Original Article

Vitamin D3 Insufficiency and Its Correlation with Disease Severity and Diagnostic Biomarkers in Rheumatoid Arthritis : A Case-Control Study

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Abstract

Background : This study aimed to identify Vitamin D3 insufficiency in patients with Rheumatoid Arthritis (RA) and investigate the correlation between Vitamin D3 and anti-cyclic Citrullinated Peptide (anti-CCP) antibodies and disease severity. The diagnostic value of Anti-CCP, RF, ESR, and hs-CRP was also evaluated.

Methods: Selectra (Pro-XL) was used to estimate the lipid profile using commercially available kits. Anti-CCP and 25-(OH) Vitamin D (Vitamin D3) levels were measured using an immunoassay (ARCHITECT System, Abbott, Japan). The ESR was estimated using the Wintrobe's tube method. RA factor and hs-CRP levels were measured using the immunoturbidity method. Disease activity/severity was estimated using the Clinical Disease Activity Index (CDAI) scoring.

Results : The RA factor, hs-CRP and anti-CCP levels were significantly higher in patients than controls ($p<0.0001$), while Vitamin D3 levels were significantly lower ($p<0.0001$). A significant correlation was found between the RA factor and anti-CCP ($r=0.678$, $p<0.0001$), ESR and anti-CCP ($r=0.469$, $p<0.0001$) and a negative correlation between Vitamin D3 and anti-CCP ($r=-0.224$, $p=0.046$). Vitamin D3 levels were significantly correlated with the RA factor ($r=-0.481$, $p=0.028$). In patients with severe disease, Vitamin D3 level was associated with anti-CCP ($\beta=0.409$, $p=0.018$). The RA factor and anti-CCP demonstrated high specificity and sensitivity, with a PPV of 66% and 68% and NPV of 99.9% each. The AUC was significantly higher for anti-CCP (0.879, $p<0.0001$) and RA factor (0.813, $p<0.0001$) than for hs-CRP and ESR, indicating superior diagnostic performance.

Conclusion : The study concludes that Vitamin D3 levels may determine the severity of RA and also suggests that the endorsed criteria should include the RA factor due to its diagnostic value equivalent to that of anti-CCP.

Key words : Vitamin D3, Anti-CCP Antibodies, Rheumatoid Factor, Rheumatoid Arthritis, CDAI Scoring.

Rheumatoid Arthritis (RA) is a chronic inflammatory disease affecting 1% of the global population, with a threefold higher prevalence in females[1,2]. It manifests with articular and extra-articular features, and its onset can be either gradual or abrupt. Key biomarkers for RA include the erythrocyte sedimentation rate, C-reactive protein level, plasma viscosity, Rheumatoid Factor (RF) and anti-cyclic Citrullinated Peptide (anti-CCP) antibody[3].

Editor's Comment :

- Low Vitamin D3 levels are linked to higher RA severity, highlighting its role in disease progression. Anti-CCP and RA factor offer excellent diagnostic value for RA, with high sensitivity and specificity. These factors also suggest Vitamin D3 may influence immune response and RA severity.

Radiological characteristics of RA include soft tissue swelling, periarticular osteoporosis, juxta-articular erosions and joint space constriction. Patients with RA have an increased risk of osteoporosis, potentially linked to Vitamin D levels. However, the relationship between RA and blood levels of 25(OH)D and 1,25(OH)2D is inconsistent[4].

Vitamin D plays a pivotal role in both innate and adaptive immunity by regulating immune cell subsets. The inflammation observed in RA shares similarities with that seen in unstable atherosclerotic plaques. Both conditions involve the expression of pro-inflammatory cytokines and increased inflammatory

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Received on : 30/11/2023
Accepted on : 29/04/2024

How to cite this article : Vitamin D3 Insufficiency and Its Correlation with Disease Severity and Diagnostic Biomarkers in Rheumatoid Arthritis : A Case-Control Study. Sharma M, Anand VK, Kumar A, Ram VS, Sharma P, Jawad K. *J Indian Med Assoc* 2025; **123(4):** 55-61.

markers like CRP and fibrinogen. These molecules may promote proatherogenic activation and endothelial dysfunction[5-7]. In active or untreated Rheumatoid Arthritis (RA), the lipid profile typically exhibits certain characteristic changes. These include decreased serum levels of High-density Lipoprotein Cholesterol (HDL-C). Concurrently, there is an increase in the ratio of Total Cholesterol (TC) to HDL-C (TC/HDL-C ratio). These lipid profile alterations indicate an elevated risk of atherosclerosis, a condition characterized by the hardening and narrowing of arteries due to plaque buildup. This underscores the importance of regularly monitoring and managing lipid levels in individuals with RA to mitigate potential cardiovascular risks[8-10]. This study aims to estimate serum Vitamin D3 and lipid profiles in RA patients to correlate these parameters with disease severity for improved diagnosis and prognosis assessment.

Material and Methods

Study Population :

This case-control study, conducted from November, 2019 to October, 2021, was a collaborative effort between the Department of Biochemistry and the Department of General Medicine at Uttar Pradesh University of Medical Sciences, Saifai, Etawah. The study encompassed 220 subjects, comprising 120 RA patients and 100 controls who were matched for age and sex, all from the same ethnic group.

The diagnosis of RA was established based on the Revised American College of Rheumatology's 2010 clinical criteria. Patients were accommodated in the rheumatology clinic's Inpatient Wards and Outpatient Departments within the Department of Medicine. A comprehensive oral questionnaire was administered to each participant after obtaining their consent. This questionnaire included a detailed history and a clinical examination based on the Clinical Disease Activity Index (CDAI). This rigorous approach ensured a thorough evaluation of each participant's condition.

Subject Selection Criteria :

The study included patients who met the 2010 Revised American College of Rheumatology/ European League Against Rheumatism (ACR/ EULAR) criteria for Rheumatoid Arthritis[11]. However, individuals taking Vitamin D supplements or the hypolipidemic drug Highly Active Anti-retroviral Therapy (HAART) were excluded. Additionally, subjects with chronic conditions such as Diabetes, Hypertension, Familial Hypercholesterolemia, Chronic Kidney Disease and Tuberculosis were not considered for the study. The Institutional Human Ethics Committee of Uttar Pradesh University of Medical Sciences, Saifai, Etawah (IEC-82/2019-20) duly approved the study protocol.

Clinical Assessment :

This study assessed disease activity and severity using the Clinical Disease Activity Index (CDAI) scoring. CDAI = SJC (28) + TJC (28) + PGA + EGA[12].

SJC (28) — Swollen 28-Joint Count (shoulders, elbows, wrists, MCPs (metacarpophalangeal joints (MCPs), PIPs (proximal interphalangeal joints and knees).

TJC (28) — Tender 28-Joint Count (shoulders, elbows, wrists, MCPs, PIPs, knees)

PGA — Patient Global Disease Activity (patient's self-assessment of overall RA disease activity on a scale of 1-10 where 10 is the maximal activity)

EGA — Evaluator's Global Disease Activity (evaluator's assessment of overall RA disease activity on a scale of 1-10 where 10 is maximal activity)

Interpretation —

Mild Disease Activity CDAI > 2.8 and $\leq$10

Moderate Disease Activity CDAI > 10 and $\leq$22

Severe Disease Activity CDAI > 22

Sample Collection :

Blood samples were collected by venipuncture into labelled plain and EDTA vials. Plain vials were centrifuged at 5000 rpm for 10 min and the serum was stored at -20^{o}C. An EDTA sample was used to estimate the Erythrocyte Sedimentation Rate (ESR).

Estimation of Biochemical and Rheumatoid-associated Markers :

Lipid profiles were estimated using a fully automated analyzer, Selectra (Pro-XL), with commercially available kits. Anti-CCP and 25-(OH) Vitamin D (Vitamin D3) levels were measured using an immuno-chemiluminescence kit (ARCHITECT System, Abbott, Japan). The immunoturbidity method measured RA factor and hs-CRP, while ESR was estimated using Wintrobe's tube method.

Data Analysis :

Data were analyzed using SPSS version 21 (Chicago, Inc. USA). Data are presented as mean ± SD. The Student's t-test was used to compare the groups for parametric data, whereas the chi-square test was used to compare the groups for non-parametric data. Receiver Operating Characteristic (ROC) curve analysis was used to determine the sensitivity and specificity of the markers. Pearson's correlation coefficient was calculated to determine the correlation between blood markers. Univariate and multivariate linear regression analyses were used to determine independent markers of Rheumatoid Arthritis (RA). Statistical significance was set at p<0.05.

Results

Clinical and Biochemicals findings of Study Population :

Table 1 shows the demographic characteristics of the study groups, including age, sex, and disease severity. The study groups' male-to-female ratio (M:F) was 1:2, indicating that the disease was more prominent in females. No significant differences were found in age (p=0.797) or sex (p=0.225), indicating an adequate matching between the case and control groups. The severity of rheumatoid arthritis was mild in 16 (13.3%), moderate in 69 (57.5%) and severe in 35 (29.2%) enlisted patients.

Elevation of Rheumatoid-associated Markers with Declining Vitamin D patients :

Lipid profiles (TC, TG, LDL-C and VLDL-C) were significantly higher in patients than in controls (p<0.0001) (Table 2). The rheumatoid-associated markers, RA factor, hs-CRP, and anti-CCP, were 9.54-fold (mean±SD; 44.46±14.97 *versus* 4.66±1.02 mg/L), 2.10-fold (3.48±3.41 *versus* 1.66±1.48 U/mL) and 8.69-fold (95.98±46.27 *versus* 11.04±3.98 U/mL), respectively, which were significantly higher than the control (p<0.0001). The ESR was also significantly (p<0.0001) higher in the patients (37.67±17.40 mm/1Hr) group as compared control (13.93±4.69 mm/1Hr). In contrast, Vitamin D was significantly decreased in rheumatoid patients (18.14±4.43 ng/mL *versus* 22.28±14.72 ng/mL) than in control (p<0.0001) (Table 2a).

Rheumatoid-associated Markers Differentiate the Disease Severity :

The lipid profile was not significantly associated with disease severity. RA factor (RF) only showed a significant difference from mild (50.38±10.13 U/mL) to moderate (43.06±16.51 U/mL,p=0.003) and severe groups (44.51±13.18 U/mL, p=0.024), while moderate and severe groups did not show a significant difference in RF levels (p=0.20). Anti-CCP mean levels were significantly 1.49-fold (78.35±30.80 *versus* 62.51±8.73 U/mL, p=0.59) in the moderate group and 2.58-fold (146.03±42.74 *versus* 62.51±8.73 U/mL, p<0.0001) higher in the severe group as compared to the mild group (62.51±8.73 U/mL). Similarly, Vitamin D only showed a significant difference from the mild (17.38 ±3.25) to moderate (18.34±3.67) and severe groups (18.06±6.05, p=0.02). In contrast, the moderate and severe groups did not significantly differ in 25-(OH) Vitamin D levels (p=0.49) (Table 2b).

Table 1 — *Demographical Characteristics of the Study Groups*

Variables		Case (n=120)	Control (n=100)	p-value
Age (Years)	Young (18-35)	17(14.2%)	15(15.0%)	0.797
	Middle (36-55)	63(52.5%)	48(48.0%)	
	Older (>55)	40(33.3%)	37(37.0%)	
	Mean±SD	49.97±11.44	50.7±12.58	0.250
Sex	Male	42(35.0%)	43(43.0%)	0.225
	Female	78(65.0%)	57(57.0%)	
Severity(CDAI)	Mild	16(13.3%)	-	
	Moderate	69(57.5%)	-	
	Severe	35(29.2%)	-	

The Chi-Square test and student t-test were used to compare the study group. p-value <0.05 was considered as statistically significant.

Table 2a — *Status of Biomarkers in Rheumatoid Arthritis*

Variables	Case (n=120) (Mean±SD)	Control (n=100) (Mean±SD)	p-value
Vitamin D3 (ng/mL)	18.14 ± 4.43	22.28 ± 14.72	<0.0001*
TC (mg/dL)	165.76 ± 19.42	156.7 ± 40.05	<0.0001*
TG (mg/dL)	151.09 ± 25.83	135.59 ± 65.01	<0.0001*
HDL-C (mg/dL)	46.91 ± 10.89	42.38 ± 10.13	0.621
LDL-C (mg/dL)	89.84 ± 19.98	96.29 ± 34.57	<0.0001*
VLDL-C (mg/dL)	30.21 ± 5.25	27.11 ± 13.0	<0.0001*
RA Factor (U/mL)	44.46 ± 14.97	4.66 ± 1.02	<0.0001*
hs-CRP (mg/L)	3.48 ± 3.41	1.66 ± 1.48	<0.0001*
Anti-CCP(U/mL)	95.98 ± 46.27	11.04 ± 3.98	<0.0001*
ESR (mm/1Hr)	37.67 ± 17.40	13.93 ± 4.69	<0.0001*

Abbreviations : TC-Total Cholesterol, TG- Triglyceride, HDL-C-High-Density Lipoprotein-Cholesterol, LDL-C- Low-Density Lipoprotein-Cholesterol, VLDL- Very-low-density Lipoprotein, RA Factor- Rheumatoid Factor, hs-CRP- High-sensitivity C-reactive protein, Anti-CCP- Anti-cyclic citrullinated peptide, ESR- Erythrocyte Sedimentation Rate. Student T-test was used to compare the group. *p-value <0.05 was considered as statistically significant.

Table 2b — *Stratification of Biomarkers according to the disease severity*

Variables	Case (n=120)			p-value		
	(A) Mildn=16	(B) Moderaten=69	(C) Severen=35	A *versus* B	B *versus* C	A *versus* C
	Mean ± SD					
Vitamin D3(ng/mL)	17.38 ± 3.25	18.34 ± 3.67	18.06 ± 6.05	0.497	0.002*	0.028*
TC (mg/dL)	172.31 ± 22.61	162.49 ± 16.86	169.22 ± 21.72	0.415	0.297	0.996
TG (mg/dL)	158.31 ± 26.72	148.46 ± 25.56	152.9714 ± 25.91	0.716	0.823	0.85
HDL-C (mg/dL)	46.56 ± 7.64	48.82 ± 11.69	43.31 ± 9.77	0.128	0.124	0.749
LDL-C (mg/dL)	94.11 ± 21.65	85.39 ± 18.82	96.64 ± 19.65	0.927	0.829	0.839
VLDL (mg/dL)	31.65 ± 5.37	29.66 ± 5.23	30.64 ± 5.20	0.79	0.944	0.835
RA Factor (U/mL)	50.38 ± 10.13	43.06 ± 16.51	44.51 ± 13.18	0.003*	0.024*	0.209
hs-CRP (mg/L)	3.08 ± 2.83	3.44 ± 3.77	3.74 ± 2.92	0.508	0.405	0.939
Anti-CCP(U/mL)	62.51 ± 8.73	78.35 ± 30.80	146.03 ± 42.74	0.059	<0.0001*	<0.0001*
ESR (mm/1Hr)	41.56 ± 19.81	38.27 ± 17.01	34.71 ± 17.05	0.992	0.323	0.584

Abbreviations: *TC-Total Cholesterol, TG- Triglyceride, HDL-C- High-Density Lipoprotein-Cholesterol, LDL-C- Low-Density Lipoprotein-Cholesterol, VLDL- Very-low-density Lipoprotein, RA Factor- Rheumatoid Factor, hs-CRP- High-sensitivity C-reactive protein, Anti-CCP- Anti-cyclic citrullinated peptide, ESR- Erythrocyte Sedimentation Rate. Student T-test was used to compare the group.*

*p-value <0.05 is considered as statistically significant.

Association among the Total Cholesterol and Rheumatoid-associated Markers in Patients :

In the univariate regression analysis, Vitamin D levels were positively associated with anti-CCP (b=0.475, p=0.004) in patients with severe Rheumatoid Arthritis. RA was also positively associated with anti-CCP in patients with severe (b=0.295, p= 0.047) and mild (b=0.373, p=0.033) rheumatoid arthritis. In contrast, hs-CRP was negatively associated with anti-CCP (b=-0.229, p=0.049) in the severe group. In the multi-regression analysis, the 25-(OH) Vitamin D level was positively associated with anti-CCP (b=0.409, p=0.018) in the severe group (Table 3).

Diagnostic Utility of Rheumatoid-associated Markers :

Elevated RF and anti-CCP titers had a specificity and sensitivity of 93% and 47%, respectively, with a positive predictive value of 66% and a negative predictive value of 99.9%. Similarly, for Anti CCP, specificity and sensitivity were 95% and 34%, respectively, with a positive predictive value of 68% and a negative predictive value of 99.9%. To further compare the diagnostic utility of each test, we constructed an ROC curve and calculated the AUC. The ROC curves of RF and Anti CCP were closer to the upper left corner than those of the other markers (hs-CRP and ESR), indicating that it can serve as a specific diagnostic marker (Fig 1). The AUC was significantly higher for anti-CCP (0.879, p<0.0001) and RF (0.813, p<0.0001) than for hs-CRP and ESR indicated a higher diagnostic performance (Table 4).

Discussion

This study was based on clinical and biochemical features with special reference to Vitamin D and lipid profiles of 120 Rheumatoid Arthritis patients and 100 controls. RA is characterized by chronic inflammation of the synovium, leading to progressive joint destruction. Periarticular bone erosion is the most specific hallmark of the disease, causing deformation, laxity, and functional disability. Inflammation plays a key role in the chronicity and progression of Rheumatoid Arthritis despite its unknown source.

Our study showed that the prevalence of RA in females was two-fold higher than in males. A previous study demonstrated that RA is twice as frequent in women than men. There is strong evidence that RA is an autoimmune disease that is under genetic control, and genes in the sex chromosome can play a role in supporting female prevalence[13]. On the other hand, it is widely accepted that sex hormones, particularly estrogens, may regulate the immune response by favoring the survival of forbidden autoreactive clones and, ultimately, the prevalence of autoimmunity in women[14].

The present study found low serum 25(OH) Vitamin D levels in the RA group and more prominent levels in the severity groups. Previous studies have reported that serum 25(OH) Vitamin D deficiency and inadequacy were observed in 34-84% of RA patients and 12-52% of RA patients[15]. However, some studies, inconsistent with our data, suggest that the number of patients with 25(OH) Vitamin D deficiency and inadequacy may vary depending on race, area, diet, sample size, age, sex, BMI and other community characteristics[16,17].

Table 3 — *Univariate and Multivariate Linear Regression model as Anti-CCP dependent variables*

Severity Groups	Univariate		Multivariate	
	Beta co-efficient	p-value	Beta co-efficient	p-value
Vitamin D3 (ng/mL)				
Mild	-0.012	0.965	-	-
Moderate	-0.148	0.224	-	-
Severe	0.475	0.004*	0.409	0.018*
TC (mg/dL)				
Mild	-0.607	0.013*	0.945	0.049*
Moderate	0.032	0.792	-	-
Severe	0.035	0.841	-	-
TG (mg/dL)				
Mild	-0.297	0.263	-	-
Moderate	-0.217	0.053	-	-
Severe	0.120	0.491	-	-
HDL-C (mg/Dl)				
Mild	-0.361	0.049*	-0.916	0.008*
Moderate	0.051	0.678	-	-
Severe	-0.284	0.048*	0.099	0.699
LDL-C (mg/dL)				
Mild	-0.431	0.033*	-0.685	0.006*
Moderate	0.030	0.808	-	-
Severe	-0.226	0.043*	0.774	0.047*
VLDL (mg/dL)				
Mild	-0.302	0.255	-	-
Moderate	-0.332	0.005*	-1.453	<0.0001*
Severe	0.115	0.510	-	-
RA Factor (U/mL)				
Mild	0.373	0.033*	0.184	0.649
Moderate	-0.273	0.051	-	-
Severe	0.295	0.047*	0.201	0.241
hs-CRP (mg/L)				
Mild	-0.226	0.053	-	-
Moderate	-0.217	0.061	-	-
Severe	-0.229	0.049*	0.109	0.511
ESR (mm/1Hr)				
Mild	0.065	0.812	-	-
Moderate	-0.123	0.312	-	-
Severe	0.062	0.724	-	-

Abbreviations : r-Pearson correlation, TC-Total Cholesterol, TG-Triglyceride, HDL-C- High-Density Lipoprotein-Cholesterol, LDL-C-Low-Density Lipoprotein-Cholesterol, VLDL- Very-low-density Lipoprotein, RA Factor- Rheumatoid Factor, hs-CRP- High-sensitivity C-reactive protein, Anti-CCP- Anti-cyclic citrullinated peptide, ESR-Erythrocyte Sedimentation Rate. Linear Regression was used to calculate Univariate and Multivariate.

*p-value <0.05 is considered as statistically significant.

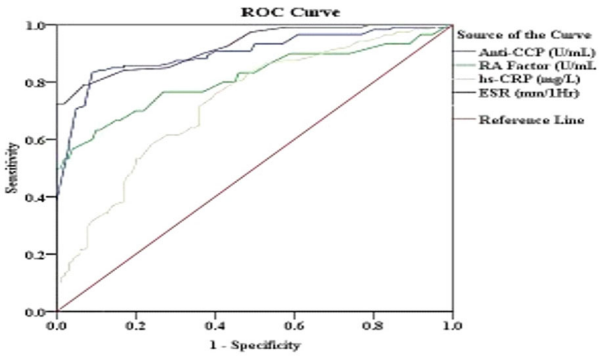

Fig 1 — ROC curve of anti-CCP, RA factors hs-CRP and ESR

Lower serum 25 (OH) Vitamin D levels may be a risk factor for the pathogenesis of Rheumatoid Arthritis, which typically affects the peripheral joints in a symmetrical pattern. Lipids play a role in RA synovitis via the arachidonic acid pathway in the joint space[18]. Various inflammatory disorders, including RA, are linked to changes in lipid levels, such as atherosclerosis and Cardiovascular Disease (CVD), which are more common in patients with RA than in the general population. Chronic inflammation has emerged as a critical component of RA development[19]. The mean C-reactive Protein (CRP) level 3 measures the chronic inflammatory burden[3].

Chronic inflammation in patients with active RA causes oxidative alterations that alter the HDL structure and lower apolipoprotein-A-1 levels[20]. As a result of inflammation, the usual anti-inflammatory, antioxidative and cardioprotective functions of triglyceride, VLDL and LDL levels are impaired, and they become pro-inflammatory. Furthermore, patients with RA have Total Cholesterol, HDL cholesterol, and LDL cholesterol levels due to a pro-inflammatory state[21]. This finding parallels the statement above[22-25]. Our results demonstrated that serum anti-CCP, RA factors and ESR were significantly elevated (three to ten-fold) in patients with RA compared to those in controls.

RF is widely used as a diagnostic indicator for RA.

Table 4 — *Analysis of Sensitivity and specificity*

Tests	Cut-off value	Area (LB-UB)	p-value	Sensitivity (%)	Specificity (%)	PPV	NNV
Anti-CCP (U/mL)	22.00	0.879 (0.833-0.926)	<0.0001*	34	95	0.68	99.93
RA Factor (U/mL)	15.00	0.813 (0.756-0.870)	<0.0001*	47	93	0.66	99.94
hs-CRP (mg/L)	0.83	0.730 (0.663-0.796)	<0.0001*	13	46	0.02	99.81
ESR (mm/1Hr)	24.50	0.924 (0.891-0.957)	<0.0001*	72	96	2	99

Abbreviations : Anti-CCP- Anti-cyclic citrullinated peptide, RA Factor- Rheumatoid Factor, hs-CRP- High-sensitivity C-reactive protein, ESR- Erythrocyte Sedimentation Rate. The Cut-off was calculated by ROC curve analysis.
*p-value <0.05 is considered as statistically significant.

However, RA factor can manifest in various autoimmune and infectious diseases and its specificity is restricted to a few percent of healthy individuals. Therefore, the pursuance of identifying indices with significant diagnostic potential or the simultaneous identification of pre-existing indices is crucial. Anti-CCP is a highly specific marker for the early detection of RA and has significant clinical diagnostic utility. It was included in the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) diagnostic criteria[12,26-28].

Anti-CCP levels were statistically elevated in individuals with RA compared to individuals without RA and healthy individuals. This study's findings suggest that anti-CCP antibodies may play a role in the clinical classification of Rheumatoid Arthritis (RA).

The study conducted a comparative analysis of the AUCs of anti-CCP and 25-(OH) Vitamin D. The results indicated that the AUC of anti-CCP demonstrated the highest magnitude, indicating its superior diagnostic efficacy. The study's results suggest that the anti-CCP test exhibited a considerable degree of sensitivity (34%) and specificity (95.0%). The findings presented herein align with earlier investigations carried out by Cui, *et al*[29] and Lin, *et al*[30]. The results of the diagnostic performance assessment indicate that the anti-CCP had the highest Positive Predictive Value (PPV) compared to other indicators. The statement above suggests that anti-CCP has the potential to function as a principal serological indicator in the differentiation of RA from alternative medical conditions. Upon isolation, the anti-CCP demonstrated the highest Youden index, measuring 0.879. Among the variables that were examined, authenticity emerged as the most robust predictor, demonstrating superior discriminatory power in distinguishing between individuals diagnosed with Rheumatoid Arthritis and those who were classified as healthy. According to Lee, *et al*[33] study, the diagnostic effectiveness of anti-CCP was superior to that of RA factors[31]. The study findings indicate that the RA factors exhibited a sensitivity of 47% and a specificity of 93%. This study underscores the significant role of certain parameters, including 25-(OH) Vitamin D, anti-CCP, hs-CRP and ESR, in the progression of RA. When assessed in serum, these parameters could potentially serve as reliable markers for RA. However, the identified correlation between 25-(OH) Vitamin D and RA factors warrants further validation due to the limited sample size of our study. Moreover, the influence of various factors such as geographic location, familial ancestry and gender on an individual's Vitamin D3 levels necessitates future research with cross-regional and larger sample sizes for a comprehensive understanding of the correlation between 25(OH) Vitamin D and RA.

Conclusion

Our findings also highlight the superior diagnostic performance of Anti-CCP and RF in RA. Furthermore, 25-(OH) Vitamin D levels may be indicative of RA severity. These insights pave the way for personalized prevention and treatment strategies for RA, underscoring the need for continued research in this area.

Acknowledgement

We thank all the participants for their co-operation.

Funding : None

Conflict of Interest : None

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