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Original Research Paper

Predicting Thrombosis Risk in Rheumatoid Arthritis: The Combined Effects of Anti-MCV Antibodies, D-dimer and Disease Activity

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Abstract: Rheumatoid arthritis (RA) carries an elevated risk of thrombotic complications, a major contributor to cardiovascular morbidity in this population. This case-control study aimed to identify predictive factors for thrombosis risk in RA and D-dimer roles, focusing on anti-mutated citrullinated vimentin (anti-MCV) antibodies and disease activity. Sixty-five RA patients and 25 age-matched female controls were recruited from Al-Sadder Teaching Hospital, Iraq (September–November 2024). Disease activity was assessed via DAS28-CRP, alongside biomarkers (CRP, ESR, D-dimer, anti-MCV), lipid profiles, and platelet counts.

RA patients exhibited significantly elevated CRP (9.19 vs. 2.45 mg/L, $p<0.0001$), D-dimer (0.66 vs. 0.29 µg/mL, $p<0.001$), anti-MCV (7.96 vs. 2.63 U/mL, $p<0.001$), and ESR (38.34 vs. 18.99 mm/hr, $p<0.001$) compared to controls. Higher disease activity (DAS28-CRP ≥3.25) correlated with older age (OR:7.600; 95%CI:2.173–26.583), elevated CRP (OR:7.000; 95%CI:3.171–15.454), and D-dimer (OR:13.176; 95%CI:2.676–64.879). Anti-MCV levels showed a weaker association (OR:3.846; 95%CI:0.452–32.695, $p=0.036$). ROC analysis identified CRP (AUC:0.99, sensitivity:100%, specificity:94%) and D-dimer (AUC:0.87) as robust discriminators of moderate-to-high disease activity, while anti-MCV demonstrated poor discriminatory capacity (AUC:0.60, $p=0.334$). Correlation analyses revealed strong associations between DAS28-CRP and CRP ($r=0.871$), D-dimer ($r=0.792$), and ESR ($r=0.541$), but only a modest link with anti-MCV ($r=0.313$).

In conclusion, systemic inflammation (CRP, D-dimer) and age, rather than anti-MCV, are critical predictors of thrombosis risk in RA. Anti-MCV's limited discriminatory utility suggests its role in RA pathophysiology may not directly translate to thrombosis risk stratification. These findings underscore the importance of integrating inflammatory biomarkers into RA management protocols to address cardiovascular morbidity.

Keywords: Rheumatoid Arthritis, Thrombosis, D-dimer, Inflammatory Markers, Anti-MCV Antibody.

1. Introduction

Venous thromboembolism (VTE), which includes pulmonary embolism (PE) and deep vein thrombosis (DVT), is a prevalent medical condition that is linked to a high rate of morbidity and death [1]. When compared to the general population, patients with autoimmune diseases, such as rheumatoid arthritis (RA), are about twice as likely to develop VTE. This elevated risk most likely results from the interaction of inflammation and coagulation, which includes endothelial dysfunction and elevated tissue factor expression brought on by inflammatory cytokines [2]. Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease characterized by synovial inflammation, bone erosion, and cartilage destruction that led to joint damage and deformity, with

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a worldwide prevalence of about 1% of the general population [3]. Patients with RA suffer from joint discomfort and physical incapacity, but their prognosis is mostly determined by cardiovascular events, such as venous thromboembolism (VTE) [4]. As clinical biomarkers, CRP and ESR are routinely used to assess the general inflammatory state of RA patients [5]

Anticyclic citrullinated peptide (anti-CCP) and anti-mutated citrullinated vimentin (/anti-MCV) antibodies are the most often used clinical tests for anticitrullinated peptide antibodies (ACPAs), which measure the quantity of ACPAs in patients' serum.[6]. Extensive epidemiological studies have indicated that individuals with rheumatoid arthritis (RA) had an elevated risk of developing venous thromboembolism (VTE) compared to age- and sex-matched controls, even after accounting for clinical risk factors and acute-phase reactants. Both diseases have shared demographic factors, including advanced age, obesity, smoking, and specific comorbidities [7].

D-dimer, a result of fibrin degradation, serves as a global biomarker for the activation of coagulation and fibrinolysis systems and appears also to reflect activation of inflammatory pathways [8] D-dimer functions as a biomarker for fibrin formation and degradation, indicating active coagulation and fibrinolysis. In addition to thrombotic disorders, cancers, and infections, D-dimer levels are elevated in autoimmune diseases [9]. This study aims identify predictive factors for thrombosis risk in RA, and D-dimer roles with focusing on anti-mutated citrullinated vimentin (anti-MCV) antibodies and disease activity.

2. Methodology

Populations and Samples collection:

This study included 65 female rheumatoid arthritis (RA) patients, diagnosed by a consultant physician according to the American College of Rheumatology 2010 ACR/EULAR criteria, and 25 age-matched female controls. RA patients, receiving standard treatment, were assessed for disease activity at Al-Sadder Teaching Hospital in Al-Najaf, Iraq, between September and November 2024. Participants with alternative autoimmune disorders, such as systemic lupus erythematosus, mixed connective tissue disease, or systemic sclerosis, were rigorously excluded from this investigation. The mean ages and gender distributions of the groups were in alignment with the recognized epidemiological patterns associated with RA. A minimal number of eight male RA patients were assessed, and due to insufficient availability of serum samples, they were subsequently omitted from the analysis. Control subjects were recruited following individual interviews, which validated the absence of any diagnoses or treatments related to inflammatory or autoimmune rheumatic disorders. Demographic data, including age and duration of disease, was meticulously gathered through comprehensive reviews of medical records and structured interviews. Patients received various anti-rheumatic drugs, including NSAIDs, corticosteroids, and both synthetic and biologic DMARDs. None had a history of cardiovascular disease or were taking anticoagulants. The assessment of disease activity was executed using the DAS28-CRP criteria, which categorized patients into low, moderate, and high activity subgroups, thereby enabling a comparative analysis of coagulation and inflammation indices across these distinct classifications.

Laboratories Assay

Human anti-mutated citrullinated vimentin antibody ELISA kit. This ELIZA uses sandwich-ELIZA as the method for the accurate quantitative detection (anti-mcv) in serum, supplied by China-CAT. No.SL0214Hu. Estimation of CRP serum levels was measured by the use of CRP kit and was done according to the company (DIRUI /CHINA) that depended on the technique of the use a (CS-T180Auto-Chemistry Analyzer). Determination of Erythrocyte Sedimentation Rate (ESR), Venous blood is drawn in EDTA and put in a vertical Westergren tube for the ESR assay. The ESR value is determined by measuring the distance in millimeters that red blood cells have settled after an hour. D-dimer was measured by Finecare FIA meter from (Wondfo company, China) is based on Fluorescence Immunoassay (FIA) technology. Estimation of the Lipid Profile Levels: TC, TG, and HDL-C in blood serum levels was measured by the use of Lipid profile kit and was done according to the company (Tokyo Boeki Medisys/Japan) that depended on the technique of the uses a (biolis 30i automated clinical Chemistry Analyzer)

Statistical analysis

Statistical analysis was conducted using the IBM SPSS Statistics package (version 28.0) and data entry was performed with Microsoft Office Excel 2021. The Kolmogorov–Smirnov test assessed data normality, while qualitative data were analyzed using the chi-square test, presented as counts and proportions (N%). Quantitative data comparisons between two groups were made with the independent t-test, reported as mean ±

standard deviation (SD). Non-normally distributed data were described by the median and interquartile range (IQR), with group differences analyzed using the Mann-Whitney U test. Differences across three groups were evaluated using one-way ANOVA and Kruskal-Wallis tests. The diagnostic values of coagulation and inflammation indices for thrombosis in RA were confirmed through receiver operating characteristic (ROC) curve analysis, which estimated the area under the curve (AUC) and 95% confidence intervals (CIs) to establish optimal cutoff values. Linear regression assessed correlations between parameters, with significance defined at $p < 0.05$. [10]

3. Results and Discussion

Demographic and Clinical Data

A comparison of the clinical and demographic traits of a control group of 25 healthy people with a group of 65 RA patients is shown in Table 1. With a p-value of 0.068, which indicates no statistically significant difference, the mean age of the RA patients was 49.51 years (±9.41 standard deviation), whereas the mean age of the healthy controls was 45.64 years (±8.26 SD). However, compared to the control group (28%), a higher percentage of RA patients (52.3%) were 50 years of age or older, according to the age distribution. The median duration of RA across patients was 4 years, with an interquartile range (IQR) of 1.75 to 10 years. In the RA group, the distribution of disease duration groups (less than a year, one to five years, six to ten years, and more than ten years) differed statistically from that of the control group (p=0.010).

Significant differences between the two groups were evident in clinical indicators. RA patients had mean C-reactive protein (CRP) values of 9.19 mg/L (±4.92 SD, median 10.1, IQR 4.33–13.7), while healthy controls had mean C-reactive protein levels of 2.45 mg/L (±0.76 SD, median 2.4, IQR 2.02–3) (p<0.001). Likewise, D-dimer levels in RA patients were 0.66 µg/ml (±0.35 SD, median 0.51, IQR 0.41–0.94), while in controls, they were 0.29 µg/ml (±0.08 SD, median 0.28, IQR 0.22–0.36) (p<0.001). In patients with RA, anti-MCV antibody levels were 7.96 U/ml (±2.62 SD, median 8, IQR 6.05–9.19), while in controls, they were 2.63 U/ml (±0.73 SD, median 2.62, IQR 2.33–2.97) (p<0.001).

In RA patients, the DAS28-CRP, a measure of disease activity, was 3.86 (±1.32 SD, median 3.72, IQR 3.25–4.89). The distribution of disease activity categories (low, moderate, and high) differed significantly from the control group (p=0.012). Compared to the control group, 60% of RA patients experienced some type of morbidity, including cardiovascular disease, hypertension, diabetes mellitus, and thyroid abnormalities (p<0.001).

RA patients had mean triglyceride levels of 173.35 mg/dl (±80.38 SD, median 160, IQR 114–213.50) and mean cholesterol levels of 167.00 mg/dl (±37.48 SD, median 169, IQR 137–193), whereas healthy controls had mean triglyceride levels of 106.56 mg/dl (±33.20 SD, median 107, IQR 75.00–136) and mean cholesterol levels of 145.00 mg/dl (±25.93 SD, median 148, IQR 120–161.50). RA patients had mean HDL levels of 39.22 mg/dl (±9.69 SD, median 40, IQR 32–47.50) while controls had mean HDL values of 44.64 mg/dl (±7.29 SD, median 45, IQR 38–50.50).

RA patients had a mean platelet count of 246.71 x 10^3/µL (±56.71 SD, median 241, IQR 205.5–271.5), while controls had a mean platelet count of 207.76 x 10^3/µL (±35.84 SD, median 210, IQR 180.5–233.5). At a mean of 38.34 mm/hr (±16.7 SD, median 37, IQR 25.5–50), RA patients had a greater erythrocyte sedimentation rate (ESR) than healthy controls (18.99 mm/hr, ±9.42 SD, median 16.72, IQR 12.2–27.5). Both the ESR and these lipid and platelet measurements showed statistical significance.

Clinical and Biomarker Predictors of Disease Activity in Rheumatoid Arthritis

The data show that several clinical and biomarker variables are significantly correlated with RA disease activity (DAS28-CRP), Table 2. A significant correlation ($p = 0.003$) was found between age and disease activity: patients under 45 years old were more likely to have low disease activity (68.8%), whereas patients over 45 years old were more likely to be in the moderate (75.8%) and high (81.3%) activity groups. The risks of moderate to high disease activity were substantially greater in older age groups (OR: 7.600; 95% CI: 2.173–26.583).

There was no significant link between RA duration (≤ 5 vs. > 5 years) and disease activity ($p = 0.340$), a relatively uniform distribution across groups, and a non-significant OR of 2.069 (95% CI: 0.583–7.344). There was a significant correlation ($p < 0.001$) between CRP levels and disease activity. 56.3% of those with low activity had low CRP (≤ 3 mg/L), whereas 100% of people with moderate and high activity had higher CRP. The risks of moderate to high disease activity were substantially higher in patients with CRP > 3 mg/L (OR: 7.000; 95% CI: 3.171–15.454).

There was also a strong correlation ($p < 0.001$) between D-dimer levels. 87.5% of the low activity group had low D-dimer (< 0.5 µg/ml), but 51.5% of moderate and 93.8% of high activity cases had increased levels (OR = 13.176, 95% CI: 2.676–64.879). Stable anti-MCV was more common in the high activity group (37.5%) than in the moderate (12.1%) and low (6.3%) groups, indicating

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a significant difference in anti-MCV status between the groups (p = 0.036). However, there was no statistically significant difference in the OR for stable anti-MCV in moderate/high versus low activity (OR: 3.846; 95% CI: 0.452–32.695).

Association of DAS28-CRP with Clinical Markers in RA

The provided data in Table 3, which compares clinical markers in rheumatoid arthritis (RA) patients with low versus moderate to high disease activity based on DAS28-CRP, reveals several significant associations. The data indicates that patients in the moderate to high disease activity group were on average older (51.65 years vs. 42.94 years) and had a longer median duration of RA (5 years vs. 1.5 years). Furthermore, the data shows a less favourable lipid profile in the higher disease activity group, with significantly elevated mean triglyceride (190.69 vs. 120.25) mg/dl and total cholesterol (177.35 vs. 135.31) mg/dl levels, alongside significantly lower mean HDL cholesterol (35.84 vs. 49.56) mg/dl. The data also demonstrates significantly higher mean levels of platelet count (253.33 vs. 226.44) x 10^3/ml, ESR (42.92 vs. 24.31) mm/hr, CRP (11.22 vs. 2.95) mg/L, and D-dimer (0.76 vs. 0.37) µg/ml in the moderate to high disease activity group, highlighting increased inflammation and coagulation. In contrast, the mean anti-MCV antibody levels (8.21 vs. 7.21) U/ml did not show a statistically significant difference between the two disease activity groups according to the data.

Correlation and Predictive Analysis

The results in Figure 1 shows correlations between inflammatory indicators and disease activity. Figure B demonstrates a substantial positive connection between DAS28-CRP and CRP (r = 0.871, p < 0.001). Figure C shows a similarly strong association between DAS28-CRP and D-dimer levels (r = 0.792, p < 0.001). Additionally, Figure A shows a moderate correlation between ESR and DAS28-CRP (r = 0.541, p < 0.001). Figure D shows that anti-MCV antibodies had statistically significant but smaller relationships with DAS28-CRP (r = 0.313, p = 0.011).

According to Figure 2, correlation analysis, CRP and ESR had a somewhat favourable relationship (r = 0.610, p < 0.001), as shown in Figure F. Figure A shows a modest correlation between D-dimer levels and ESR (r = 0.495, p < 0.001), while Figure B shows a substantial correlation with CRP (r = 0.781, p < 0.001). Additionally, Figure D shows a substantial correlation between Anti-MCV levels and all three inflammatory indicators, including ESR (r = 0.326, p = 0.008). Figure E shows CRP (r = 0.387, p = 0.001), while Figure C shows D-dimer (r = 0.286, p = 0.021).

Discriminatory Capacity of Biomarkers in Rheumatoid Arthritis Disease Activity Levels

The results in the figure 3. CRP exhibits the strongest discriminatory power, with an AUC of 0.99 (p<0.001), according to the data, which also includes p-values, 95% CI, ideal cut-offs, sensitivity, and specificity. CRP has 100% sensitivity and 94% specificity in detecting moderate to high disease activity at a threshold of 4.31 mg/L. With an 81% specificity and 76% sensitivity at a threshold of 30.50 mm/hr, ESR likewise exhibits high discriminating (AUC=0.83, p<0.001). D-dimer has moderate discrimination (AUC=0.87, p<0.001), with 82% sensitivity and 75% specificity at a threshold of 0.45 µg/ml. However, the data for Anti-MCV indicates that it is ineffective at differentiating between the disease activity groups, with low discrimination (AUC=0.60, p=0.334) and a non-significant p-value. Anti-MCV has a low sensitivity of 37% and a high specificity of 88% at a cut-off of 8.87 U/ml.

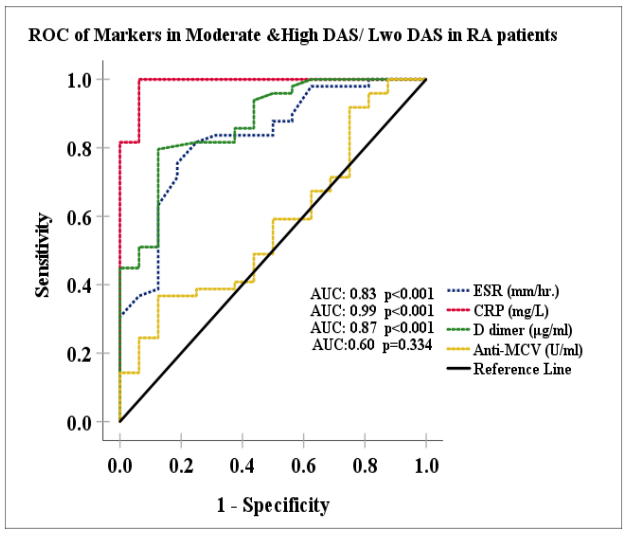

Fig 3. ROC Curves and AUC for Biomarkers in Differentiating RA Disease Activity Scores

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Table 1. Demographics and Clinical Categories in Rheumatoid (RA) Patients and Healthy Controls

Demographics and Clinical Categories		**RA Patients N=65**	**Healthy control N=25**	**p-value**
Age (year)	Mean ± SD	49.51±9.41	45.64±8.26	0.068 ¥ ns
	30-39 year	9(13.8%)	8(32%)	X^2= 5.684
	40-49 year	22(33.8%)	10(40%)	0.058 ns
	≥ 50 years	34(52.3%)	7(28%)	
Period_ RA (year)	Median (IQR)	4(1.75–10)		X^2= 11.369
	< 1 year	13(20%)	-	0.010*
	1-5 years	28(43.1%)	-	
	6-10 year	12(18.5%)	-	
	> 10 years	12(18.5%)	-	
CRP (mg/L)	Mean ± SD	9.19±4.92	2.45±0.76	0.0001**
	Median (IQR)	10.1(4.33–13.7)	2.4(2.02–3)	
	< 3 mg/L	9(13.8%)	25(100%)	X^2= 12.585
	3.1 - 10 mg/L	24(36.9%)	(16%)	0.002*
	> 10 mg/L	32(49.2%)	0(0%)	
D dimer (µg/ml)	Mean ± SD	0.66±0.35	0.29±0.08	0.0001**
	Median (IQR)	0.51(0.41–0.94)	0.28(0.22–0.36)	
	<0.5 µg/ml	31(47.7%)	25(100%)	X^2= 0.138
	≥0.5 µg/ml	34(52.3%)	0(0%)	0.710 ns
Anti-MCV (U/ml)	Mean ± SD	7.96±2.62	2.63±0.73	0.0001**
	Median (IQR)	8(6.05–9.19)	2.62(2.33–2.97)	
	Disappear	54(83.1%)	25(100%)	X^2= 28.446
	Stable	11(16.9%)	-	0.0001**
DAS28-CRP	Mean ± SD	3.86±1.32	–	0.0001*
	Median (IQR)	3.72(3.25–4.89)	–	
Disease Activity (DAS 28-CRP)	Low	16(24.6%)	-	X^2= 8.892
	Moderate	33(50.8%)	-	0.012*
	High	16(24.6%)	-	
Complications Morbidity	Non	26(40%)	25(100%)	X^2= 32.015
	CVD	10(15.4%)	-	0.0001**
	Hyper.	9(13.8%)	-	
	Hyper. & DM.	13(20%)	-	
	Thyroids	4(6.2%)	-	
	Thyroids & DM	3(4.6%)	-	
TG (mg/dl)	Mean ± SD	173.35±80.38	106.56±33.20	0.0001**
	Median (IQR)	160(114–213.50)	107(75.00–136)	
CHOL (mg/dl)	Mean ± SD	167.00±37.48	145.00±25.93	0.008**
	Median (IQR)	169(137–193)	148(120–161.50)	
HDL (mg/dl)	Mean ± SD	39.22±9.69	44.64±7.29	0.013*
	Median (IQR)	40(32–47.50)	45(38–50.50)	
PLT (103/µL)	Mean ± SD	246.71±56.71	207.76±35.84	0.002*
	Median (IQR)	241(205.5–271.5)	210(180.5–233.5)	
ESR (mm/hr.)	Mean ± SD	38.34±16.7	18.99±9.42	0.0001**
	Median (IQR)	37(25.5–50)	16.72(12.2–27.5)	

Significant differences at p-value<0.05*, <0.01**. ¥: Independent t-test, or Mann Whitney. SD: Standard deviation. IQR: inter quartile range. X^2: Chi-square test. Ns: non-significant. D.D: Disease duration. DAS28: Disease Activity Score 28

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Table 2. Clinical and Biomarker Predictors of Disease Activity in Rheumatoid Arthritis

Categories		**Disease Activity (DAS 28-CRP)**						**P-value**
		Low		**Moderate**		High		
		N	**%**	**N**	**%**	N	%	
Age (year)	≤ 45 yr.	11	68.8%	8	24.2%	3	18.8%	X2= 11.69
	> 45 yr.	5	31.3%	25	75.8%	13	81.3%	0.003*
Period_ RA	≤ 5 yr.	12	75.0%	21	63.6%	8	50.0%	X2= 2.16
	> 5 yr.	4	25.0%	12	36.4%	8	50.0%	0.340 ns
CRP mg/L	Low ≤ 3	9	56.3%	0	0.0%	0	0.0%	X2= 31.99
	Mild _Severe >3	7	43.8%	33	100.0%	16	100.0%	0.0001**
D-dimer	<0.5	14	87.5%	16	48.5%	1	6.3%	X2= 21.19
µg/ml	≥0.5	2	12.5%	17	51.5%	15	93.8%	0.0001**
Anti-MCV	Disappear	15	93.8%	29	87.9%	10	62.5%	X2= 6.66
status	Stable	1	6.3%	4	12.1%	6	37.5%	0.036*
Moderate & High DAS vs. Low DAS.				**OR (95% CI)**				
Age (> 45 / ≤ 45 yr.)				7.600 (2.173 – 26.583)				0.002*
Period RA (> 5 / ≤ 5 yr.)				2.069 (0.583 – 7.344)				0.261 ns
CRP (Mild/Severe > 3 / Low ≤ 3 mg/L)				7.000 (3.171 – 15.454)				0.0001**
D-dimer (≥ 0.5 / < 0.5 µg/ml)				13.176 (2.676 – 64.879)				0.002*
Anti-MCV (Disappear / Stable)				3.846 (0.452 – 32.695)				0.217 ns

Significant differences at p-value<0.05*, <0.01**. Ns: non-significant. X^2: Chi-square test. D.D: Disease duration. DAS28: Disease Activity Score 28

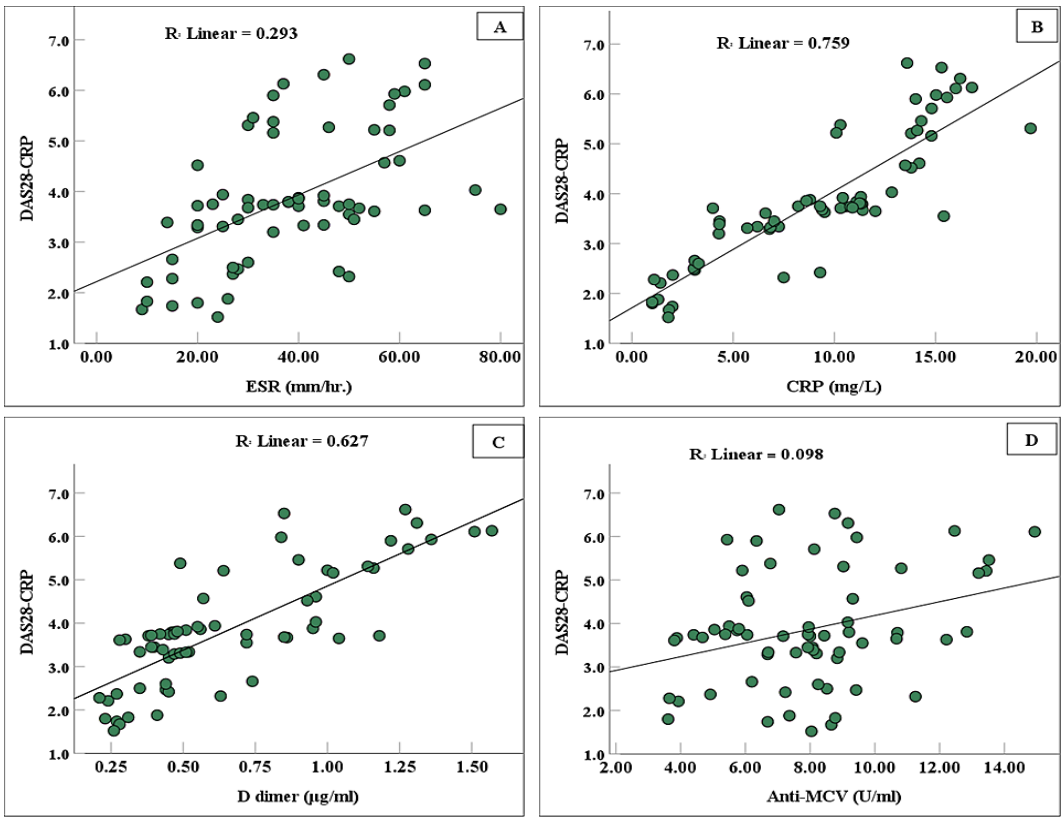

Fig1. Correlations of Disease Activity with Inflammatory and Coagulation Markers in RA

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Table 3. Association of DAS28-CRP with Clinical Markers in RA

Parameters	Disease Activity (DAS28-CRP) Mean ± SD		P-value
	Low (N=16)	Moderate & High (N=49)	
Age (year)	42.94 ± 7.73	51.65 ± 8.58	0.001
Period_ RA (year)	1.5 (29-5.75)	5 (2.0-10.5)	0.008
TG (mg/dl)	120.25 ± 69.02	190.69 ± 76.67	0.002
CHOL (mg/dl)	135.31 ± 24.94	177.35 ± 35.14	0.001
HDL (mg/dl)	49.56 ± 5.77	35.84 ± 8.22	0.001
PLT (10^3/ml)	226.44 ± 45.48	253.33 ± 58.83	0.001
ESR (mm/hr.)	24.31 ± 12.44	42.92 ± 15.37	0.001
CRP (mg/L)	2.95 ± 2.36	11.22 ± 3.65	0.001
D dimer (µg/ml)	0.37 ± 0.15	0.76 ± 0.35	0.001
Anti-MCV (U/ml)	7.21 ± 2.23	8.21 ± 2.71	0.188

Significant differences at p-value<0.05*, <0.01**. Ns: non-significant. D.D: Disease duration. DAS28: Disease Activity Score 28

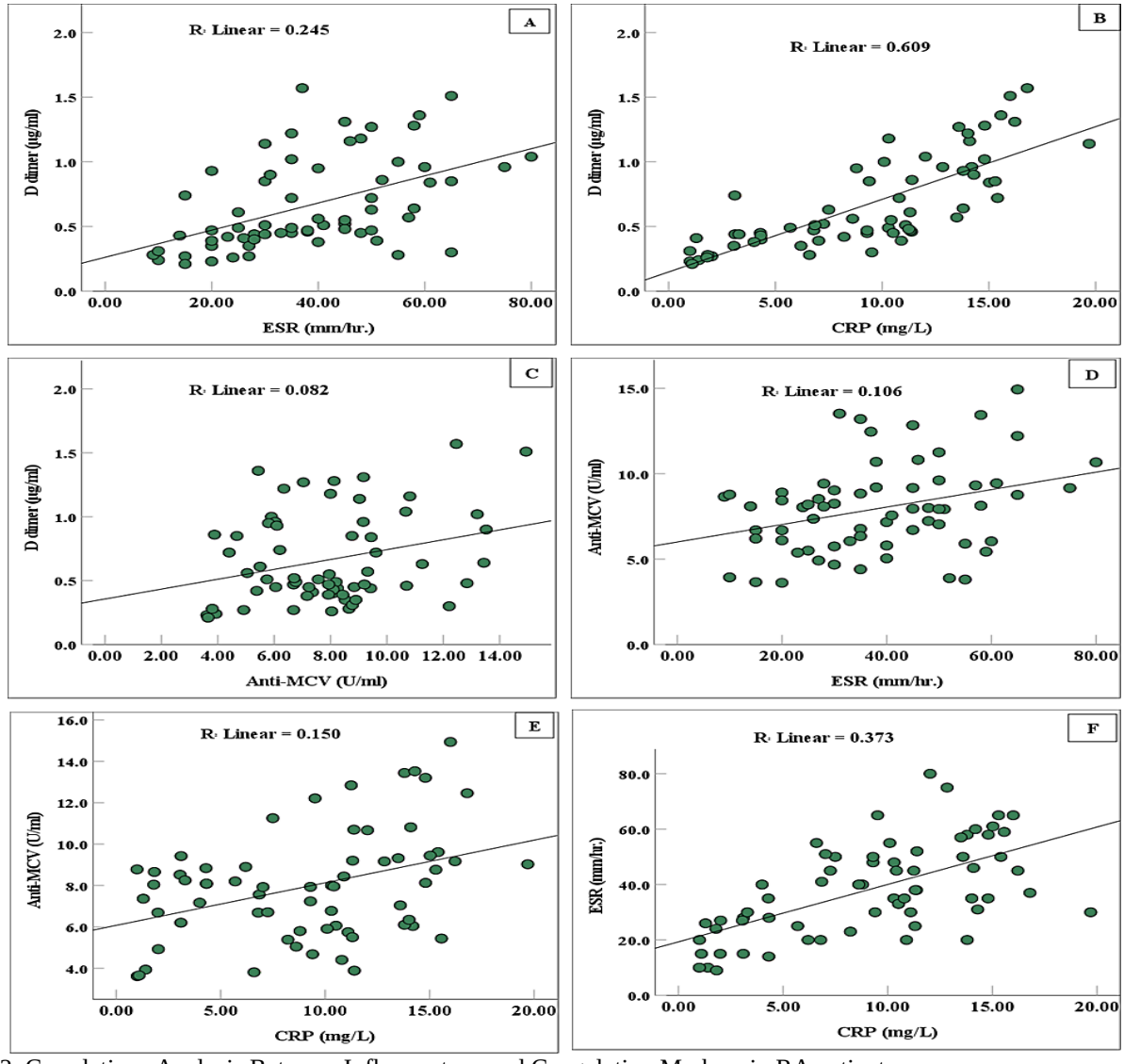

Fig 2. Correlations Analysis Between Inflammatory and Coagulation Markers in RA patients

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Characteristics and Clinical Biomarkers

In the study, although the mean age difference between RA patients and controls was not statistically significant ($p = 0.068$), a higher proportion of RA patients were ≥50 years. This age-related skew is aligned with epidemiological findings, where RA incidence increases with age, especially in post-menopausal women. Since aging increases endothelial dysfunction and coagulopathy, it is also a risk factor for thrombosis in RA. Even in the absence of statistical age significance, this lends credence to the current finding of a possible thrombotic predisposition. [11] This supports the current observation of potential thrombotic predisposition even in the absence of statistical age significance.

The higher incidence of RA in older adults could be influenced by factors such as hormonal changes, immune system aging (immunosenescence), and the accumulation of environmental exposures over time. These factors may lead to increased susceptibility to rheumatoid arthritis after menopause, as estrogen has immunomodulatory effects. The documented increase in endothelial dysfunction and coagulopathy in older RA patients highlights crucial mechanisms through which aging exacerbates the disease. Endothelial dysfunction can lead to a pro-inflammatory state, facilitating the development of comorbidities such as cardiovascular disease (CVD). RA itself is associated with increased cardiovascular morbidity and mortality, making this relationship particularly concerning. [12]

An atherogenic lipid pattern associated with RA is consistent with the dyslipidemia seen in the RA population, which is characterized by decreased HDL and higher triglycerides. [13]. Heart disease is exacerbated by this pro-thrombotic lipid environment. Both thrombotic events and disease activity in RA have been linked to inflammation-induced lipid changes, such as HDL dysfunction and increased triglycerides.

The levels of CRP, D-dimer, and anti-MCV antibodies in the RA and control groups were shown to differ statistically significantly. These results are consistent with research demonstrating that high levels of CRP and D-dimer are indicative of inflammatory activity and hypercoagulability in RA. Finding particular biomarkers like CRP, D-dimer, fibrinogen, and platelet counts offers important information on estimating the risk of VTE in RA patients taking tofacitinib or TNF inhibitors. [14]

In patients with RA, higher levels of anti-MCV antibodies are substantially linked to more severe clinical symptoms. Greater systemic inflammation and more noticeable joint involvement are indicated by higher antibody levels, which suggests that these antibodies may be used as markers of disease activity. [15] Recent research has demonstrated a correlation between elevated anti-MCV levels and the degree of joint erosion or damage seen in RA. These findings demonstrate the potential of anti-MCV as a biomarker for predicting the disease's structural progression and improved the accuracy of RA diagnosis, particularly in the early stages and for people who are seronegative for common RA-associated antibodies such as rheumatoid factor or ACPAs. [16] Particular different hematological markers that shown strong associations with conventional disease activity measurements were found in the study of Choe (2023). In line with our findings that the increased ESR and platelet counts in the RA group reflect chronic inflammation and are recognized RA biomarkers, these indices comprised characteristics such as leukocyte counts and platelet counts. [17]

Activity of the Disease and Predicted Risk Factors for Thrombosis

The older patients have higher Disease Activity Score-28 using CRP (DAS28-CRP) scores is in line with research showing that RA disease severity increases with age. As people age, the combined effects of comorbidities and persistent inflammation can make RA's clinical symptoms worse. Increased systemic inflammation is common in older persons, and this can lead to higher levels of disease activity. This is an important consideration since it may have an impact on treatment choices and the timing of therapeutic actions. [18]

It has been found that elevated CRP and D-dimer levels may accurately predict moderate to high disease activity in RA patients. A well-known indicator of inflammation, CRP has been used extensively to evaluate RA disease activity. Increased D-dimer levels are a sign of systemic inflammation and hypercoagulability, two important factors to take into account when treating RA, particularly in elderly patients who are more susceptible to thrombotic events. According to recent study observed a substantial risk factor for VTE in rheumatoid arthritis patients is persistent high disease activity as indicated by time-averaged DAS28-CRP. [19] In order to reduce the risk of thrombotic events in this population, it is imperative that disease activity be aggressively managed. Since these markers are associated with thrombotic risk, it is

important to closely monitor RA patients, particularly those who are elderly or show signs of increased disease activity. [20] Chronic inflammation in RA causes endothelial dysfunction, which increases the risk of thromboembolic events. [21] Strong associations between DAS28-CRP and markers such as ESR, D-dimer, and CRP are in line with new research showing them to be reliable predictors of RA disease activity. [19] The most responsive biomarker is still CRP, although D-dimer is showing promise as an additional tool for evaluating the inflammatory and vascular burden. A non-significant odds ratio (OR) indicates weak predictive potential for evaluating disease activity, even if the presence of anti-MCV antibodies was linked to increased disease activity. This is consistent with earlier studies showing that anti-MCV is more useful as a diagnostic marker than as a means of assessing disease activity. [22] The most discriminative biomarker for moderate to high disease activity, according to ROC analysis, is CRP (AUC = 0.99), followed by D-dimer and ESR. These results verify current data suggesting the inclusion of D-dimer in RA risk stratification models and support the use of CRP thresholds in clinical practice. [23] Recent comparative studies have confirmed that anti-MCV lacks discriminative capacity for disease activity, despite its diagnostic relevance. [22]

Conclusion

In conclusion, systemic inflammation (CRP, D-dimer) and age, rather than anti-MCV, are critical predictors of thrombosis risk in RA. Anti-MCV's limited discriminatory utility suggests its role in RA pathophysiology may not directly translate to thrombosis risk stratification. These findings underscore the importance of integrating inflammatory biomarkers into RA management protocols to address cardiovascular morbidity.

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Author's Contributions

The author, Intisar Razzaq Sharba, were responsible for planning, supervising the work, drafting the manuscript, and designing the figures. Asmaa Abdulrasool Gaafar conducted the measurements and processed the experimental data. Both authors collaboratively contributed to the research's design and implementation, analyzed the results, and participated in writing the manuscript.

Ethics

This study was conducted under approval by the medical ethics committee at the University of Kufa (2024). Verbal consent was provided from all participates.

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