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Original Article

Evaluating the Prognostic Potential of MCP-1 in Patients with Rheumatoid Arthritis

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ABSTRACT

Background: Rheumatoid Arthritis (RA) is a pervasive, chronic inflammatory condition. Swift diagnosis and intervention are crucial to manage the disease effectively, increasing remission prospects, and preventing long-term clinical complications. Objectives: The study aims to investigate and evaluate the potential role of certain inflammatory biomarkers - specifically Monocyte Chemoattractant Protein-1 (MCP-1) as an indicator of Rheumatoid Arthritis. Methods: An experimental study was conducted from April to June 2023, encompassing 80 individuals, 40 with chronic Rheumatoid Arthritis (RA) and 40 healthy controls. RA patients, from Azadi Teaching Hospital in Kirkuk Governorate, were selected based on a positive RF analysis. Demographic data were collected, and serum samples were obtained for biomarker analysis. MCP-1 levels were determined using ELISA. Statistical evaluations employed descriptive statistics, T-tests, and Pearson correlation via SPSS version 26. Results: In the study, 77.5% of (RA) patients in the 40-60 years bracket compared to 67.5% of healthy individuals. (RA) patients exhibited a striking increase in MCP-1, registering at 393.33 pg/ml versus the healthy individuals at 70.66 pg/ml, a moderate positive correlation was observed between BMI and MCP-1 levels (Pearson r = 0.446, p = 0.004). Conclusion: One of the pivotal revelations from the study was the significant correlation between BMI and MCP-1 levels in (RA) patients, contrasting with the healthy population. The pronounced elevation of MCP-1 levels in (RA) patients, when juxtaposed against healthy individuals, substantiate its role as a crucial inflammatory marker for (RA). Its potential utility as a diagnostic or prognostic tool is evident, especially given the marked statistical significance of the observed differences.

Keywords: Rheumatoid Arthritis, Monocyte Chemoattractant Protein, Plasminogen Activator Inhibitor, Soluble E-Selectin

Introduction

Rheumatoid Arthritis (RA) is a chronic and prevalent systemic inflammatory disease. Early (RA) diagnosis and therapy are critical for good disease management, increased chances of recovery, and avoiding lasting clinical and radiographic damage. Although RA remains a clinical diagnosis, the application and identification of biomarkers are increasingly important. The lifetime prevalence rate is as high as 1% in the world. The progression of RA might last for several years. One of the major contributors to (RA) patients' reduced quality

of life is joint swelling and discomfort brought on by ongoing inflammation, an issue that patients aim to recover as soon as possible (1). Biomarkers may develop into a tool that has a greater capacity to forecast the health effects of medical treatments, expanding their use beyond initial detection to prompt prognosis evaluation, selection of the most effective and safest therapy, and monitoring disease activity, leading to greater preservation of the joint cavity and movement in (RA) patients (2). Monocyte chemoattractant protein 1 (MCP-1) is extensively expressed in (RA) patients' joints, according to mounting research (3). Endothelial, epithelial, fibroblast, monocyte-macrophage, and vascular smooth muscle cells have all been found to express MCP-1, a chemokine (4, 5). Monocytes and macrophages are drawn to MCP-1, which plays a significant role in inflammation (6). MCP-1 levels were shown to be greater in (RA) patients compared to controls in prior research involving 92 participants (5).

Although MCP-1 is essential for the onset and progression of arthritis, it is uncertain whether it directly damages joints by altering FLSs' ability to proliferate, invade, and differentiate. MCP-1 has the power to alter the phenotype of numerous cells, including their propensity for invasion and differentiation. The ability of renal cancer cells to proliferate and migrate was reported to be stimulated by MCP-1 (7). However, it was discovered that MCP-1 produced in the herniated nucleus pulposus promoted osteoclast genesis in the vertebral column, causing more bone erosion (8). In vitro and in vivo, MCP-1 can influence angiogenesis and tumor development through Vascular Endothelial Growth Factor (VEGF) (9). Although MCP-1 is essential for the initiation and progression of arthritis, it's still not fully understood whether it causes joint destruction by altering the function of Fibroblast-Like Synoviocytes (FLSs), including their proliferation, invasion, and differentiation capacities. MCP-1 is known to alter the phenotype of several cell types, including their invasion capacity and differentiation potentials (8). This study aimed to understand the levels of inflammatory biomarkers –Monocyte Chemoattractant Protein-1 MCP-1 correlate with the severity of the RA disease or the rate of its progression.

Methods

An experimental study design was conducted on eighty individuals, including forty patients diagnosed with Rheumatoid Arthritis and forty healthy controls. The study was conducted between April 2023 and October 2023. The study sample size was determined based on the number of patients to be enrolled to obtain meaningful data and was done in consultation with a statistician using convenient sampling. The study sample included a group of patients diagnosed with Rheumatoid Arthritis after a positive RF analysis and with a record in the Joint and Medical Rehabilitation Center at Azadi Teaching Hospital in Kirkuk Governorate.

Procedure

Five ml blood were collected by vein puncture 5 ml syringes from each patient with (RA) and individual control enrolled in this study. Blood samples were placed into three sterile test tubes and1.5 ml of blood was put in the test tube. The tubes then were centrifuged (3000 rpm) for 15 min. The clear serum was pipetted into clear dry Eppendorf's tubes and stored at -20°C for determination of MCP-1 by ELISA. The Serum MCP-1 levels were determined using a quantitative sandwich enzyme-linked immunosorbent assay (Human MCP-1 ELISA kit, Bioscience, Inc., Catalogue Number: SLD037Hu. The sensitivity of the assay was 15.63 pg/ml-1000 pg/ml for MCP-1 (10).

Statistical analysis was performed using the SPSS version 26 statistic program. The difference was carried out using a T-test, ANOVA test, and pearson correlation for the determination of probability value (P-value).

Inclusion Criteria

Healthy adults without a history of inflammatory or autoimmune diseases and not on medications that can influence the biomarker levels.

Exclusion Criteria

Individuals smoking cigarettes, having chronic illness, active infections, or recent trauma/surgery.

Ethical Considerations

- Approval of the council of the College of Medicine/ Tikrit University was obtained for the study
- Approval permission was presented to the director of Kirkuk Health Directorate /Azadi General Hospital.
- An interview was carried out with these patients using a questionnaire form designed by the investigator including age, gender, BMI, and RF.

Results

Table 1. Demographic characteristics of the patients with (RA) and healthy persons in the study

Demographic characteristics		F	Percent	Mean	Std. Deviation
Patients With (RA)	Female	36	90.0	---	---
	Male	4	10.0		
	Less Than 40	7	17.5		
	40-60	31	77.5	1.87	0.46
	More Than 60	2	5.0		
	Less Than 18.5	3	7.5		
	18.5-24.9	16	40.0	2.62	0.86
	25-29.9	14	35.0		
	30- More	7	17.5		
Healthy persons	Female	36	90.0	---	---
	Male	4	10.0		
	Less Than 40	11	27.5		
	40-60	27	67.5	1.77	0.53
	More Than 60	2	5.0		
	Less Than 18.5	8	20.0		
	18.5-24.9	21	52.5	2.18	0.87
	25-29.9	7	17.5		
	30- More	4	10.0		
Total		40	100.0		

F= frequency,

In each group, a majority of females were observed, constituting 90% (or 36 individuals), leaving males with a minor representation of just 10% (or 4 individuals). Age distribution presented more variability. The healthy group showed a broader distribution, with 67.5% (or 27 individuals) in the 40-60 years range. This under 40 group was less prevalent in the (RA) group at just 17.5% (or 7 individuals). In the healthy group, the normal weight category had a pronounced lead with 52.5% (or 21 individuals) compared to 40% (or 16 individuals) of (RA) patients. However, when shifting the lens to the overweight segment, (RA) patients exhibited a higher prevalence at 35% (or 14 individuals) versus 17.5% (or 7 individuals) in the healthy cohort.

Table 2. Inflammatory biomarkers levels, E-selection, MCP-1, and PAI-1 in the patients with (RA) and healthy persons

Inflammatory biomarkers		N	Min	Max	Mean	Std. Deviation
Patients with (RA)	MCP-1	40	236.67	586.67	393.33	88.25
Healthy Persons	MCP-1	40	27.55	110.67	70.66	17.57

N: Number

Table 2, The study analyzed the levels of the inflammatory biomarker MCP-1 in both patients diagnosed with Rheumatoid Arthritis (RA) and in healthy individuals. For the (RA) patient cohort, the recorded MCP-1 levels demonstrated a range between a minimum of 236.67 pg/ml and a maximum of 586.67 pg/ml, with an average concentration of 393.33 pg/ml. In contrast, the healthy individuals exhibited considerably lower MCP-1 levels, spanning from a minimum of 27.55 pg/ml to a maximum of 110.67 pg/ml. The mean concentration in this group was 70.66 pg/ml. This stark difference in MCP-1 levels between the two groups underscores its potential role in the inflammatory response associated with (RA). The elevated mean level of MCP-1 in (RA) patients, in comparison to the significantly lower mean concentration in the healthy population, reinforces the biomarker's relevance in understanding the pathophysiological processes underpinning (RA).

Table 3. Correlation between BMI and inflammatory biomarkers MCP-1 in patients with Rheumatoid Arthritis and healthy persons

Correlations		MCP_1
Patients with (RA)	Pearson Correlation	0.446**
	P Value	0.004
Healthy persons	Pearson Correlation	0.092
	P Value	0.573

Table 3, In an examination of the relationship between BMI and the inflammatory biomarker MCP-1 in two distinct groups of patients diagnosed with (RA), a moderate positive correlation was observed between BMI and MCP-1 levels (Pearson r = 0.446, p = 0.004). In contrast, the correlation among healthy participants was found to be weak and statistically non-significant (Pearson r = 0.092, p = 0.573). This suggests that while an increased BMI might be associated with elevated MCP-1 levels in individuals with (RA), a similar trend is not apparent in the general healthy population.

Table 4. The Difference in the MCP-1 levels as a progressive marker in patients with Rheumatoid Arthritis and healthy persons.

Group	N	Mean	Std. Deviation	T.TEST	P-Value	ASS
Patients with (RA)	40	393.33	88.25	22.67	0.000	S
Healthy persons	40	70.66	17.57			

ASS: Assessment, N: Number, S: Significance

Table 4, Among the 40 patients diagnosed with (RA), the average MCP-1 level was notably higher, measured at 393.33 pg/mg. The standard deviation for this group, which quantifies the variability from the average, was 88.25. Contrastingly, the 40 healthy individuals demonstrated a significantly lower average MCP-1 level at 70.66 pg/mg. Moreover, the spread of MCP-1 values in this cohort, as described by the standard deviation of 17.57. The t-test yielded a value of 22.67. The p-value, associated with this test, was 0.000. Generally, in the realm of statistical analysis, a p-value of less than 0.05 is deemed to be statistically significant.

Discussion

This study aims to evaluate the potential role of Monocyte Chemoattractant Protein-1 (MCP-1) as indicators of (RA) progression, by examining whether the levels of these biomarkers increased with disease severity or its rate of advancement. Both groups manifested an overwhelming female representation at 90%. Such a pronounced gender difference might hint at females' heightened susceptibility to (RA). According to WHO RA affects women are more likely to have the condition than males (11).

The study demonstrated that levels of MCP-1 inflammatory biomarkers concentration increased in the (RA) patients with mean concentrations (393.3 pg/ml). Notably, these figures confirm the literature, wherein diabetic patient serum samples manifested the presence of MCP 1, with concentrations oscillating between (135.6-543.5 pg/ml) (12). However, the study offers valuable insights into the inflammatory profile of (RA) patients, particularly concerning MCP-1 levels. The resonance of these findings with those from diabetic patient samples is intriguing, suggesting potential shared inflammatory mechanisms. A deeper exploration of these parallels, and understanding the implications of MCP-1 modulation, could pave the way for innovative therapeutic strategies in managing RA.

Additionally, MCP-1 levels showed an even weaker positive correlation with BMI, indicated by a Pearson correlation coefficient (r of 0.092), and this association was similarly non-significant in healthy individuals. The current findings agree with (13), who demonstrated a negative association between the component variety and MCP-1. While there is limited information on the association between diet quality and MCP-1. The consumption of a healthy diet such as the Mediterranean diet, or a higher intake of fruits and vegetables and vitamin C is associated with a lower level of systematic inflammation (14).

RA patients manifested markedly elevated MCP-1 levels, accumulating at 393.33 pg/ml, a stark contrast to the 70.66 pg/ml noted in healthy individuals. This amplification attests to the central role of MCP-1 in orchestrating monocyte infiltration to sites of inflammation, emblematic of RA's pathological processes. These disparities highlight the biochemical changes characteristic of RA affording critical perspectives on its underlying mechanisms and prospective therapeutic interventions. In line with these findings study (15), demonstrates that the plasma MCP-1 levels were higher in patients with anemia (109.5 pg/mL) in comparison with patients who had normal hemoglobin values (78.9 pg/mL), also (16), showed that MM cells increase the production of MCP-1 by bone marrow stromal cells.

Conclusion

The study highlighted a significant female predominance in both rheumatoid arthritis (RA) patients and healthy cohorts. It found a moderate positive correlation between Body Mass Index (BMI) and the inflammatory biomarker MCP-1, suggesting that higher BMI may exacerbate inflammatory responses in RA patients. Notably, there was a clear difference in MCP-1 levels between RA patients and healthy individuals, reinforcing MCP-1's potential as a critical indicator of RA progression. These results underscore the importance of understanding demographic factors, inflammation, and their relationship with RA, supporting future diagnostic and therapeutic developments.

Conflict of Interest

The author declares that there are no conflicts of interest regarding the publication of this manuscript.

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