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Evaluate the Diagnostic and Prognostic Significance of ANA, CRP, and ESR In RA Patients

Sikna Ali Salman [1*], Nihad Nejres Hilal [1], Mohammed M.Abdul-Aziz[2]

[1] Department of Biochemistry, College of Medicine, University of Tikrit,Salah Al-deen, Iraq
[2] Department of Surgery, College of Medicine, University of Tikrit, Salah Al-deen, Iraq

Corresponding Author Email: sa240019me@st.tu.edu.iq

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Abstract

Rheumatoid arthritis (RA) is an autoimmune disease marked by systemic inflammation and joint damage. CRP and ESR are commonly used to assess disease activity, while ANA is frequently detected in autoimmune diseases, though its role in RA remains debated. To assess the relationship of ANA, CRP, and ESR with disease activity in RA patients and evaluate their diagnostic and prognostic value. A case-control study was conducted at Marjan Teaching Hospital and Al-Mahaweel General Hospital with 90 participants: 60 RA patients (25 males, 35 females) and 30 healthy controls (15 males, 15 females), aged 20–55. ANA and CRP were measured using ELISA, and ESR was analyzed using standard methods. Statistical tests included Mann-Whitney U, Spearman's correlation, and ROC curve analysis. patients had significantly elevated CRP and ESR levels compared to controls ($p < 0.001$). ANA was positive in 35% of patients and was linked to more severe symptoms. CRP and ESR showed a strong correlation ($r = 0.79$, $p < 0.001$), while ANA had a moderate correlation with disease severity ($r = 0.45$, $p < 0.05$). CRP and ESR had good diagnostic accuracy (AUC = 0.905 and 0.832), while ANA was less useful diagnostically.CRP and ESR are reliable indicators of inflammation and disease activity in RA. While ANA is not a key diagnostic marker, it may suggest more severe disease when present. These markers can aid in clinical assessment and management.

1. Introduction

A degenerative autoimmune disease that damages joints and causes other body dysfunctions, rheumatoid arthritis (RA) develops over time. There are many variables that contribute to the development of RA, including genetics, epigenetics, the immune system, and metabolism [1] . The correlation between aging and autoimmune diseases has received a lot of research interest. Recent research has linked accelerated biological aging to a higher risk of RA [2] . The disorder is more common in women and is characterized by morning stiffness, edema, and discomfort in the joints. The clinical appearance of RA is strongly related with extra-articular symptoms in addition to these classic signs. Among them, you could find rheumatoid nodules and vasculitis. The progression of RA may impact many organ systems due to the disease's systemic nature.[3] The broad category of autoantibodies known as antinuclear antibodies (ANAs) focus on particular parts of cells, including their nuclei and cytoplasm. Multiplex assays, line immunoassay formats, indirect

immunofluorescence assays (IIFAs), and enzyme-linked immunosorbent assays (ELISAs) are among the immunochemical approaches that aid in the detection of ANA. Reliability and accuracy have long made the IIFA using HEp-2 cells the gold standard for ANA detection [4,5] Blood tests for anaemia are crucial in diagnosing certain systemic autoimmune illnesses, including SLE, SS, SSc, PM, and MCTD (mixed connective tissue disease).It is unclear; however, what role ANA plays in RA treatment and how it relates to other serological markers. The purpose of this investigation was to clarify the relationship between serum ANA and RA. Additionally, the disease's acute phase reactants (such as C-reactive protein and erythrocyte sedimentation rate) and several autoantibodies (such as CCP and(MCV) were studied [6].

2.Materials and Methods

Research Methods and Subjects
Marjan Teaching Hospital and Al-Mahaweel General Hospital collaborated for three months from October to December at 2024 to carry out this case-control research. The study included 90 individuals: 30 healthy controls of the same sex and 20–55 years old, and 60 RA patients (25 men and 35 women) diagnosed using the 2010 ACR/EULAR criteria.
Evaluation of Biomarkers: Enzyme-linked immunosorbent assay (ELISA) was used to determine the levels of ANA and CRP. The Westergren technique was used to calculate ESR.
Statistical Analysis: The Mann-Whitney U Biomarker levels in RA patients and controls were compared using a U test. The connections between biomarkers and illness severity were assessed using Spearman's correlation. To assess the diagnostic efficacy of every biomarker, ROC curve analysis was carried out. We considered $p < 0.05$ to be statistically significant.

3.Results

The levels of C-reactive protein and endothelium-sensitive receptor were noticeably higher in RA patients when compared with controls ($p < 0.001$) as seen in figures (1) and (2).When compared to healthy controls, RA patients had higher levels of ANA. figure (3) Figure (4) and (5) display the results of the diagnostic performance (ROC) analysis, which reveals a weak and non-significant correlation between ANA and ESR (r=0.03) and ANA and CRP (r=0.106), respectively, suggesting that there is no relevant association in the patients investigated.
The diagnostic performance of ANA, CRP, and ESR is shown in Table (1), which displays the ROC analysis: ANA (>0.18): AUC 0.870, specificity 96.67%, sensitivity 63.33%. With CRP levels more than 398 pg/ml, the most accurate result was an area under the curve (AUC) of 0.941, a sensitivity of 85.00% and a specificity of 100%. Sensitivity (83.33%), specificity (83.33%), and area under the curve (AUC) were achieved for ESR (>10 mm/hr). Figures 6, 7, and 8 and table (1) both demonstrate this.

4.Discussions

Antinuclear antibodies (ANA), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) were assessed for their diagnostic and prognostic value in rheumatoid arthritis (RA) patients in this research. While ANA has limited diagnostic usefulness in this setting, our data demonstrate that CRP and ESR are valid biomarkers for RA disease activity. One possible use for ANA, however, is to identify a subgroup of RA patients with more severe illness or shared autoimmune characteristics, as it was linked to more severe disease symptoms.
Previous research has shown that CRP and ESR are useful in evaluating RA disease activity, and our results are in line with that. One example is the frequent use of CRP and ESR in clinical settings to track inflammatory activity; according to a research, these markers are strongly associated with the severity of RA illness [7] . Similarly, these indicators have been shown to be predictive of disease progression and treatment efficacy in a previous study [8] . Based on the ROC analysis, which showed that CRP and ESR had good diagnostic accuracy and substantial associations with RA severity, our results corroborate these findings. But ANA's function in RA is still up for debate. According to prior research, ANA positive is somewhat common in RA patients, which is in line with our findings. Despite its low diagnostic specificity for RA, ANA positive was seen in 30–40% of RA patients in one research [9] . Although ANA is more typically linked to systemic lupus erythematosus (SLE) and other autoimmune diseases, other research have shown a higher correlation between ANA and RA disease activity. Despite this, some studies have claimed that ANA testing is useless for routine RA diagnosis. An example of this is the association between ANA titers and inflammatory markers in RA patients, which was shown [10] . This suggests that ANA may play a role in disease monitoring [11] But our results show that ANA does not significantly indicate inflammatory load in RA; weak and non-significant associations were seen between ANA and CRP and ESR.

5.Conclusion

Reliability and accuracy of CRP and ESR as inflammatory indicators for RA disease activity are well-established. Though ANA isn't usually used to diagnose RA, it may be a sign of severe disease phenotypes or autoimmune overlap syndromes when it is present. Early diagnosis, illness monitoring, and individualized treatment methods might be improved by incorporating these biomarkers into clinical practice.

Table 1. show ROC for Evaluated parameters

Parameters	Cut-off value	sensitivity	specificity	+PV	-PV	Youden index J	AUC
ANA (index)	> 0.18	63.33	96.67	97.4	56.9	0.60	0.870
CRP (pg/ml)	>398	85.00	100.00	100.00	76.9	0.8500	0.941
ESR (mml/hr)	>10	83.33	83.33	90.9	71.4	0.6667	0.882

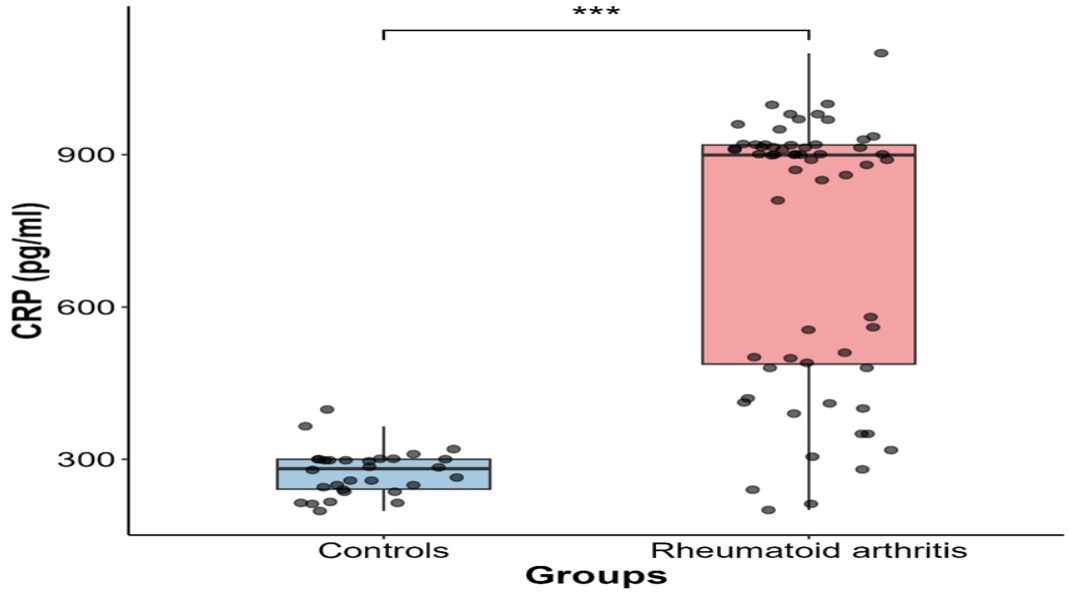

Fig.1.Boxplot of CRP by studied groups.

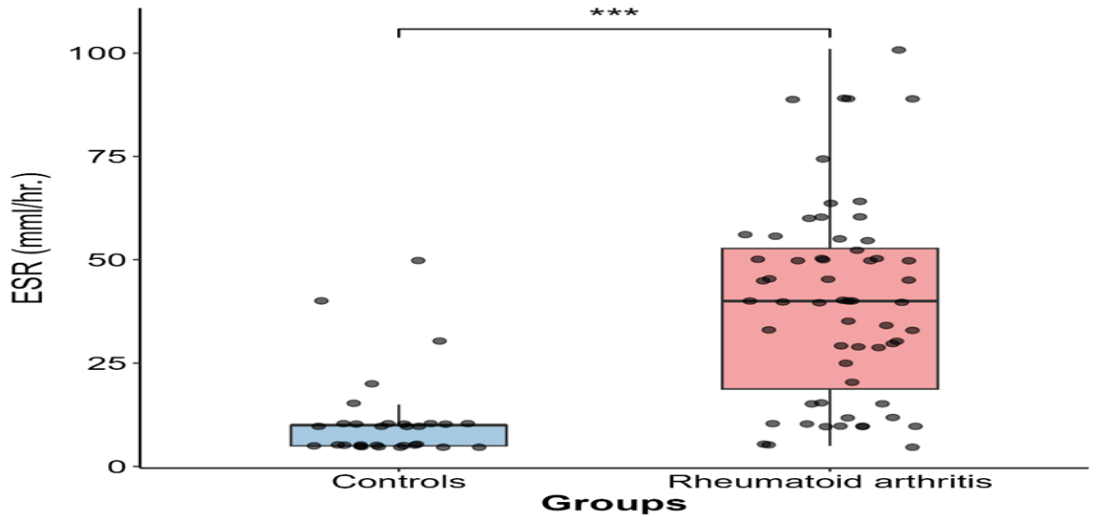

Fig.2.Boxplot of ESR by studied groups

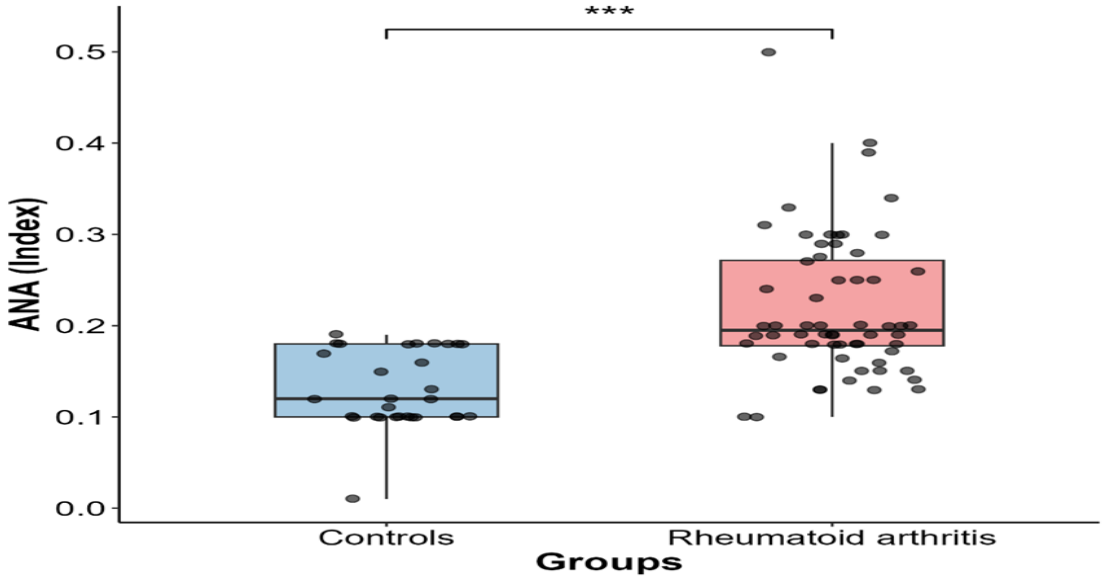

Fig.3. Boxplot of ANA by studied groups .

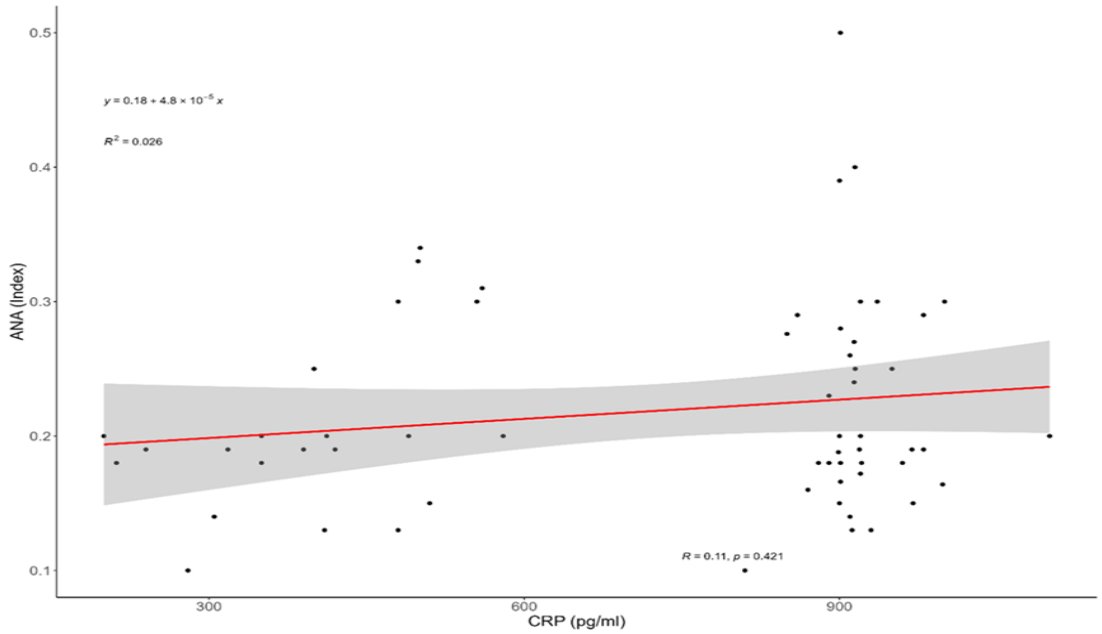

Fig.4.Correlation between ANA and CRP

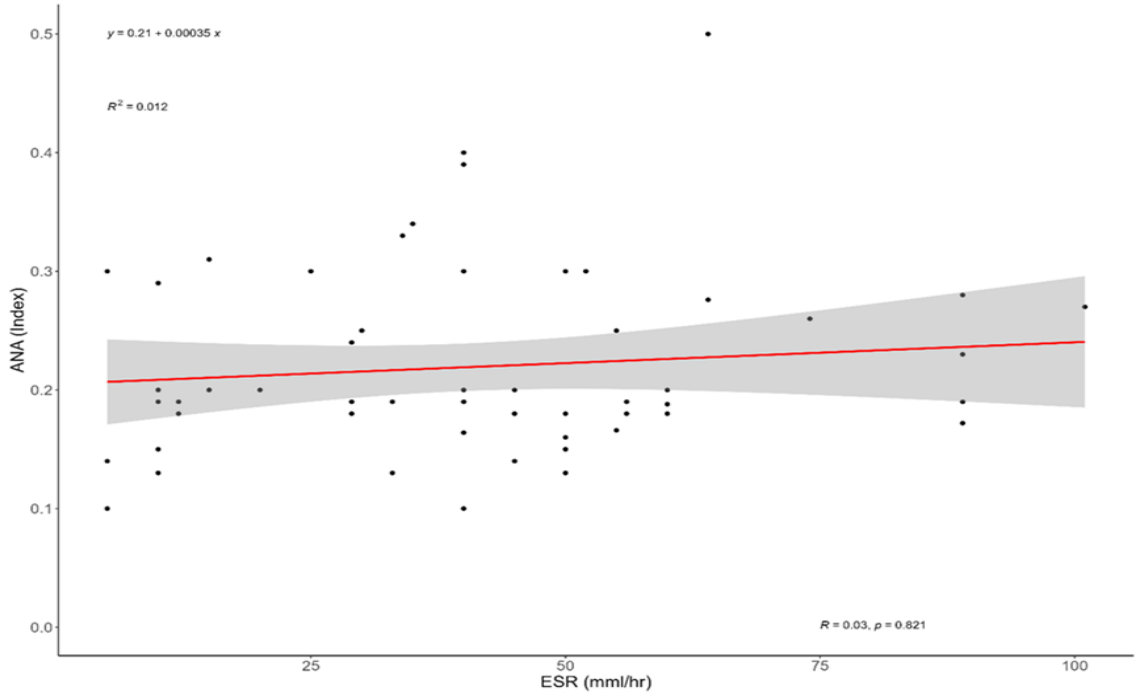

Fig.5.Correlation between ANA and ESR.

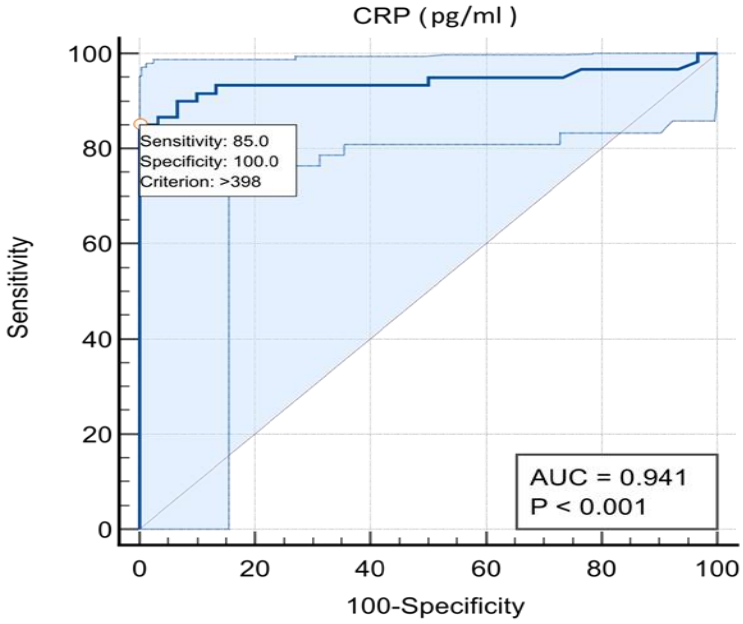

Fig.6.Receiver operating characteristic (ROC) curve of serum CRP as diagnostic marker in rheumatoid arthritis

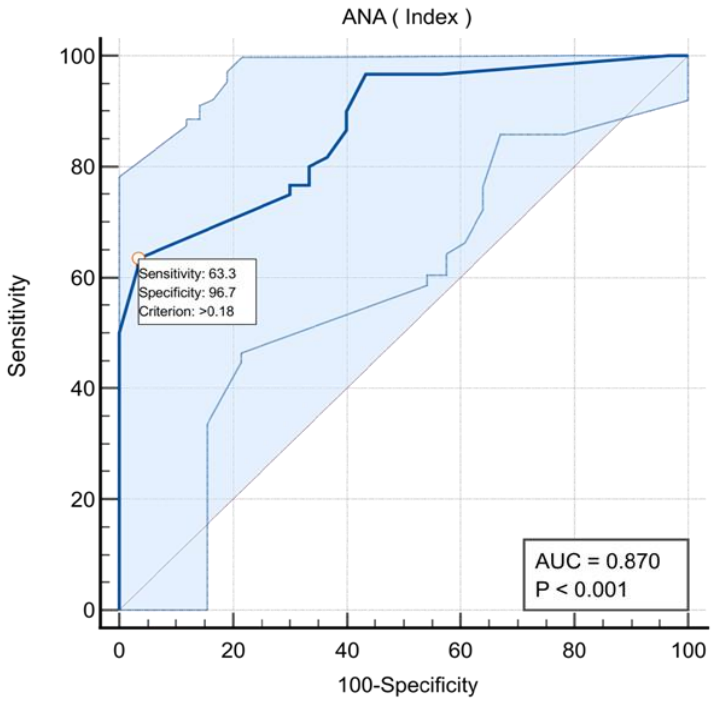

Fig.7.Receiver operating characteristic (ROC) curve of serum ANA as diagnostic marker in rheumatoid arthritis

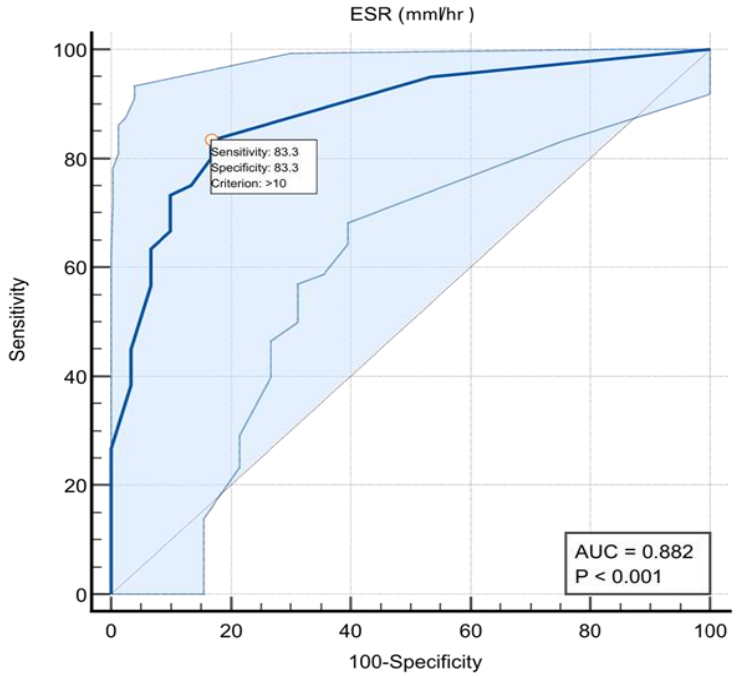

Fig.8.Receiver operating characteristic (ROC) curve of serum ESR as diagnostic marker in rheumatoid arthritis.

References

1-Symolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. Lancet. 2016;388(10055):2023–38. Doi:10.1016/S0140-6736(16)30173-8.

2-Chen L, Wu B, Mo L, Chen H, Zhao Y, Tan T, et al. Associations between biological ageing and the risk of, genetic susceptibility to, and life expectancy associated with rheumatoid arthritis: A secondary analysis of two observational studies. Lancet Healthy Longev. 2024;5:e45–e55. Doi:10.1016/S2666-7568(23)00220-9

3- Chen L, Wu B, Mo L, Chen H, Zhao Y, Tan T, et al. Associations between biological ageing and the risk of, genetic susceptibility to, and life expectancy associated with rheumatoid arthritis: A secondary analysis of two observational studies. Lancet Healthy Longev. 2024;5:e45–e55. doi:10.1016/S2666-7568(23)00252-

4-Bossuyt X, De Langhe E, Borghi MOMeroni PL. Understanding and interpreting antinuclear antibody tests in systemic rheumatic diseases. Nat Rev Rheumatol. (2020) 16:715–26. doi: 10.1038/s41584-020-00522-wPubMed Abstract | CrossRef Full Text | Google Scholar

5-Stochmal A, Czuwara J, Trojanowska MRudnicka L. Antinuclear antibodies in systemic sclerosis: an update. Clin Rev Allergy Immunol. (2020) 58:40–51. doi: 10.1007/s12016-018-8718-8PubMed Abstract | CrossRef Full Text | Google Scholar

6-Aringer M, Costenbader K, Daikh D, Brinks R, Mosca M, Ramsey-Goldman R, et al. 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. Ann Rheum Dis. (2019) 78:1151–9. doi: 10.1002/art.40930PubMed Abstract | CrossRef Full Text | Google Scholar

7-Aletaha, Daniel, and Josef S Smolen. “Diagnosis and Management of Rheumatoid Arthritis: A Review.” JAMA vol. 320,13 (2018): 1360-1372. doi:10.1001/jama.2018.13103

8-Shapiro SC. Biomarkers in Rheumatoid Arthritis. Cureus. 2021 May 16;13(5):e15063. doi: 10.7759/cureus.15063. PMID: 34141507; PMCID: PMC8205440.

9-Liu F, Wang XQ, Zou JW, Li M, Pan CC, Si YQ. Association between serum antinuclear antibody and rheumatoid arthritis. Front Immunol. 2024 Apr 22;15:1358114. doi: 10.3389/fimmu.2024.1358114. PMID: 38711518; PMCID: PMC11070521.

10-Bossuyt, Xavier et al. “Understanding and interpreting antinuclear antibody tests in systemic rheumatic diseases.” Nature reviews. Rheumatology vol. 16,12 (2020): 715-726. doi:10.1038/s41584-020-00522-w

11-Stochmal, Anna et al. “Antinuclear Antibodies in Systemic Sclerosis: an Update.” Clinical reviews in allergy & immunology vol. 58,1 (2020): 40-51. doi:10.1007/s12016-018-8718-8