-reactive protein. MedlinePlus. Retrieved 23 April 2015.

20. Lloyd-Jones DM, Liu K, Tian L, Greenland P. Assessment of C-reactive protein in risk prediction for cardiovascular disease". Annals of Internal Medicine 2006; 145 (1):35–42.

21. Yiu KH, Yeung CK, Chan HT, Wong RM, Tam S, Lam KF, Yan GH, Yue WS, Chan HH, Tse HFB. Increased arterial stiffness in patients with psoriasis is associated with active systemic inflammation. Br J Dermatol. 2011 Mar;164(3):514-20.

22. Lucy Piper .CRP proposed as marker for psoriasis severity. J Eur Acad Dermatol Venereol 2009; Advance online publication.

23. Agravatt A M and Sirajwala. H B. A Study of serum hsCRP levels to assess severity in patients with Psoriasis. IJBAR 2013; 04 (07).

24. Jagannath S, Meera. S , Jayaram S , Sahithya C S. Study of High Sensitive C Reactive Protein and Lipid Profile in Psoriasis. IJCBR 2014; 1(1): 1-6.

25.Gaspari AA. Innate and adaptive immunity and the pathophysiology of psoriasis. Journal of the American Academy of Dermatology. 2006;54 67-80.

26. Prinz JC. The role of T cells in psoriasis. Journal of European Academy of Dermatology Venerology. 2003;17 257-70.

27. Rocha Pereire P. The inflammatory response in mild and severe psoriasis. British Journal of Dermatology. 2004;150 917-928.

28. Ridker PM. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. New England Journal of Medicine. 2000;342 836-883.

29. Blake GJ, Ridker PM. Novel clinical markers of vascular wall inflammation. Circulation Research. 2001;89 763-771.

30. Ridker PM. C-reactive protein: Eighty years from discovery to emergence as a major risk marker for cardiovascular disease. Clin Chem. 2009;55:209–15.

31. Yeh ET, Palusinski RP. C-reactive protein: The pawn has been promoted to queen. Curr Atheroscler Rep.2003;5:101–5.

32. Ridker PM, Wilson PW, Grundy SM. Should C-reactive protein be added to metabolic syndrome and to assessment of global cardiovascular risk? Circulation. 2004;109:2818–25.

33. Gerkowicz A, Pietrzak A, Szepietowski JC, Radej S, Chodorowska G. Biochemical markers of psoriasis as a metabolic disease. Folia Histochem Cytobiol. 2012;50:155–70.

34. Coimbra S, Oliveira H, Reis F, Belo L, Rocha S, Quintanilha A, et al. C-reactive protein and leucocyte activation in psoriasis vulgaris according to severity and therapy. J Eur Acad Dermatol Venereol.2010;24:789–96.

35. Coimbra S, Oliveira H, Reis F, Belo L, Rocha S, Quintanilha A, et al. Circulating adipokine levels in portugese patients with psoriasis vulgaris according to body mass index, severity and therapy. J Eur Acad Dermatol Venereol. 2010;24:1386–94.

36. Vadakayil A R, Dandekeri S, Kambil S M., Ali N M.. Role of C-reactive protein as a marker of disease severity and cardiovascular risk in patients with psoriasis. Indian Dermatol Online J. 2015 Sep-Oct; 6(5): 322–325.