ORIGINAL ARTICLE

Eastern Journal of Medicine
East J Med 30(4): 653-662, 2025
DOI: 10.5505/ejm.2025.72687

Correlation of Anti-MCV and Anti-CarP Antibodies with Other Clinical and Laboratory Parameters in Patients with Rheumatoid Arthritis

Khalid W Al-Maola[1], Ali A. Younis[2], Firas M Al-Tae[1], Ahmed A Al-Harbi[1]

[1]*University of Mosul, College of Medicine, Department of Microbiology, Iraq*
[2]*University of Mosul, College of Medicine, Department of Microbiology, Iraq*

ABSTRACT

Anti-cyclic citrullinated peptides (anti-CCP) antibodies and rheumatoid factor (RF) represent the key biomarkers that are harnessed to diagnose rheumatoid arthritis (RA). This work stands to appraise other less ascertainable antibodies, such as anti-mutated citrullinated vimentin (anti-MCV) or anti-carbamylated protein (anti-CarP), to be used for RA diagnosis.
The current study was designed as a case-referent model including 60 RA patients and 30 controls. Sera levels of antibodies and RF were estimated via ELISA and correlated with each other and the DAS28 score.
Sera of 43.3% of patients own anti-MCV, while only 30% and 61.7% own anti-CarP antibodies and RF, respectively. Furthermore, 66.7% tested positive for anti-CCP antibodies. Patients' anti-MCV was notably greater than among healthy controls (P value=0.0061). Statistically there is no significant difference between early and established or between seronegative and seropositive patients. The sensitivity and specificity of anti-MCV for the diagnosis of RA were 43.3% and 96.7%. In regard to anti-CarP antibody, RA patients have significantly higher ODs than controls. Anti-CarP possessed a lower sensitivity (28.3%) and specificity (93.3%) in contrast to anti-MCV antibodies. The validity of anti-Carp antibodies to discriminate between early and established or between seronegative and seropositive RA seems to be low. Although both anti-MCV and anti-CarP antibodies were correlated with each other, neither of them showed correlation with RF, anti-CCP, or DAS 28 score.
Anti-MCV and anti-CarP antibodies are not superior to anti-CCP and RF as diagnostic indicators for RA, with limitations in discrimination between early, late, seronegative, and seropositive RA.

Keywords: Rheumatoid arthritis, anti-CarP antibodies, anti-MCV antibodies, rheumatoid factor, anti-CCP antibodies

Introduction

Rheumatoid arthritis (RA) is a lifelong systemic inflammatory autoimmune disease affecting synovium and precipitating joint degradation (1,2). It affects both men and women in a ratio of 3:1, with general prevalence among the population ranging between 0.5% and 1% (3). The disease is pathologically heterogeneous. Measurements of autoantibodies have long been a part of the medical team's care for patients (4). Furthermore, seropositivity is linked to significant discomfort and damage to the joints. (5). Antibodies targeting cyclic citrullinated peptides (anti-CCP) as well as the rheumatoid factor (RF) are the two main clinically significant autoantibodies in RA patients (6). The 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) diagnostic criteria for classifying rheumatoid arthritis now include RF and anti-CCP (7). Nevertheless, RF's specificity for RA is limited. When diagnosing RA, the anti-CCP used to be specific but not sufficiently sensitive (8). In addition to anti-CCP, RA patients may also have other autoantibodies that target structurally related determinants (9). Anti-carbamylated proteins (ACP) are among these antibodies. An example of a non-enzymatic post-translational modification is carbamylation, which occurs when isocyanic acid interacts with amino acid free groups (10). Research data showed that proteins that are carbamylated can elicit strong principal immunological reactions, including T cell activation, antibody generation, cytokine expression, andchemotaxis. Furthermore, the detection of these carbamylated and citrullinated biomolecules within the joints is made feasible by T cells as well as antibody

***Corresponding Author:** Ahmed Abdullah Ahmed Department of Microbiology, College of Medicine, University of Mosul
E-mail: ahmabdahmad@uomosul.edu.iq, Mobile number: 009647740942809
ORCID ID: Khalid W Al-Maola: 0000-0003-0227-7305, **Ali A. Younis:** 0000-0003-4561-8528, **Firas M Al-Tae:** 0000-0003-1177-897X, **Ahmed A Al-Harbi:** 0000-0002-5624-3525
Received: 04.11.2024, **Accepted:** 01.10.2025

immune responses. Eminent evidence supports the contribution of these peptides in erosive arthritis (11). Anti-CarP antibody frequency in RA varies but is generally reported to be between 16% and 45% (12).

Another class of autoantibodies associated with RA is the anti-mutated citrullinated vimentin (MCV). Vimentin is generated from the cytoskeleton's intermediate filament and is synthesized by diverse cells such as mesenchymal cells, endothelial cells, fibroblasts, and other mononuclear cells. Vimentin undergoes two stages of differentiation during its release from apoptotic macrophages in the joint's synovium, which are citrullination and mutation. In genetically predisposed individuals, DNA damage can change genes in the rheumatoid synovium and synoviocytes, explaining the formation of novel epitopes that may compromise immunological tolerance and cause the generation of anti-MCV abs (13, 14). The anti-MCV abs are considered one of the newly studied abs for the diagnosis of RA. Although a number of studies showed a controversy of its utility as a diagnostic tool (15, 16), others revealed an optimistic result of 95% specificity and 78% sensitivity (17). In addition, these antibodies are also proposed as a further indicator of the severity of construction. Patients who expressed anti-MCV abs may show greater risk of getting early joint erosions in comparison to Ab-free patients (18, 19).

The present study aims to appraise the performance of these two antibodies, anti-MCV and anti-CarP, in the diagnosis of RA. Moreover, this study further extended to correlate the level of these antibodies with clinical and laboratory parameters, namely DAS 28 score, anti-CCP, and RF levels.

Materials and Methods

Ethical considerations and consent approval: This work has been ratified by the Medical Research Committee (MREC) at the College of Medicine, University of Mosul, on 23/10/2022 in concurrence with the Helsinki Declaration for Medical Research. All related individuals signed written consent to take part in this study.

Subjects: Between January 2022 and May 2023, a case-referent study was accomplished at the University of Mosul-College of Medicine. 90 subjects participated in this study; 60 of them are RA patients attending a private rheumatology specialized clinic in Mosul City. The ACR/EUROLAR 2010 criteria were followed by the second author, a rheumatologist, to confirm the RA diagnosis in these patients (7). The remaining subjects are 30 age- and sex-matched apparently healthy individuals with no previous history of RA or other rheumatic illnesses. Different illnesses that might alter the concentration of antibodies, such as other autoimmune rheumatic illnesses, immunological deficiencies, infections, malignancy, pregnancy, and liver and kidney disorders, were among the exclusion criteria. Each patient had a detailed history taken, a thorough clinical examination, and a disease activity score (DAS28) assessment (20). Furthermore, individuals with one year of the disease or less were classified as early RA, and those with more than one year were classified as established RA (21). Additionally, patients were categorized as seropositive (anti-CCP antibody and/orRF positive) or seronegative for both parameter categories (22). Other laboratory parameters, such as complete blood count (CBC) and erythrocyte sedimentation rate (ESR), were assessed for the patients. All studied groups were investigated for RF, anti-CCP, anti-MCV, and anti-CarP abs.

Blood sampling and Collection: Under sterile conditions, blood samples equal to 5 ml were collected by venipuncture from participants, clotted, and then sera separated using a centrifuge at 4000 rpm. The obtained sera are then frozen at -20ºC for later use.

Serological Estimations: Sandwich ELISA kits from Sunlong Biotech Co. LTD, China, were used to evaluate serum levels of these studied factors as follows: RF (SL1538Hu), anti-CCP abs. (SL0154Hu), anti-MCV abs. (SL0214Hu), and anti-CarP abs. (SL2657Hu). The procedure was correctly accomplished in compliance with the manufacturer guidelines. The RF and the other two antibodies of concern (anti-CCP and anti-MCV antibodies) serum concentrations were calculated utilizing the standard curve. Concentrations were reported as U/ml. However, because the kit was qualitative, the anti-CarP antibody cut-off values were expressed as estimated optical density (OD) measurements at 450 nm. According to manufacturer recommendations, the critical (cut-off) OD value to differentiate between RA and healthy controls was determined as follows: Critical cutoff = average value of negative control + 0.15. The decision to use a qualitative kit was based on resource constraints and the limited availability of validated quantitative kits in our locality. Since the primary aim was to compare the presence of

anti-CarP antibodies across groups rather than to determine their exact concentrations, the OD-based approach provided a consistent method for group comparison and aligned with the scope of the study.

Statistics: All statistical assessments in this study were carried out via the "MedCalc®20 software package (Belgium)." The graph setup was performed by Microsoft Excel 10. Minimum (min), maximum (max), mean, median, standard deviation (SD), and 95% confidence interval (CI) are used to summarize the data when appropriate. Statistical tests, such as the non-parametric Mann-Whitney test or the parametric "Student t-test," were used to test the means whenever indicated. Serum anti-MCV and anti-CarP antibodies (antibodies of interest) were examined for their ability to diagnose RA at various cut-off values depending on the "Area under the Receiver Operating Characteristics (AUC-ROC) curve. Fisher's exact test was chosen to compare the category data. The pearson correlation coefficient assessed the relationships between the factors under study. P values $\leq$ 0.05 were assumed statistically significant.

Results

Characteristics of the samples: The participant's clinical, laboratory, and demographic details were compiled in Table 1. They include sixty RA (49 female and 11 male) together with 30 healthy individuals (22 female and 8 male). No significant difference was detected between the patients and the controls regarding their age or sex ($P > 0.05$). Family history regarding RA proved positive in 20% of patients, and smoking was reported in 31.7%. Dry eye was the most popular extra-articular feature, detected among 15% of patients. Most patients have moderate-to-severe RA with average DAS scores ranging from 4.09 to 5.57. The medications most prescribed to the patient group are NASIDs, prednisolone, and methotrexate.

Table 2 classified the RA patients according to duration of illness and seropositivity. In this context, 14 patients (23.3%) had early RA, and 46 patients (76.7%) had established RA. Moreover, 57 patients (95.0%) were seropositive, and only 3 patients (5.0%) were seronegative.

Frequencies and serum levels of anti-MCV, anti-Carp, RF, and anti-CCP antibodies among patients and controls: Anti-MCV antibody testing revealed that 26 individuals (43.3%) with RA tested positive at the universal cut-off value of 20.2 U/ml, while 34 patients (56.7%) tested negative, in contrast to 2 individuals (6.7%) positive and 28 individuals (93.3%) negative in the control group (Table 3). Using an OD cut-off value of 0.235, 18 patients (30%) are positive for the anti-carp antibody, while 42 patients (70%) tested negative (**Table 3**). Additionally, when the cut-off value is 20 U/ml, 37 RA patients (61.7%) tested positive for RF, and 40 patients (66.7%) tested positive for anti-CCP in contrast to the controls.

Anti-MCV abs. level in RA patients' sera (25.42 ± 16.69, n=60) was notably greater than those of the healthy controls (16.08 ± 7.99, n=30), (P=0.0061) (Table 4). However, the anti-MCV abs concentrations did not express any significant difference between early and established RA patients (P=0.092). In the same manner, anti-MCV abs serum levels did not differ significantly between seronegative and seropositive groups ($P = 0.447$) (Table 4). In regard to anti-CarP antibody, since the ELISA kit used for measuring anti-CarP antibodies in this study was a qualitative kit, therefore, the OD measurements at 450 nm were used as an indirect indicator of its serum level in both RA patients and healthy individuals. RA patients have significantly higher OD values (0.23 ± 0.14) in contrast to controls (0.15 ± 0.05, $P = 0.002$) (Table 4).

Diagnostic utility of Anti-MCV and anti-CarP among patient group: Table 5 summarizes the efficacy of both anti-MCV and anti-CarP abs. in diagnosing RA depending on ROC curve analysis. The sensitivity of anti-MCV abs. at a best cut-off value of 20.29 U/ml was 43.3% with a specificity of 96.7% (AUC = 0.678, P = 0.0020). Meanwhile, anti-CarP antibody expressed a lower sensitivity (28.3%) with specificity (93.3%) in comparison to anti-MCV antibody at the best cut-off value of 0.235 (AUC=0.641, P=0.0236). In addition, the validity of both antibodies to discriminate between early and established RA or between seronegative and seropositive RA seems to be low.

As shown in Figure 1, anti-CarP antibodies and the serum level of anti-MCV antibodies were positively correlated with one another ($r=0.5836$, $P < 0.0001$). However, neither of them showed any correlation with RF, anti-CCP, or DAS 28 score.

Table 1: Demographic, Clinical, and Laboratory Properties of Studied Subjects

Subjects	Patients	Controls		
Female	49/60 (81.67%)	22/30 (73.33%)		* P = 0.4159 (ns)
Male	11/60 (18.33%)	8/30 (26.67%)		
Age in years (mean ± SD)	20-68 (47.48±11.35)	24-77 (45.57±16.16)		**P = 0.3604 (ns)
Family history of RA	12/60 (20%)	-		
Smoking	19/60 (31.7%)	-		
Extra-articular manifestation				
Negative	41/60 (68.2%)	-		
Dry eye	9/60 (15.0%)	-		
ILD (Interstitial lung diseases)	3/60 (5.0%)	-		
Rheumatoid nodules	2/60 (3.3%)	-		
	1/60 (1.7%)	-		
Felty syndrome				
Rheumatoid nodules	1/60 (1.7%)	-		
Sjogren syndrome	1/60 (1.7%)	-		
Rh. nodules+ Sjorgen syndrome	1/60 (1.7%)	-		
Vasculitis	1/60 (1.7%)	-		
Severity of RA	Remission	Mild	Moderate	Severe
Number	7	8	29	16
***Duration (years)	9.29±11.03	10.13±12.70	6.43±6.52	3.1±3.56
***DAS score	2.29±0.19	2.93±0.16	4.09±0.54	5.57±0.22
***Hb (gm/dl)	12.8±0.69	12.67±1.83	12.04±1.57	11.51±1.31
***Platelets (x103/ mm3)	320.5±110.04	304.29±110.04	369.5±144.72	310.42±147.10
***WBC/ mm3	7.98±2.61	7.87±2.54	8.98±3.68	9.9±4.13
***ESR (mm/hr)	28.86±12.47	33.63±16.95	43.79±25.60	74.31±27.89
Current Medication				
NSAID		27/60 (45%)		
Prednisolone		14/60 (23.3%)		
Methotrexate		45/60 (75%)		
Hydroxychloroquine		6/60 (10%)		
Etanercept		12/60 (20%)		
Leflunomide		2/60 (3.3 %)		

* Fisher's exact test and ** Mann-Whitney test were used for calculation of P value; "ns" means not significant, "ILD" means interstitial lung diseases, "DAS28" means disease activity scoring, "Hb" means hemoglobin, "ESR" means erythrocyte sedimentation rate, and "NSAID" means non-steroidal anti-inflammatory drugs. *** Results presented as means ± standard deviations (SD).

Table 2: Classification of RA Depending On Seropositivity and Duration of Illness

	Early (≤1 1)	Established (>1)	Seronegative	Seropositive
* Number	14 (23.3%)	46 (76.7%)	3 (5.0%)	57 (95.0%)
* Duration (years)	0.79±0.30	8.02±8.035	6±5.20	6.32±7.80
* DAS score	4.13±1.41	4.11±1.07	3.23±0.91	4.16±1.15
* Hb (gm/dl)	11.81±1.59	12.17±1.49	12±0.46	12.09±1.55
* Platelets (x103/ mm3)	287.92±84.07	357.78±134.43	249.33±73.66	347.52±128.40
* WBC/ mm3	6.9±2.81	9.31±3.53	7.47±2.99	9.46±3.57
* ESR (mm/hr)	48.36±28.29	48.98±29.18	33.33±22.55	49.65±28.96

* Results presented as means ± standard deviations (SD)

Table 3: Frequencies of anti-MCV, anti-CarP, RF and anti-CCP in the studied groups

	Anti-MCV		Anti-CarP		RF		Anti-CCP	
	Negative	Positive	Negative	Positive	Negative	Positive	Negative	Positive
RA	34 (56.7%)	26 (43.3%)	42 (70%)	18 (30%)	23 (38.3%)	37 (61.7%)	20 (33.3%)	40 (66.7%)
HC	28 (93.3%)	2 (6.7%)	28 (93%)	2 (6.7 %)	26 (86.7%)	4 (13.3%)	27 (90%)	3 (10%)

Table 4: Anti-MCV, anti-CarP, RF and anti-CCP Levels Among Studied Groups

	Remission	Mild	Moderate	Severe	All	Control	RA vs HC
Anti-MCV(U/ml)	19.48±9.42	30.08±28.87	23.54±14.52	29.09±15.10	25.42±16.69	16.08±7.99	*P = 0.006(s)
Anti-CarP (OD=450nm)	0.14±0.01	0.46±0.61	0.20±0.11	0.19±0.07	0.23± 0.14	0.15± 0.05	* P= 0.002 (s)
RF (U/ml)	31.66±42.80	22.5±18.10	106.31±105.79	96.25±96.28	83.74±94.95	14.33±6.08	
Anti-CCP (U/ml)	148.57±185.38	156.38±216.68	156.03±197.47	183.31±168.05	162.48±186.86	13.47±7.60	
	Early RA	Late RA					
Anti-MCV(U/ml)	18.84±10.55	27.42±17.76	P= 0.092 (ns)				
Anti-CarP (OD=450nm)	0.16±0.05	0.25±0.28	P = 0.2389 (ns)				
RF (U/ml)	40.54±41.59	96.89±102.78	P = 0.0510 (ns)				
Anti-CCP (U/ml)	262.07±214.09	132.17±168.86	P = 0.0214 (s)				
	Seronegative	Seropositive					
Anti-MCV(U/ml)	32.63±14.59	25.04±16.82	P = 0.447 (ns)				
Anti-CarP (OD=450nm)	0.38±0.30	0.22±0.24	P = 0.269 (ns)				
RF (U/ml)	≤20	87.62±95.88	P = 0.2305 (ns)				
Anti-CCP (U/ml)	≤20	170.24±188.57	P = 0.1763 (ns)				

Table 5: Diagnostic Utility of anti-MCV and anti-CarP abs. to Diagnose RA at the best cut-off Values

	Cut-Off	AUC	Sensitivity	Specificity	Youden index (%)	P value
RA vs HC						
Anti-MCV (U/ml)	20.29	0.678	43.3%	96.7%	0.40 (40.0%)	*0.0020
Anti-CarP (OD=450nm)	0.235	0.641	28.33%	93.33%	0.30 (30.0%)	*0.0236
Anti-CCP (U/ml)	19	0.891	66.7%	96.7%	0.63 (63%)	*P<0.001
RF (U/ml)	19	0.789	61.7%	86.7%	0.48 (48%)	*P<0.001
Early vs Late RA						
Anti-MCV (U/ml)	20.29	0.700	45.7%	71.4%	0.447 (44.7%)	*0.0163
Anti-CarP (OD=450nm)	0.235	0.609	34.78%	92.86%	0.276 (27.6.0%)	0.2049
Anti-CCP (U/ml)	23	0.717	54.3%	85.7%	0.40 (40%)	*P=0.004
RF (U/ml)	20	0.645	65.2.7%	57.1%	0.48 (48%)	*P<0.05
Seronegative vs Seropositive						
Anti-MCV (U/ml)	20.29	0.708	59.6%	66.7%	0.473 (47.3%)	0.108
Anti-CarP (OD=450nm)	0.235	0.711	73.7%	66.7%	0.596 (59.6%)	0.395
Anti-CCP (U/ml)	19	0.868	66.7%	100.0%	0.67 (67%)	*P<0.001
RF (U/ml)	20	0.930	63.2	100/0%	0.63(63%)	*P<0.001

* Significant
Anti-MCV and anti-CarP abs.correlation with DAS 28 score and RF and anti-CCP

Discussion

The current study is concerned with the utility of anti-MCV and anti-CarP antibodies to diagnose RA and the investigation of their relation with other lab or clinical characteristics in those patients. Compared to 6.7% of healthy controls, 43.3 percent of those with RA yielded positive results for anti-MCV antibodies at the threshold level of 20.2 U/ml. The frequency of anti-MCV autoantibody positivity was greater than that detected by Iwaszkiewicz et al. 2015, who showed that 3.1% of participants without RA and 36.6% of RA patients had anti-MCV antibody positivity (23). The percentage of anti-MCV antibody positivity, however, was less than that seen in other studies. For example, Marina et al., 2010 demonstrated that 80% of those with RA had anti-MCV antibody positivity, compared to just 40.5% of non-rheumatoid arthritis patients (24). Similarly, 72.5% of those suffering from RA and 12% of the control group yielded positive results for anti-MCV autoantibodies, as outlined in the study by Al-Shukaili et al.,2012 (25). The discrepancy in antibody frequencies may be due to the variation in autoantibody prevalence across patient populations or the application of disparate methodologies for the detection of antibodies. In contrast to the healthy control group, participants with RA had noticeably higher serum levels of anti-MCV antibody. The finding of the present study supports earlier studies showing those with RA had noticeably greater levels of anti-MCV than healthy controls (26, 27, 28).

It is noteworthy that the anti-MCV levels didn't correlate with the disease activity index (DAS28 scores) or two other recognized RA indicators, namely anti-CCP and RF. This may imply that

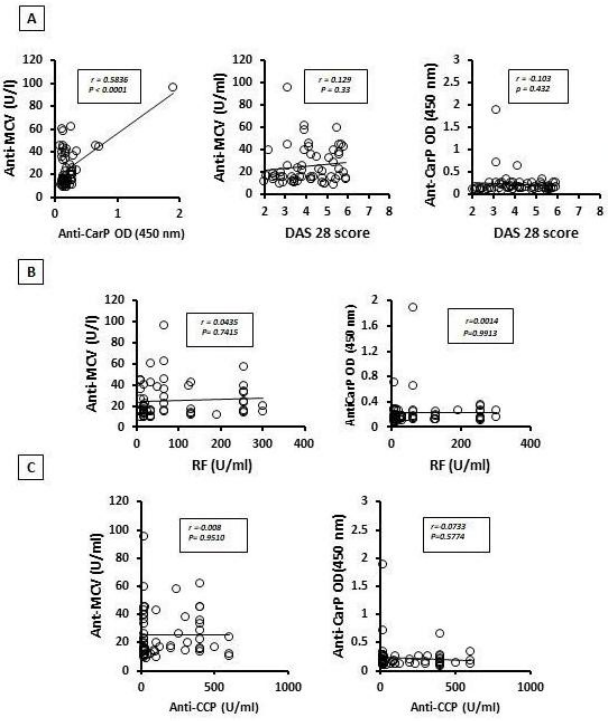

Fig. 1. Correlation of serum anti-MCV (u/ml) and serum anti-CarP (OD 450 nm) antibodies and with DAS 28 score and correlation of anti-CarP OD (450 nm) with DAS 28 score (A); and correlation of anti-MCV (u/ml) or anti-CarP OD (450 nm) with RF (B); and the correlation of anti-MCV (u/ml) or anti-CarP OD (450 nm) and anti-CCP (U/ml) (C).

anti-MCV may be a marker of autoimmunity in RA rather than a direct reflection of ongoing inflammatory processes.

Nearly a third of RA sufferers in the current study showed positive results for the presence of anti-CarP abs. This is consistent with what earlier studies have shown (29-31) and lower than that detected by other studies (32, 33, 34). Akin to anti-MCV findings, RA patients have far higher anti-CarP levels than controls. This finding is consistent with earlier studies (6, 30, 35) that found a link between anti-CarP autoantibodies and rheumatoid arthritis. Unfortunately, using a qualitative ELISA kit limited our ability to assess anti-CarP's diagnostic significance. Anti-CarP exhibited the same lack of correlation with recognized markers of RA or disease activity as anti-MCV. According to the study conducted by Othman et al. 2017, anti-CarP autoantibodies have a correlation with RF but not anti-CCP autoantibodies (35). Moreover, anti-CarP autoantibodies had no meaningful correlation with DAS28. Yee and colleagues, 2015 did not discover any correlation between the DAS28 score and anti-CarP antibody levels (29).

Anti-CCP autoantibodies have the greatest sensitivity and specificity in the current study (66.7% and 96.7%, respectively), whereas RF antibodies demonstrated 61.7% and 86.7%, respectively. The sensitivity of anti-MCV autoantibodies was just 43.3%, despite having a strong specificity of 96.7% for diagnosing RA. This suggests that anti-MCV alone may overlook a sizable fraction of those patients with RA. In keeping with Kondo et al, 2005, anti-MCV antibodies exhibited a 37% sensitivity and a 98% specificity (36). According to Dejaco et al.2006, the anti-MCV ELISA showed a sensitivity of about 69.5% and specificity of 90.8%, while the anti-CCP2 assays were 70.1% and 98.7% (37). The study conducted by Maraina and colleagues revealed that anti-mutated citrullinated vimentin antibodies exhibited sensitivity equal to 80%, while their specificity was nearly 60%; RF antibodies demonstrated an 85% sensitivity and a specificity of about 75%; on the other hand, anti-CCP abs sensitivity exceeded 70% with specificity equal to 94.8% (24). In an Italian multicentric study, Bartoloni et al., 2012 disclosed that anti-MCV antibodies possess 59 percent sensitivity and 92 percent specificity, whereas anti-CCP antibodies showed a 77% sensitivity and 96% specificity (38). In a Chinese study, the detected anti-MCV sensitivity as well as specificity were 78.6% and 73.8%, respectively; anti-CCP had a 67.9% sensitivity and a 97.6% specificity; while RF had a 71.4% sensitivity and a 78.6% specificity (39). While the performance of kits from various manufacturers may have an impact, the heterogeneity in autoantibody prevalence in various patient populations is more likely to be the cause of the discrepancy.

In comparison to anti-MCV, anti-CarP exhibited considerably lower sensitivity (28%) and specificity (93%). According to a study done on Egyptian patients suffering with RA, anti-CarP antibodies showed a 32.2% sensitivity and a 96.7% specificity; for anti-CCP antibodies they were 61.1% and 97.8%, and for RF they were 66.7% and 91.1% (34). Li et al. 2016, reported in their meta-analysis that anti-CarP autoantibodies had pooled sensitivity and specificity of 42% and 96%, respectively (39). In an Iraqi study on patients with RA, anti-CarP autoantibodies showed 46% sensitivity and 97.1% specificity for diagnosing RA; anti-CCP antibodies revealed 66% sensitivity and 65.7% specificity, while RF exhibited 86% sensitivity and 100% specificity (40). Another

study conducted by Pecani et al., 2016 found that anti-CarP antibodies had 46.8% sensitivity and 91.95% specificity in an Italian cohort with RA (6). In comparison, ACPA showed a 61.8% sensitivity and 89.9% specificity, whilst RF exhibited 64.4% sensitivity and 76.5% specificity. Shi and colleagues (2015) demonstrated that the specificity values for anti-CarP autoantibodies, anti-CCP2, and RF were 89%, 96%, and 91%, respectively, and that the sensitivity was 44%, 54%, and 59%, respectively (41). A possible explanation is the difference in sample size and the population studied.

The evident positive correlation between anti-MCV and anti-CarP implies a possible common pathway in their formation. It needs more investigation to clarify this connection, though. However, anti-CarP and anti-MCV autoantibodies did not correlate with RF, anti-CCP, or DAS28 score, in contrast to previous studies (29, 35). This supports the notion that distinct facets of RA pathophysiology may be reflected by various antibodies.

The prime drawback of the current study was its rather small sample number that might limit the overall applicability of the findings. The ability to perform a more thorough evaluation was hindered by the use of a qualitative assay for anti-CarP. Since the number of seronegative patients was inadequate, conclusions regarding this group should be interpreted very cautiously and in a limited manner. In the future, these results need to be confirmed by larger cohort studies. Furthermore, exploring the exact mechanisms via which RA produces anti-MCV and anti-CarP can shed light on how the disease develops. To ascertain whether anti-MCV and anti-CarP can be employed as prognostic indicators for RA or to assess the effectiveness of treatment, further studies are required. Both anti-MCV and anti-CarP autoantibodies appear to have minimal diagnostic usefulness, despite an association with RA. To precisely characterize their significance in RA diagnosis and prognosis, more investigation is required.

References

1. Khafar K., Karim M., Qadr N., Noori S., Mohammed S., Salah S. Analysis of Hematological and Biochemical Parameters in Patients with Rheumatoid Arthritis in Sulaymaniyah. Mosul Journal of Nursing, 2024; 12: 144-152.
2. Al-Hasso IK. Evaluation of HLA-G 14 base-pair insertion/deletion polymorphism and soluble HLA-G level in patients with rheumatoid arthritis in Mosul City: a case-control study. Al-Rafidain J Med Sci 2023; 5: 119-124.
3. Intriago M, Maldonado G, Cárdenas J, Ríos C. Clinical characteristics in patients with rheumatoid arthritis: differences between genders. Sci World J 2019; 2019: 8103812.
4. Al-Tae FM, Al-Harbi AA, Turki KW, Sood M. Interleukin-37 in rheumatoid arthritis: correlation with clinical severity and genetic polymorphisms in Mosul City, Iraq. Egypt J Immunol 2023; 30: 162-173.
5. Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. Lancet 2016; 388: 2023-2038.
6. Pecani A, Alessandri C, Spinelli FR, et al. Prevalence, sensitivity, and specificity of antibodies against carbamylated proteins in a monocentric cohort of patients with rheumatoid arthritis and other autoimmune rheumatic diseases. Arthritis Res Ther 2016; 18: 276.
7. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO 3rd, et al. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum 2010; 62: 2569-2581.
8. Zhu T, Feng L. Comparison of anti-mutated citrullinated vimentin, anti-cyclic citrullinated peptides, anti-glucose-6-phosphate isomerase, and anti-keratin antibodies and rheumatoid factor in the diagnosis of rheumatoid arthritis in Chinese patients. Int J Rheum Dis 2013; 16: 157-161.
9. Trouw LA, Huizinga TW, Toes RE. Autoimmunity in rheumatoid arthritis: different antigens—common principles. Ann Rheum Dis 2013; 72: 132-136.
10. Mueller AL, Payandeh Z, Mohammadkhani N, Mubarak SMH, Zakeri A, Alagheband Bahrami A, et al. Recent advances in understanding the pathogenesis of rheumatoid arthritis: new treatment strategies. Cells 2021; 10: 3017.
11. Fang Q, Ou J, Nandakumar KS. Autoantibodies as diagnostic markers and mediators of joint inflammation in arthritis. Mediators Inflamm 2019; 2019: 6363086.
12. Kumar A, Singh S, Verma SK, et al. From rheumatoid factor to anti-citrullinated protein antibodies and anti-carbamylated protein antibodies for diagnosis and prognosis prediction in patients with rheumatoid arthritis. Int J Mol Sci 2021; 22: 686.

13. Reyes-Castillo Z, Palafox-Sánchez CA, Parra-Rojas I, Martínez-Bonilla GE, del Toro-Arreola S, Ramírez-Dueñas MG, et al. Comparative analysis of autoantibodies targeting peptidylarginine deiminase type 4, mutated citrullinated vimentin, and cyclic citrullinated peptides in rheumatoid arthritis: associations with cytokine profiles, clinical and genetic features. Clin Exp Immunol 2015; 182: 119-131.
14. Firestein GS. Somatic mutations and anti-mutated citrullinated vimentin antibodies in rheumatoid arthritis: comment on the editorial by Levesque et al. Arthritis Rheum 2010; 62: 303-304.
15. Kurowska W, Kuca-Warnawin EH, Radzikowska A, Maśliński W. The role of anti-citrullinated protein antibodies (ACPA) in the pathogenesis of rheumatoid arthritis. Cent Eur J Immunol 2017; 42: 390-398.
16. Mohammed HS, Ahmed GH, Tawfik NM, Sayed SK, Ahmed AS. Anti-mutated citrullinated vimentin antibodies in rheumatoid arthritis: diagnostic utility and association with deformities and disease activity. Egypt J Immunol 2023; 30: 105-115.
17. Degboé Y, Constantin A, Nigon D, Tobon G, Cornillet M, et al. Predictive value of autoantibodies from anti-CCP2, anti-MCV, and anti-human citrullinated fibrinogen tests in early rheumatoid arthritis patients with rapid radiographic progression at 1 year: results from the ESPOIR cohort. RMD Open 2015; 1 :e000180.
18. Montes A, Perez-Pampin E, Calaza M, et al. Association of anti-citrullinated vimentin and anti-citrullinated alpha-enolase antibodies with subsets of rheumatoid arthritis. Arthritis Rheum 2012; 64: 3102-3110.
19. Mansour HE, Metwaly KM, Hassan IA, Elshamy HA, Elbeblawy MM. Antibodies to mutated citrullinated vimentin in rheumatoid arthritis: diagnostic value, association with radiological damage, and axial skeleton affection. Clin Med Insights Arthritis Musculoskelet Disord 2010; 3: 33-42.
20. Prevoo ML, van't Hof MA, Kuper HH, van Leeuwen MA, van de Putte LB, van Riel PL. Modified disease activity scores that include twenty-eight joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. Arthritis Rheum 1995; 38: 44-48.
21. Chatzidionysiou K, Fragoulis GE. Established rheumatoid arthritis: Redefining the concept. Best Pract Res Clin Rheumatol 2019; 33: 101476.
22. Carbonell-Bobadilla N, Soto-Fajardo C, Amezcua-Guerra LM, Batres-Marroquín AB, Vargas T, Hernández-Diazcouder A, et al. Patients with seronegative rheumatoid arthritis have a different phenotype than seropositive patients: A clinical and ultrasound study. Front Med 2022; 9: 978351.
23. Iwaszkiewicz C, Puszczewicz M, Białkowska-Puszczewicz G. Diagnostic value of the anti-Sa antibody compared with the anti-cyclic citrullinated peptide antibody in rheumatoid arthritis. Int J Rheum Dis 2015; 18: 46-51.
24. Maraina CH, Nurdayana AK, Rusni D, Azwany Y. Diagnostic value of anti-modified citrullinated vimentin in rheumatoid arthritis. Int J Rheum Dis 2010; 13: 335-339.
25. Al-Shukaili A, Al-Ghafri S, Al-Marhoobi S, Alkaabi J. Evaluation of anti-mutated citrullinated vimentin antibodies, anti-cyclic citrullinated peptide antibodies, and rheumatoid factor in Omani patients with rheumatoid arthritis. Int J Rheumatol 2012; 2012: 285854.
26. El-Shazly RI, Hussein SA, Rashan HZ, Elgogary AA. Anti-mutated citrullinated vimentin antibodies in rheumatoid arthritis patients: Relation to disease activity and manifestations. Egypt Rheumatol. 2014; 36: 65-70.
27. Keskin G, Inal A, Keskin D, et al. Diagnostic utility of anti-cyclic citrullinated peptide and anti-modified citrullinated vimentin antibodies in rheumatoid arthritis. Protein Pept Lett 2008; 15: 314-317.
28. Ebrahimi-Rad M, Khatami S, Akhbari H, et al. Evaluation of autoantibodies against vimentin and α-enolase in rheumatoid arthritis patients. Reumatologia 2020; 58: 350-356.
29. Yee A, Webb T, Seaman A, Infantino M, Meacci F, Manfredi M, et al. Anti-CarP antibodies are a promising marker to measure joint damage and disease activity in patients with rheumatoid arthritis. Immunol Res 2015; 61: 24-30.
30. Montes A, Regueiro C, Perez-Pampin E, Boveda MD, Gomez-Reino JJ, Gonzalez A. Anti-Carbamylated Protein Antibodies as a Reproducible Independent Type of Rheumatoid Arthritis Autoantibodies. PLoS One 2016; 11: e0161141.
31. Mohamed SR, Neseem NO, Metwally SS, El-Kady BA. Diagnostic value and clinical significance of anti-carbamylated protein (anti-CarP) antibodies in Egyptian patients with rheumatoid arthritis. Egypt Rheumatol 2020; 42: 1-6.
32. Challener GJ, Jones JD, Pelzek AJ, et al. Anti-carbamylated protein antibody levels correlate with anti-Sa (citrullinated vimentin) antibody levels in rheumatoid arthritis. J Rheumatol 2016; 43: 273-281.

33. Verheul MK, van Erp SJH, van der Woude D, et al. Anti-carbamylated protein antibodies: a specific hallmark for rheumatoid arthritis. Comparison to conditions known for enhanced carbamylation: renal failure, smoking, and chronic inflammation. Ann Rheum Dis 2016; 75: 1575-1576.
34. Shi J, Knevel R, Suwannalai P, van der Linden MP, Janssen GM, van Veelen PA, et al. Autoantibodies recognizing carbamylated proteins are present in sera of patients with rheumatoid arthritis and predict joint damage. Proc Natl Acad Sci U S A 2011; 108: 17372-17377.
35. Othman MA, Ghazali WSW, Hamid WZWA, Wong KK, Yahya NK. Anti-carbamylated protein antibodies in rheumatoid arthritis patients and their association with rheumatoid factor. Saudi Med J 2017; 38: 934-941.
36. Kondo H, Sakai M. Immunological tests: anti-vimentin antibodies. Nihon Rinsho 2005; 63: 646-649.
37. Dejaco C, Klotz W, Larcher H, et al. Diagnostic value of antibodies against a modified citrullinated vimentin in rheumatoid arthritis. Arthritis Res Ther 2006; 8: R119.
38. Bartoloni E, Alunno A, Bistoni O, et al. Diagnostic value of anti-mutated citrullinated vimentin in comparison to anti-cyclic citrullinated peptide and anti-viral citrullinated peptide 2 antibodies in rheumatoid arthritis: an Italian multicentric study and review of the literature. Autoimmun Rev 2012; 11: 815-820.
39. Li L, Deng C, Chen S, Zhang S, Wu Z, Hu C, et al. Meta-analysis: Diagnostic accuracy of anti-carbamylated protein antibody for rheumatoid arthritis. PLoS One 2016; 11: e0159000.
40. Ali J, Saleh B, Gorial F. Diagnostic value of serum anti-carbamylated protein antibodies in Iraqi patients with rheumatoid arthritis: a case-control study. GJBB 2018; 7: 15-18.
41. Shi J, van Steenbergen HW, van Nies JAB, et al. The specificity of anti-carbamylated protein antibodies for rheumatoid arthritis in a setting of early arthritis. Arthritis Res Ther 2015; 17: 339.