Original Article

Recognize the Relationship Between Autoimmune Disease as Rheumatism with Multi Vitamin Deficiency

Mohammed Mousa Atta and Ashraf Fadhil Jomah

ABSTRACT

Objective: To identify associated risk factors in RA. The highest reported prevalence for RA was in the 42-52 years age group, with lower prevalence in over 80-year-old, for whom diagnosis may be more difficult.

Study Design: Cross-sectional case-control study

Place and Duration of Study: This study was conducted at the Thi-Qar Governorate in south of Iraq from 1st February 2025 to 30th June 2025.

Methods: The link between vitamin D deficiency and rheumatoid arthritis and its possible consequences on disease activity and coexisting diseases were assessed. Fifty patients who had been clinically diagnosed with rheumatoid arthritis according to the 2010 ACR/EULAR classification criteria were enrolled from rheumatology clinics and hospitals in the area. A group of healthy subjects, age- and sex-matched and without any autoimmune and chronic inflammatory diseases was also studied for comparisons.

Results: Males had a higher prevalence of Anaplasia compared to females, which might be associated with genetic and immune-related differences between males and females. Diabetic patients were more frequently infected (42%) than hypertensive patients (36%), indicating different effects of comorbidities on the progression of infection. In terms of hematological findings, mild anemia due to chronic inflammation was suspected in all cases, with significant vitamin D3 deficiency identified in more than 80% of cases

Conclusion: Vitamin D has an immunity-regulating role and could be useful in rheumatoid arthritis treatment. A global integrated strategy taking into account comorbid conditions, nutritional deficiencies and demographics in relation to vitamin D supplementation could potentially result better outcomes. In the future, more studies are required to improve the diagnosis and treatment of rheumatoid arthritis.

Keywords: Rheumatoid arthritis, Vitamin D3, Chronic inflammation, Personalized medicine, Hematological markers

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INTRODUCTION

Autoimmune conditions such as RA occur when your body's immune system which is supposed to protect against viruses, bacteria, and other pathogens attacks healthy cells within the body.[1] Rheumatoid arthritis (RA) is a systemic inflammatory disorder with a chronic course that is characterized by synovial inflammation, joint destruction and systemic manifestations including fatigue and cardiovascular disease.[2] It is multifactorial in etiology and includes genetic propensity, environmental factors, level of hormones, and most recently nutritionally condition.[3]

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Vitamin D deficiency is vulnerability for autoimmune disease and is a risk factor for nutritional diseases. Vitamin D, first known for its effects on calcium and bone metabolism, has a strong impact on the immune system.[4] It is involved in both innate immunity, activation of macrophages and dendritic cells, and adaptive immunity through modulation of T cell differentiation and cytokine production.[5] In particular, vitamin D suppresses pro-inflammatory thymic stromal lymphopoietin (Th1 and Th17) cytokines and induces Tregs that promote immune tolerance and prevent autoimmunity.[6]

Surveys of people in various regions of the world have demonstrated that the common the prevalence of deficiency of 25 hydroxy vitamin D (25(OH)D) deficiency in the Middle East is amongst the most common, characterized by low sun exposure (attributed in part to traditional clothing and skin pigmentation and dietary insufficiency.[7] ThiQar is a southern Iraqi governorate, which has the same risk factors of RRMs, but few studies have been carried out on the risk factors linked with VDD and the prevalence of ADs indicate RA particularly.[8] There is a regional gradient that stresses the importance of regional investigation, since

such interaction between IABS and vitamin D status depending on local socio-cultural circumstances is important regarding efficient public health interventions and clinical guidelines.[9]

The immunologic basis to study vitamin D in RA is supported by mechanistic and clinical phenotypic evidence.[10] Mechanistically, stimulation of vitamin D receptor (VDR) in immune cells influences gene expression networks essential in the control of inflammation.[11] Low vitamin D status has been associated with worse disease activity in RA in clinical studies as well as in meta-analyses, and with more pain and lower functional capacity.[12] In addition, some studies, for example of vitamin D supplementation, have found for a possible role of this agent in either symptom relief in RA or in halting its progression findings are controversial.[12,13]

Clasen et al[14] reviewed in meta-analysis of the effect of vitamin D on the risk of rheumatoid arthritis. These workers observed that low circulating levels of 25(OH)D were associated with a slightly increased risk of the incidence of RA, offering a preventive hint to maintain an adequate 25(OH)D status.

Dupuis et al[15] investigated, whether sex has any impact on vitamin D role in autoimmune diseases, including RA. They noted that sex-related effects in vitamin D metabolism and immunity might alter disease risk or presentation and it is critical to account for gender-specific physiological differences in both research and clinical practice when optimizing vitamin D levels with autoimmune disease.

Although an increasing amount of evidence was being collected in this way[16,17], few regional data are available, particularly from Iraqi populations. Yet there has been no large study of vitamin D status among RA patients in ThiQar who were analyzed with respect to demographic factors, seasonal exposure to sunlight, dietary habits, or cultural habits of dress, all of which could skew vitamin D synthesis effects.

The main aim of the present study is to investigate the role of vitamin D deficiency in rheumatoid arthritis and other autoimmune diseases in Thi-Qar province. The goal of this project is to provide insights into the role of vitamin D in the development of autoimmune disease by examining vitamin D levels in healthy and RA individuals and their relevance to the severity and outcome of disease.

METHODS

This cross-sectional case-control study, conducted in Thi-Qar Governorate in south of Iraq from 1st February 2025 to 30th June 2025 vide letter No.202 dated 8-1-2025. The link between vitamin D deficiency and rheumatoid arthritis (RA) and its possible consequences on disease activity and coexisting diseases were assessed. Fifty patients who had been clinically diagnosed with RA according to the 2010 ACR/EULAR classification criteria were enrolled from rheumatology clinics and hospitals in the area. A group of healthy subjects, age- and sex-matched and without any autoimmune and chronic inflammatory diseases was also studied for comparisons. All participants had their venous blood samples taken aseptically. Two portions of the blood samples were separated. White blood cell count (WBC), red blood cell count (RBC), hemoglobin concentration, platelet count, and packed cell volume (PCV) were among the hematologic parameters evaluated by Complete Blood Count (CBC) analysis. Serum from the second part was obtained by centrifugation and kept at -20°C until the levels of 25-hydroxyvitamin D [25(OH)D] and autoimmune markers were analyzed.

Following the manufacturer's instructions, serum 25(OH)-vitamin D levels were measured using a D Xpress ELISA kit, and a Biotek ELX-800 microplate reader was used to measure absorbance. The assay used a monoclonal antibody specific to 25(OH)-vitamin D3 in a competitive ELISA format. The status of vitamin D was categorized as optimal: 30–70 ng/mL; insufficient: 20–30 ng/mL; deficient: <20 ng/mL

Autoimmune Marker Analysis: Commercially available immunoassay kits were used to measure Rheumatoid Factor (RF) and Anti-Citrullinated Protein Antibodies (ACPA) in order to confirm the diagnosis and evaluate autoimmune activity. The RA group consisted of only those patients who tested positive for RF and/or ACPA.

Assessment of Disease Activity: **T**he Disease Activity Score 28 (DAS28), which incorporates the sedimentation rate of erythrocytes (ESR), painful and swollen joint counts, and the patient's overall health evaluation was used to assess the progression of rheumatoid arthritis (RA).In order to gather a thorough medical history from the participants, comorbidities such as diabetes mellitus and hypertension which were verified by patient records and ongoing medical treatment were the focus of the interviews.

The data was entered and analyzed through SPSS-26. Vitamin D levels were compared across age and disease activity groups using one-way ANOVA and independent t-tests. Serum vitamin D levels and RA disease activity were compared using Pearson correlation coefficients. A p-value <0.05 was deemed statistically significant.

RESULTS

The findings indicate a higher prevalence of rheumatoid arthritis in males compared to females, with males constituting 62% of the cases (Table 1). The 41–50-year age group accounted for 30% of our series, which is the greatest prevalence among our 50 cases. This was followed by the 51–60 years age group (22% of cases). In comparison, the lowest number (4%) were found amongst those aged under thirty, while those aged 80 years or more made up 2% of the total (Fig. 1).

42% of participants were diagnosed with diabetes, 36% with hypertension, and 22% reported no chronic illnesses. Figure 2 provides an overview of the prevalence of these illnesses within the sample, emphasizing the substantial proportion of persons afflicted by diabetes and hypertension.

Table No. 1: Distribution of rheumatoid arthritis infection according to sexual category (n=50)

Gender	No.	%
Male	31	62
Female	19	38

X^2= 3.84 DF= 1 P<0.016 (Significant)

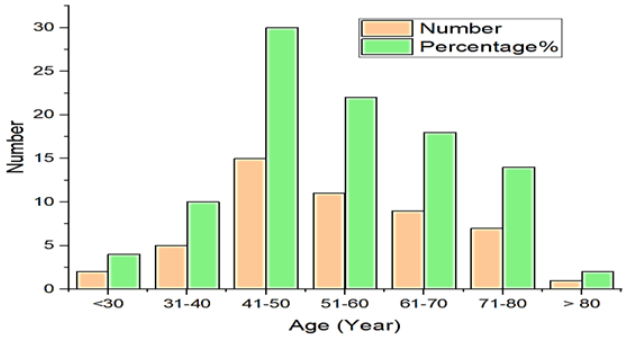

Figure No. 1: Age-wise distribution of rheumatoid arthritis cases

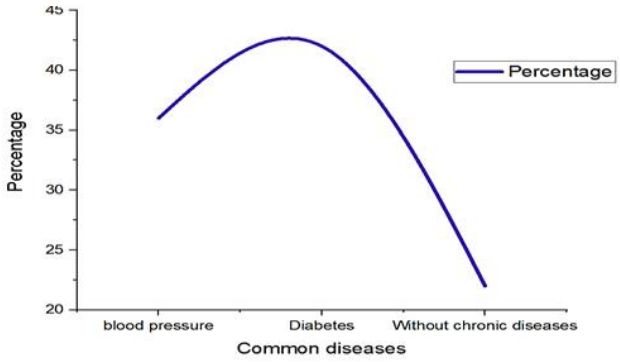

Figure No. 2: The association between rheumatoid arthritis and other common diseases.

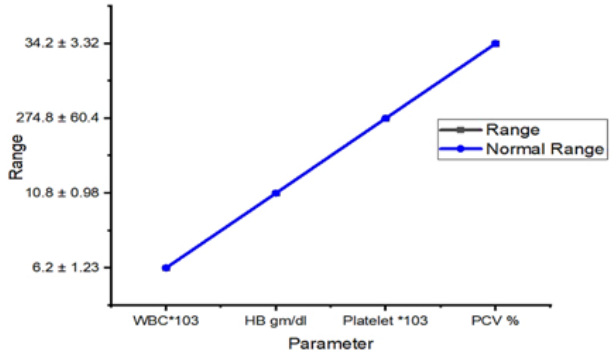

Figure No. 3: Hematological profile of study participants

The Chi-square score of 6.32 exceeds the crucial criterion of 5.99 in the statistical analysis (Fig. 2).

The majority of subjects have blood characteristics within normal limits. However, there were some clinically relevant discrepancies. However, there was a minimal decrease in hemoglobin concentration and packed cell volume (PCV) and this may be suggestive of a mild anemia (Fig. 3).

DISCUSSION

Interesting details regarding the epidemiology and clinical profile of RA were revealed by this investigation. The disease was most common in women aged 42 to 52 (30%). With a 2% prevalence rate in the elderly, the prevalence decline was, nevertheless, highly notable in the older age groups. According to this pattern, middle-aged adults are the ones who are diagnosed with RA the most frequently; underreporting or the presence of conflicting old age symptoms may make it difficult to detect RA in the elderly.[18]

Given the overall epidemiological trend in RA, the high percentage of males in this cohort (62% vs. 38%) is noteworthy. Variations in immune system activity, genetic susceptibility, or other biological and environmental factors that influence disease risk could be reflected in this unexpected sex distribution. The included RA patients' comorbidities were also examined. 42% of RA patients had diabetes mellitus, which seemed to be a serious risk factor. This association is most likely due to the fact that diabetes patients are frequently immunocompromised, which puts them at risk for autoimmune diseases like RA.[19] Although hypertension was found in 36% of patients, it did not appear to have had a comparable impact on immune function; that is, there was a weaker correlation between the development of RA and high blood pressure.[20]

WBCs and platelets, among other hematological parameters, were elevated in the blood (CBC) examination, although they were still within the normal range. Additionally, there were slight drops in hemoglobin and RBC levels, which could be indicators of anemia. One important finding of the present study was that serum 25(OH)-vitamin D levels were significantly lower among patients with RA (80% had vitamin D insufficiency). This finding further substantiates the action of vitamin D on the immune and emphasizes its therapeutic potential in cases of RA. The high insufficiency rate indicates that supplementation might contribute to the adjustment of disease activity and patient outcome. The results emphasize the multifactorial nature of RA, influenced by age, sex, comorbidities, hematological markers, and nutritional condition.[21] These findings reinforce the need for a multidimensional, patient-centered approach to the diagnosis and treatment for RA, considering the

range of clinical and demographic factors that influence disease course and responses to therapy.

The 41–50-year age group accounted for 30% of our series, which is the greatest prevalence among our 50 cases. This was followed by the 51–60 years age group (22% of cases). In comparison, the lowest number (4%) were found amongst those aged under thirty, while those aged 80 years or more made up 2% of the total (Fig. 1). A statistical analysis showed a significant relationship between age and RA prevalence value was greater than the critical table value (12.59) and $p<0.001$). This validates a significant correlation and indicates that age plays an important role in the development and progression of RA. The findings show that most patients with RA had been diagnosed between the ages of 30 to 60, and the group 41–50-year had the highest proportion, which was coincident with the common age of RA onset. The significance of age in RA prevalence, detection, and clinical manifestation is highlighted by these findings. Additionally, they encourage further research on the role of aging-related physiological factors and healthcare access in the onset and diagnosis of RA in older adults.[22]

The total amount of patients with cases of viral rheumatoid arthritis and the associated percentages for each gender (Table 1). There were 31 were male (62%) and 19 were female (38%). The Chi-square value of 5.76 exceeds the crucial value of 3.84; the p-value of 0.016 is statistically significant ($p<0.05$). This indicates a significant sex-specific disparity in the prevalence of rheumatoid arthritis. The findings indicate a higher prevalence of rheumatoid arthritis in males compared to females, with males constituting 62% of the cases.

This does not conform to the usual trend of elevated prevalence of autoimmune illnesses, such as rheumatoid arthritis[23], observed in women. However, it appears that within this particular analyzed population, males exhibit greater susceptibility, since a higher number of instances was identified among them. This may indicate several explanations, including environmental, genetic, or lifestyle factors leading to the heightened frequency of RA in males within this community.

The statistical significance ($P<0.0001$) of this study verifies that the gender distribution in the RA is not attributable to chance. This outcome warrants a comprehensive investigation of the gender disparities in the manifestation and progression of the illness[24], which may enhance the knowledge of the processes driving gender bias in rheumatoid arthritis, thereby facilitating personalized preventative and treatment strategies.

42% of participants were diagnosed with diabetes, 36% with hypertension, and 22% reported no chronic illnesses and the prevalence of these illnesses within the sample, emphasizing the substantial proportion of persons afflicted by diabetes and hypertension. The Chi-square score of 6.32 exceeds the crucial criterion of 5.99 in the statistical analysis. A p-value of 0.042 is statistically significant ($p < 0.05$), indicating that the distribution of chronic illnesses is unlikely to be attributable to chance (Fig. 2). This signifies a substantial correlation between the existence of these chronic illnesses and the study population.

The data indicate that diabetes is the predominant chronic illness in the sample, impacting 42% of individuals, while hypertension affects 36%. This corresponds with overarching public health trends, wherein diabetes and hypertension are significantly widespread worldwide especially among older demographics or those with certain lifestyle variables.[25] The very low number of persons devoid of chronic illnesses (22%) indicates the significant prevalence of these ailments within the sample.

The results summarized in Figure 3 reveal that the majority of subjects have blood characteristics within normal limits. However, there were some clinically relevant discrepancies. However, there was a minimal decrease in hemoglobin concentration and packed cell volume (PCV) and this may be suggestive of a mild anemia. These hematological alterations are commonly observed in chronic inflammatory and immune process such as rheumatoid arthritis (RA).[26]

At the time of testing, there were no hematologic neoplasms, active bleeding, or hypercoagulable state, as evidenced by the WBC and platelet results being within the normal range for age. Despite the fact that these findings are somewhat comforting, they should be interpreted in light of the overall clinical picture, which includes the disease's stage, symptoms, and medication.[27]

CONCLUSION

The low vitamin D levels may exacerbate rheumatoid arthritis severity and activity. The findings clarify the impact of demographic and clinical factors, including age, gender, and comorbidities like diabetes, on the prevalence and progression of rheumatoid arthritis. These findings highlight the importance of vitamin D as both a biomarker and a therapeutic strategy for the optimal management of rheumatoid arthritis.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Mohammed Mousa Atta, Ashraf Fadhil Jomah
Drafting or Revising Critically:	Mohammed Mousa Atta, Ashraf Fadhil Jomah
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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