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Association Between Disease Activity and C-reactive Protein to Serum Albumin Ratio in Patients with Ankylosing Spondylitis

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Abstract

Background and objectives: Ankylosing spondylitis is a persistent inflammatory rheumatic condition that predominantly affects the axial skeleton. The current research aims to assess the correlation between disease activity and the C-reactive protein to serum albumin ratio among individuals diagnosed with ankylosing spondylitis.

Patients and methods: This cross-sectional study was undertaken at Sulaymaniyah Shahid Hemn Teaching Hospital. The study encompassed a cohort comprising 100 patients who were diagnosed as ankylosing spondylitis. The study was conducted between December 2022 and August 2023. By referring to the patients' medical files and by assessing the disease activity using bath ankylosing spondylitis disease activity index and ankylosing spondylitis disease activity score required data were gathered.

Results: The patients' age ranged from 20 to 60 years, and (70%) were males. The most common comorbidities included sacroiliitis in (100%) of the patients, enthesitis in (39%) of them, peripheral arthritis in (37%) of them, and dactylitis in (20%) of them. All of the patients received anti-tumor necrosis factor therapy, (21%) and (6%) also received NSAID and DMARD treatments, respectively. CRP/S. albumin CAR was found to have statistically significant relationships with BASDAI and ASDAS scores (p-value<0.001) but not with HLAB27 (p-value=0.46). It was also found that CRP/S. albumin CAR had significant correlations with BASDAI scores (p-value=0.03) and ASDAS scores (p-value<0.001).

Conclusion*:* C-reactive protein-to-serum albumin ratio can be utilized as a reliable indicator to assess disease activity in individuals diagnosed with ankylosing spondylitis.

Keywords: Ankylosing spondylitis, C-reactive protein, Disease activity, Serum albumin

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Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease that primarily impacts the axial skeleton, leading to inflammatory back pain, stiffness, and a decline in spinal mobility. It is estimated to affect approximately 0.1-1.4% of the global population, with a higher prevalence observed among young males.[1] The precise pathogenesis of AS remains uncertain. Prolonged inflammation can result in the development of new bone and eventual fusion of the spine.[2] Effective AS management requires monitoring disease activity to control inflammation, minimize structural damage, and improve physical function. However, assessing disease activity presents challenges. Patient-reported outcomes, such as the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), offer insight into symptoms but are subjective. Conventional inflammatory markers like Erythrocyte sedimentation rate (ESR) and C-Reactive protein (CRP) lack specificity and sensitivity in detecting active AS. Thus, research focuses on exploring alternative biomarkers for a more accurate reflection of inflammation and disease activity.[3] The C-reactive protein ratio to albumin ratio (CAR) is an experimental biomarker that has garnered attention. C-reactive protein ratio as an acute phase reactant produced by the liver in response to cytokines like interleukin-6 increases in the presence of inflammation. Conversely, albumin levels decrease as a negative acute phase reactant. Consequently, CAR serves as a comprehensive indicator of the acute phase response. The CAR has demonstrated prognostic significance in predicting mortality and complications in various inflammatory disorders, including cardiovascular disease, stroke, and cancer.[4] Several recent studies have conducted assessments on the utilization of (CAR) in individuals with AS. Significantly, two separate research groups indicated that CAR has a positive correlation with clinical disease activity scores such as ASDAS and BASDAI indicated by bath ankylosing spondylitis functional index (BASFI), and conventional inflammatory markers. In addition, CAR levels were higher in AS patients compared to healthy individuals. Preliminary outcomes indicate that CAR holds promise as a cost-effective and readily available biomarker for assessing inflammation and guiding treatment decisions in (AS).[5] ,[6] Despite recent advancements in understanding the role of (CAR) in AS, significant knowledge gaps persist. Published studies, which mostly encompassed small sample sizes of fewer than 200 patients and were conducted in single centers, highlight the need for larger multi-center cohort studies. Additionally, existing research has primarily been cross-sectional in nature, providing only a momentary snapshot of CAR's association with AS disease activity.[7] Longitudinal studies are essential to ascertain whether alterations in CAR correspond to disease flare-ups and remission in ankylosing spondylitis (AS). Additionally, there is insufficient understanding regarding the relative effectiveness of CAR compared to conventional inflammatory markers like (ESR) and (CRP).[8] There is an increasing interest in employing composite measures that combine multiple parameters of disease activity, such as the CAR (CRP/albumin ratio). This ratio is a potential composite marker in inflammatory conditions like rheumatoid arthritis (RA) and inflammatory bowel disease (IBD). While albumin levels alone reflect systemic inflammation and nutritional status, CRP provides a specific indicator of inflammatory activity. The CAR may offer additional insights compared to each parameter assessed individually.[9] The utility of the CRP/albumin ratio in (AS) has been inadequately investigated. Gaining

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knowledge about the relationship between this composite marker and established assessments of (AS) disease activity, like BASDAI, can offer valuable insights into how systemic inflammation acts in AS.[10] Therefore, the present study was aimed to examine the correlation between disease activity and CAR in individuals suffering from AS.

Patients and methods

The present cross-sectional study was carried out in Sulaymaniyah Shahid Hemn teaching hospital, Kurdistan region, Iraq from December 2022 to August 2023.The study cohort comprised 100 individuals diagnosed with ankylosing spondylitis, a well-prepared questionnaire was distributed to patients selected based on specific inclusion criteria, including meeting the diagnostic criteria outlined in the modified New York criteria, age ranging from 20 to 60 years, and providing informed consent. [11] Conversely, individuals outside the age range of 20 to 60 years, those who declined to provide informed consent, and individuals with cardiac, liver, or renal failure were excluded from the study. The disease activity was assessed using ASDAS and BASDAI, and the patients were sent for investigations including C reactive protein to albumin ratio, ESR, and HLA B27. Verbal and written consent were taken from each individual for the purpose of getting Data regarding demographic characteristics, smoking habit, duration of smoking, educational level, and Ethical approval has been taken from ethical committee from Kurdistan Higher council for Medical Specialties. Statistical analysis: The collected data was subjected to statistical analysis using SPSS (version 24), and required analyses were conducted via both inferential and descriptive statistical tests. It's important to mention the normal CRP/S. albumin (CAR)-There isn't a universally accepted "normal" range for CAR, as it can vary based on the population being studied and the specific context (such as chronic disease or acute conditions). Generally, lower CAR values are associated with lower levels of inflammation and better nutritional status. Elevated CAR: An increased CAR value often indicates higher levels of inflammation or poor nutritional status, as it reflects elevated CRP levels relative to albumin levels.)

Results

The demographic data collected showed that the patients' ages ranged from 20 to 60 years. Among them, 26 patients (26%) were aged 20 to 30 years, 34 patients (34%) were aged 31 to 40 years, 31 patients (31%) were aged 41 to 50 years, and 9 patients (9%) were aged 51 to 60 years. Regarding their gender, the results showed that 70 (70%) were males, and 30 (30%) were females. Seventy-five (75%) were found to be married, 22 (22%) were single, and 3 (3%) were divorced. Most of the patients (60%) were unemployed, while 40% were employed. Moreover, 63 patients (63%) were literate, and the rest (37%) were illiterate. Most of the patients (90%) lived in cities and 10% in rural areas. Moreover, 60 patients (60%) never smoked, while 33% were current smokers, and 7% were ex-smokers. The results also indicated that 40 patients (40%) had family history of ankylosing spondylitis, while 60% did not. It was also observed that 96 patients (96%) did not have past history of comorbidity (diabetes mellitus and hypertension), while 4 (4%) did, Table (1).

Table (1): The patients' sociodemographic information

		Frequency (N)	Percentage (%)
Age group	20 - 30	26	26.0
	31 - 40	34	34.0
	41 - 50	31	31.0
	51 - 60	9	9.0
Gender	Male	70	70.0
	Female	30	30.0
	Single	22	22.0

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Marital status	Married	75	75.0
	Divorced	3	3.0
Occupation	Employed	40	40.0
	Unemployed	60	60.0
Education	Educated	63	63.0
	Illiterate	37	37.0
Residence	Urban	90	90.0
	Rural	10	10.0
Smoking history	Current	33	33.0
	Ex-smoker	7	7.0
	Never	60	60.0
Family history	Yes	40	40.0
	No	60	60.0
Comorbidity	Positive	4	4.0
	Negative	96	96.0
Total		100	100.0

In terms of the patients' medical conditions, the results showed that 37 of them (37%) had peripheral arthritis, 20 (20%) had dactylitis, all of them (100%) had sacroiliitis, 21 (21%) had uveitis, 39 (39%) had enthesitis, and 62 (62%) had HLA-B27, Table (2).

Table (2): The patients' medical profile

Medical Condition	Positive N (%)	Negative N (%)	Total N (%)
Peripheral arthritis	37 (37%)	63 (63%)	100 (100%)
Dactylitis	20 (20%)	80 (80%)	100 (100%)
Sacroiliitis	100 (100%)	0 (0%)	100 (100%)
Uveitis	21 (21%)	79 (79%)	100 (100%)
Enthesitis	39 (39%)	61 (61%)	100 (100%)
HLA-B27	62 (62%)	38 (38%)	100 (100%)

Regarding the treatments provided to the patients, the results indicated that all of them (100%) received anti-TNF alfa treatment, of whom 6 patients (6%) received DMARD treatment and 21 (21%) received NSAID treatment, Table (3).

Table (3): Treatments provided to the patients

Treatment	Frequency (N)	Percentage (%)
Anti-TNF alfa	100	100.0
DMARD	6	6.0
NSAID	21	21.0
Total	100	100.0

Analyzing the relationships between the studied variables revealed that there was a significant relationship between CRP/S. albumin CAR and BASDAI scores (p-value<0.001). The relationship between CRP/Albumin (CAR) and ASDAS scores was also found to be significant (p-value<0.001). However, there was not a significant relationship between CRP/S. albumin CAR and HLA-B27 (p-value=0.46), Table (4).

Table (4): Relationship between CRP/S. albumin CAR and BASDAI, ASDAS, and HLA-B27 scores

	CRP/S. albumin CAR	N	Mean ± SD	95% CI	Min - Max	p value
BASDAI Score	Low < 2	38	1.34 ± 1.86	0.73 - 1.95	0.04 - 10.09	<0.001
	Moderate ≥ 2 - < 4	21	2.44 ± 2.84	1.15 - 3.73	0.07 - 12.50	
	High ≥ 4 - ≤ 6	37	1.36 ± 1.56	0.84 - 1.87	0.02 - 5.85	
	Very high > 6	4	7.86 ± 9.74	-7.63 - 23.35	0.17 - 22.11	
	Total	100	1.84 ± 2.91	1.26 - 2.41	0.02 - 22.11	

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ASDAS Score	Inactive < 1.3	13	0.67 ± 0.56	0.34 - 1.01	0.04 -1.89	<0.001
	Low disease activity 1.3 - < 2.1	24	0.93 ± 0.86	0.57 - 1.29	0.07 - 2.74	
	High disease activity 2.1 - 3.5	45	1.59 ± 1.97	1.01 - 2.19	0.02 - 10.09	
	Very high disease activity > 3.5	18	4.51 ± 5.28	1.89 - 7.14	0.17 - 22.11	
	Total	100	1.84 ± 2.91	1.27 - 2.42	0.02 - 22.11	
HLA-B27	Positive	62	1.67 ± 1.87	-1.62 – 0.75	0.06 – 10.9	0.46
	Negative	38	2.11 ± 4.07	-1.85 – 0.97	0.02 – 22.11	
	Total	100	1.84 ± 2.9	-1.74 – 0.86	0.02 – 22.11	

Analyzing the correlation between CRP/S. albumin CAR and BASDAI scores using the coefficient of determination (R^2 linear) indicated that there was a significant correlation between the two variables (p-value=0.03), Figure (1).

The results of R^2 linear also revealed a significant correlation between CRP/S. albumin CAR and ASDAS scores (p-value<0.001), Figure (2).

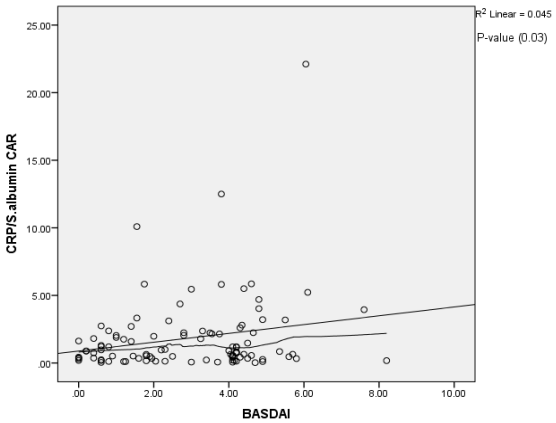

Figure (1): Correlation between CRP/S. albumin CAR and BASDAI scores

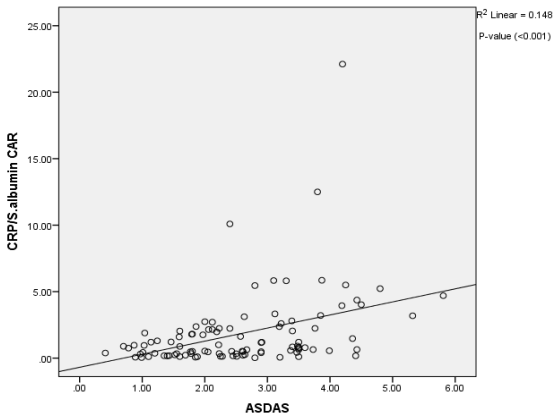

Figure (2): Correlation between CRP/S. albumin CAR and ASDAS scores

Discussion

The present study aims to investigate the relationship between the severity of AS and the ratio of C-reactive protein (CRP) to serum albumin in patients with AS. Based on the data achieved from this study, it was observed that more than two-thirds of patients with AS are male. Moreover, it was observed that AS primarily affects younger and middle-aged adults. The high rate of smoking among participants is alarming, as it can exacerbate the disease and lead to more severe spinal damage. Less than half of patients have a family history of AS,

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supporting the genetic component of the disease. Surprisingly, only 4% of patients have comorbidities, which may not be representative of the broader AS population. In contrast to the data from a recent study, the incidence of AS did not differ significantly between women and men in a large study of military service members.[12] In our study, we assessed the BASDAI score, which includes a component specifically related to fatigue among other disease activity measures. Previous research has demonstrated that severe fatigue is a prevalent issue in individuals with ankylosing spondylitis, often leading to reduced productivity and limitations in leisure activities. Although our study did not collect specific data solely on fatigue, the inclusion of the fatigue component in the BASDAI score highlights its significance. Implementing early management strategies for fatigue could be beneficial in mitigating its impact on daily life and work for patients with ankylosing spondylitis.[13] Our results align with recent research indicating that, although AS has a significant genetic component, the actual likelihood of AS being inherited within families is lower than earlier estimates. These finding challenges previously cited figures from other populations.[14] The results presented in Table (4) demonstrate a significant association between the CAR and disease activity measures in patients with AS. A strong correlation was observed between CAR and both the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Ankylosing Spondylitis Disease Activity Score (ASDAS), with p-values <0.001 for both measures. This suggests that CAR may be a useful biomarker for assessing disease activity in AS patients. Notably, patients with very high BASDAI scores (>6) showed markedly elevated CAR values (mean 7.86 ± 9.74) compared to those with lower scores. Similarly, patients with very high disease activity according to ASDAS (>3.5) exhibited substantially higher CAR values (mean 4.51 ± 5.28) than those with lower disease activity. These findings indicate that CAR may be particularly valuable in identifying patients with severe disease activity. A study also found that the C-reactive protein to albumin ratio (CAR) was elevated in patients with active axial spondylarthritis (axSpA). This suggests that CAR may be a useful and accurate biomarker for assessing disease activity in axSpA patients, including those with ankylosing spondylitis (AS). This reinforces our findings that CAR is elevated in AS.[15] A study in 2022 suggested a revised cut-off point for the BASDAI score, which is widely used internationally, based on their data. Implementing this proposed change could enhance treatment decisions for ankylosing spondylitis (AS) patients by allowing for earlier initiation or adjustment of biological therapy, as a lower BASDAI cut-off would trigger these actions sooner.[16] Recent research has consistently shown that the (CAR) is a valuable inflammatory marker with significant predictive power in a range of diseases.[17,18] Consistent with our results, a study in 2018 found that CRP levels can forecast the development of spinal immobility in ankylosing spondylitis (AS) patients. Additionally, the CRP-to-albumin ratio (CAR) has been identified as a reliable biomarker for evaluating disease activity in axial spondylarthritis (axSpA) patients, as it is positively correlated with BASDAI and BASFI scores.[19] A study found that ASDAS outperforms BASDAI and CRP in measuring disease activity, making it a preferred choice. However, there is a lack of evidence on the benefits of using Ankylosing Spondylitis Disease Activity Score Inactive Disease (ASDAS-ID) as a treatment goal.[20] Another study in 2018 found that CRP is typically viewed as a short-term indicator of inflammation, but emerging research highlights its broader significance in the

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inflammatory process. As the primary mediator of the acute-phase response, CRP is mainly produced in the liver through a process dependent on IL-6.[21] Based on the evidence achieved from the present study and previous research, the positive correlation between (CAR) and disease activity scores (BASDAI and ASDAS) in ankylosing spondylitis patients supports CAR as an effective inflammation marker for several reasons. Firstly, it combines two key indicators - CRP, an acute-phase protein that increases during inflammation, and serum albumin, which decreases during inflammatory states - into a single, more comprehensive measure. This ratio provides a balanced view of both the inflammatory response and nutritional status. Secondly, the statistically significant relationships observed between CAR and both BASDAI and ASDAS demonstrate its consistency across different disease activity measures. The strong correlation with ASDAS, in particular, underscores CAR's potential as a reliable, objective biomarker. Lastly, as CAR utilizes readily available laboratory parameters, it offers a cost-effective and easily implementable tool for monitoring disease activity and treatment response in ankylosing spondylitis, complementing existing patient-reported outcome measures.

Conclusion

This study confirms the value of the C-reactive protein-to-serum albumin ratio (CAR) as an effective marker for assessing disease activity in ankylosing spondylitis (AS). The significant correlation between CAR and both the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Ankylosing Spondylitis Disease Activity Score (ASDAS) indicates CAR's reliability in reflecting disease severity. CAR integrates both C-reactive protein and serum albumin levels, providing a comprehensive view of inflammation and nutritional status, independent of HLA-B27 status. CAR's practicality and cost-effectiveness make it a useful tool for monitoring disease activity and guiding treatment decisions. Future research should further validate CAR's effectiveness and explore its application across diverse patient populations and disease stages.

Conflict of interest:

None

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