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Systemic Immune-Inflammation Index and C-Reactive Protein in Rheumatoid Arthritis Patients Attending Specialist Hospital, Owerri, Nigeria

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Abstract

Rheumatoid arthritis (RA) is a long-lasting inflammatory illness that affects the whole body and causes inflammation and problems with the immune system. For assessing inflammatory state and disease activity in RA, dependable and readily accessible biomarkers are crucial. The Systemic Immune-Inflammation Index (SII), calculated from neutrophil, lymphocyte, and platelet counts, has been established as a new indicator of systemic inflammation, in addition to the commonly utilized C-reactive protein (CRP). This study sought to evaluate and compare the levels of SII and CRP in individuals with rheumatoid arthritis and ostensibly healthy controls. A comparative cross-sectional study was performed with rheumatoid arthritis patients and healthy controls matched for age and sex. Standard hematological procedures were used to look at the number of neutrophils, lymphocytes, and platelets in peripheral blood samples. To find SII, we used the formula (Neutrophils × Platelets) / Lymphocytes. Standard immunoassay methods were used to find the levels of CRP in serum. The data were presented as mean ± standard deviation, and group differences were analysed using suitable statistical tests, with significance established at $p < 0.05$. Rheumatoid arthritis (RA) patients had much higher neutrophil counts (6.47 ± 1.53 $\times 10^9$/L) and platelet counts (359.8 ± 78.5 $\times 10^9$/L) than controls (3.82 ± 0.86 $\times 10^9$/L and 266.9 ± 56.2 $\times 10^9$/L, respectively; $p < 0.001$). On the other hand, RA patients had much lower lymphocyte counts (1.94 ± 0.58 $\times 10^9$/L) than controls (2.67 ± 0.57 $\times 10^9$/L; $p < 0.001$). The mean SII was significantly higher in RA patients (1199.95 ± 207.1) than in controls (381.9 ± 84.8; $p < 0.001$). In the same way, CRP levels were much higher in RA patients (28.2 ± 12.8 mg/L) than in controls (4.6 ± 2.1 mg/L; $p < 0.001$). The markedly increased SII and CRP values in RA patients signify augmented systemic inflammation and immunological dysregulation. SII, in particular, may be a simple, cheap, and reliable way to measure inflammation in rheumatoid arthritis, along with other markers like CRP.

Keywords: systemic immune-inflammation index; c-reactive protein; rheumatoid arthritis; Owerri

Introduction

Rheumatoid arthritis (RA) affects about 1% of the world's population and is one of the most frequent chronic inflammatory autoimmune diseases in the world. It is linked to significant morbidity, advancing functional deterioration, diminished quality of life, and heightened healthcare expenses. The condition mostly affects synovial joints, which can cause discomfort, swelling, stiffness, and, if not treated properly, joint deformity. Rheumatoid arthritis (RA) is increasingly recognised as a systemic illness with extra-articular symptoms, including cardiovascular, pulmonary, and hematological problems, all of which contribute to increased mortality among affected patients [1].

The pathophysiology of RA is intricate and multifactorial, encompassing genetic predisposition, environmental stimuli, and immune system dysregulation. A loss of immunological tolerance lies at the heart of disease development. This leads to constant stimulation of both innate and adaptive immune responses. Neutrophils, lymphocytes, macrophages, and platelets are important parts of the inflammatory cascade. These immune cells emit pro-inflammatory cytokines such tumour necrosis factor-alpha (TNF-α), interleukin-1 (IL-1), and interleukin-6 (IL-6), which cause inflammation in the synovial membrane, the creation of pannus, the degradation of cartilage, and the erosion of bone. Over time, this ongoing condition of inflammation causes damage to joints that can't be fixed and makes it impossible to move [2].

Because RA is a long-term and progressive disease, it is important to quickly and accurately measure inflammation. For early diagnosis, assessing disease activity, tracking how well treatments are working,

and predicting long-term results, we need reliable biomarkers. In clinical practice, laboratory indicators of inflammation augment clinical evaluation and imaging modalities, offering objective metrics of disease burden. C-reactive protein (CRP) is still one of the most common and well-known signs of systemic inflammation in RA [3].

CRP is an acute-phase protein produced mostly by hepatocytes in response to pro-inflammatory cytokines, especially IL-6. CRP is found in modest amounts in the blood while the body is working normally. But when there is acute or chronic inflammation, its levels can go up a lot in just a few hours. In rheumatoid arthritis (RA), high levels of CRP are closely linked to active illness, higher disease activity scores, and radiographic progression. Consistently elevated CRP levels have been associated with expedited joint degradation and inferior functional results [4]. Moreover, CRP is included in widely utilized composite disease activity indices, such as the Disease Activity Score in 28 Joints (DAS28), underscoring its pivotal position in standard RA management [5].

In addition to joint disease, CRP functions as a significant prognostic indicator for systemic consequences of RA. Chronic inflammation leads to endothelial dysfunction and atherosclerosis, elucidating the heightened risk of cardiovascular disease in individuals with rheumatoid arthritis. In this group of people, increased CRP levels have been linked to a higher risk of heart attacks, strokes, and heart failure. So, CRP shows not only how active inflammatory diseases are, but also how they affect health in general [6].

CRP is helpful in the clinic; however, it has several problems. It is not unique to RA and may be increased in other circumstances, including infections, malignancies, trauma, and other autoimmune illnesses. This lack of specificity can make it harder to understand, especially in places where infectious diseases are common. Additionally, certain rheumatoid arthritis patients may present with active illness despite having relatively normal CRP levels, particularly in early or seronegative instances. These constraints have incited interest in supplementary biomarkers that can offer complementary or more extensive insights into the inflammatory and immunological status of RA patients [7].

In this setting, the Systemic Immune-Inflammation Index (SII) has arisen as a promising new biomarker. To find SII, use the following formula:

SII = (Neutrophils × Platelets) ÷ Lymphocytes

This indicator combines three easily accessible blood test results from routine complete blood counts. SII, on the other hand, shows how the pro-inflammatory and regulatory parts of the immune system work together. Neutrophils are the first line of defense in innate immunity and are very important in the early stages of inflammation because they may engulf and destroy pathogens, release reactive oxygen species, and many other things. In rheumatoid arthritis (RA), neutrophils gather in the synovial fluid and destroy tissues by producing proteolytic enzymes and inflammatory mediators [8].

Platelets, which have long been thought of as important for stopping bleeding, are now seen as important for controlling inflammation and the immune system. Activated platelets interact with leukocytes and endothelial cells, facilitating cytokine release, enhancing vascular permeability, and attracting inflammatory cells to areas of tissue damage. In RA, high platelet counts are generally a sign of persistent inflammation and are linked to worse disease severity [9].

Lymphocytes, especially T and B lymphocytes, play a key role in adaptive immunity and the production of autoantibodies in RA. Peripheral lymphopenia is often seen in chronic inflammatory conditions, likely due to the redistribution of lymphocytes to inflamed tissues, immunological exhaustion, or heightened apoptosis. Lower lymphocyte counts show that the immune system isn't working properly and that immunological homeostasis has been lost [10].

SII gives a better overall picture of systemic immune activation by combining these three factors. A high SII means that pro-inflammatory dominance is on the rise. This is shown by more activity in neutrophils and platelets and less regulation by lymphocytes. Multiple worldwide studies have shown that a higher SII is linked to higher disease activity ratings, more damage to joints shown on X-rays, and worse functional status in people with RA. Additionally, SII has been investigated as a prognostic indicator in several inflammatory and neoplastic disorders, hence reinforcing its biological significance [11].

One of the best things about SII is that it is easy to use and doesn't cost much. It doesn't need any special tests, and you can figure it out with regular lab tests that are easy to find even in places with few resources.

This makes SII especially useful in low- and middle-income nations, where it may be hard to get advanced immunological markers.

Even though more and more people throughout the world are interested in SII, there isn't much evidence from African and Nigerian clinical contexts. The majority of studies on SII in RA have been executed in Europe, Asia, and North America, regions where healthcare facilities and disease profiles markedly contrast with those in sub-Saharan Africa. In Nigeria, rheumatoid arthritis (RA) is frequently underdiagnosed and undertreated due to insufficient awareness, delayed presentation, and limited access to rheumatology treatments. Moreover, the significant prevalence of infectious disorders may complicate the interpretation of conventional inflammatory markers, including C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) [12].

Consequently, this study concentrates on RA patients at Specialist Hospital, Owerri, highlighting the assessment of SII and CRP as indicators of inflammation within a practical Nigerian clinical context. The results offer significant understanding of the inflammatory and immunological characteristics of RA patients in this context. High levels of CRP confirm that there is active systemic inflammation, which is in line with what is known around the world. More critically, the much higher SII values show how badly the immune system is out of balance in this group of people with RA. In Nigerian clinical environments like Specialist Hospital, Owerri, the integration of SII with CRP may augment diagnostic precision, enhance the surveillance of disease activity, and eventually lead to improved patient outcomes and quality of life.

Materials and Methods

Study Design and Population

This observational cross-sectional study involved adult RA patients attending the rheumatology or internal medicine clinics at Specialist Hospital, Owerri, Imo State, Nigeria. Patients diagnosed with RA based on the 2010 ACR/EULAR classification criteria were included. Individuals with concurrent infections, malignancies, or other autoimmune diseases were excluded.

Ethical Consideration

Ethical approval for the study was obtained from the Ethics Committee of Specialist Hospital, Owerri, Imo State. Written informed consent was obtained from all participants prior to enrolment, and the study was conducted in accordance with the principles of the Declaration of Helsinki

Data Collection

A structured and standardized questionnaire was administered to all participants to obtain relevant demographic information and clinical history after informed consent was obtained. Venous blood samples were subsequently collected from all participants for laboratory analysis. Demographic and clinical data were collected from patient records, including age, sex, disease duration, and current medications. Venous blood samples were obtained for Complete blood count (CBC) and C-Reactive Protein (CRP) assay.

From the CBC: neutrophil count, lymphocyte count, and platelet count were recorded to compute SII.

Statistical Analysis

Data obtained from the study was presented in the form of tables, while the results were analysed using SPSS statistical computer software (Version 21). Students T- test, Correlation, mean and standard deviations were determined. The values expressed as mean ± S.D. The level of significance was set at 95% confidence interval.

Results

Table: The levels of systemic immune-inflammation index and C-Reactive protein in rheumatoid arthritis patients.

Parameter	RA Patients (Mean ± SD)	Controls (Mean ± SD)	p-value
Neutrophils ($\times 10^9$/L)	6.47 ± 1.53	3.82 ± 0.86	<0.001
Lymphocytes ($\times 10^9$/L)	1.94 ± 0.58	2.67 ± 0.57	<0.001
Platelets ($\times 10^9$/L)	359.8 ± 78.5	266.9 ± 56.2	<0.001
SII	1199.95 ± 207.1	381.9 ± 84.8	<0.001
CRP (mg/L)	28.2 ± 12.8	4.6 ± 2.1	<0.001

Discussion

This study showed that patients with rheumatoid arthritis (RA) had much higher levels of C-reactive protein (CRP) and the Systemic Immune-Inflammation Index (SII) than healthy controls. This confirms that RA is linked to increased systemic

inflammation and immune dysregulation. The noted elevations in neutrophil and platelet counts, along with diminished lymphocyte numbers, further exemplify the intricate inflammatory environment that defines RA pathophysiology [13].

CRP is still one of the most dependable and commonly used indicators for inflammatory activity in RA. As an acute-phase reactant produced by the liver in response to pro-inflammatory cytokines like interleukin-6 (IL-6), CRP levels increase swiftly during active inflammation. In this investigation, rheumatoid arthritis patients had significantly elevated CRP levels (28.2 ± 12.8 mg/L) in contrast to controls (4.6 ± 2.1 mg/L), corroborating findings in the current literature. Consistently high CRP levels have been linked to more severe illness, faster joint damage, and worse long-term consequences. CRP is also commonly used in disease activity indices like the Disease Activity Score (DAS28), and it is a useful tool for keeping track of how well treatments are working and making changes to them in clinical practice [14].

The Systemic Immune-Inflammation Index, in addition to CRP, offers a more comprehensive assessment of inflammatory status by integrating three essential biological components of the immune system: neutrophils, lymphocytes, and platelets. In this study, the SII was markedly elevated in RA patients (1199.95 ± 207.1) compared to controls (381.9 ± 84.8), signifying a strong pro-inflammatory change. Neutrophilia in RA patients indicates robust innate immune responses and the secretion of inflammatory mediators that lead to synovial inflammation and joint destruction. Platelets, historically known for their function in hemostasis, are progressively recognised as significant inflammatory cells that engage with leukocytes and endothelial cells to enhance cytokine production and vascular inflammation. On the other hand, the lower number of lymphocytes in RA patients could mean that their immune system is worn out or that lymphocytes are being sent to inflamed tissues [15].

Recent evidence substantiates the clinical significance of SII as a biomarker for disease activity in rheumatoid arthritis (RA). Higher SII values correlate with elevated disease activity scores, increased radiographic damage, and enhanced functional impairment [16]. SII, on the other hand, shows the dynamic balance between pro-inflammatory and regulatory immune processes. This makes it a better way to measure systemic immune status than single indicators. The increased SII noted in this study highlights its prospective value as a surrogate measure for disease surveillance, especially in resource-constrained environments where sophisticated immunological tests may be inaccessible [17,18].

Conclusion

The elevated levels of CRP and SII in RA patients underscore the chronic inflammatory load and immunological dysregulation characteristic of the condition. CRP is still a key biomarker for measuring systemic inflammation, but SII adds to that by looking at how immune cells work together. In clinical settings like Specialist Hospital, Owerri, where routine, cost-effective, and accessible indicators are essential, the simultaneous application of CRP and SII may augment diagnostic precision, enhance disease activity evaluation, and facilitate more informed therapeutic decision-making. Ultimately, adding SII to established inflammatory markers could help better group patients, keep a closer eye on how they respond to treatment, and enhance long-term results for people with rheumatoid arthritis.

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