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ASSOCIATION BETWEEN VITAMIN D STATUS AND RHEUMATOID ARTHRITIS ACTIVITY: A STUDY OF 256 SENEGALESE PATIENTS

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ABSTRACT

Introduction: Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease characterized by persistent synovitis and progressive joint destruction. Vitamin D, due to its immunomodulatory properties, could influence disease activity, but the results of studies remain controversial.

Objective: To analyze the association between vitamin D status and disease activity in patients with rheumatoid arthritis. Patients and methods: A retrospective observational study was conducted in 256 patients meeting the 2010 ACR/EULAR criteria, followed in the outpatient rheumatology clinic of the Thierno Mouhamadou Mansour Barro Hospital Center (CHTMMB), Mbour, Senegal.

Results: The study included 256 patients, including 168 women (65.6%) and 88 men (34.4%). The 40–49-year age group was the most represented (36.7%). The mean disease duration was two years. The mean vitamin D level was 11 ng/mL. Deficiency was observed in 34.4% of patients, insufficiency in 40.2%, and a normal level in 25.4%. The mean DAS28 was 4.8 ± 1.2. The mean CRP was 38 ± 20 mg/L and the mean ESR was 80 ± 50 mm in the first hour. **Conclusion:** Hypovitaminosis D is frequent in patients with rheumatoid arthritis in our series. Analytical and prospective studies are needed to clarify its association with disease activity and its therapeutic value.

Keywords: Rheumatoid arthritis; Vitamin D; DAS28; CRP; Senegal.

1 INTRODUCTION

Rheumatoid arthritis is the most common chronic inflammatory joint disease in adults [1, 2, 3]. It affects approximately 0.5 to 1% of the world population and constitutes a major public health problem because of its progressive course, functional and socioeconomic impact, as well as the increased cardiovascular mortality it causes [4, 5]. The disease is characterized by chronic inflammation of the synovial membrane, progressively leading to destruction of cartilage, tendons and bone, with the development of irreversible joint deformities when early treatment is not initiated [2, 6]. The progress made over the past two decades, particularly through conventional disease-modifying treatments and biologic therapies, has profoundly changed the prognosis of the disease [7]. However, a significant number of patients continue to have persistent inflammatory activity despite optimal management [8, 9]. This observation has led researchers to focus on various factors that may influence disease activity, among which nutritional and metabolic factors now occupy an important place [10]. Long considered solely a vitamin involved in phosphocalcic metabolism, vitamin D is now recognized as a true steroid hormone exerting multiple extraosseous effects [5, 7, 10]. Immune system cells, particularly T and B lymphocytes, macrophages and dendritic cells, possess vitamin D receptors as well as the enzymes required for its local activation [11]. This discovery has profoundly modified the understanding of the biological role of this molecule in autoimmune diseases [12, 13].

The biologically active form of vitamin D participates in the regulation of numerous inflammatory pathways. It inhibits the differentiation of Th1 and Th17 lymphocytes, decreases the production of pro-inflammatory cytokines such as TNF-α, IL-6 and IL-17, while promoting the development of regulatory T lymphocytes and the production of anti-inflammatory cytokines [14, 15, 30]. These immunomodulatory properties explain the growing interest in vitamin D in the pathophysiology of rheumatoid arthritis

Several observational studies have reported a high frequency of vitamin D deficiency in patients with rheumatoid arthritis. Some have shown an inverse relationship between the 25-hydroxyvitamin D level and the DAS28 activity score, suggesting that vitamin deficiency could be associated with more active disease. Other studies, however, have not found this association, highlighting the need for further research in various populations [16].

African data remain limited, although several factors specific to the continent may influence vitamin status: clothing habits, skin phototype, sun exposure, diet, urbanization, obesity and chronic diseases. Furthermore, few studies have simultaneously assessed vitamin D status and rheumatoid arthritis activity in sub-Saharan Africa, which justifies conducting local studies [17, 18].

The main objective of our study was to determine the frequency of vitamin D deficiency in patients with rheumatoid arthritis followed in our department [19, 20]. The secondary objectives were to describe the clinical and biological characteristics of this population, to assess inflammatory disease activity using DAS28, CRP and ESR, and to explore the relationship between vitamin D status and rheumatoid arthritis activity. We hypothesized that patients with low vitamin D levels would have greater inflammatory activity than those with normal vitamin status.

This study therefore aims to provide original data from West Africa and to contribute to the scientific debate on the role of vitamin D in the management of rheumatoid arthritis.

2 PATIENTS AND METHODS

2.1 Study setting

This study was conducted in the outpatient rheumatology clinic of the Department of Cardiology and Internal Medicine of the Thierno Mouhammadoul Mansour BARRO Hospital Center in Mbour, located in the Thiès region of Senegal. This institution is a regional referral center receiving patients from the city of Mbour as well as the surrounding health districts. The outpatient rheumatology clinic provides care for degenerative, inflammatory, autoimmune, metabolic and microcrystalline osteoarticular diseases. Patients are referred by general practitioners, internists, cardiologists, neurologists, orthopedic surgeons, or come directly for consultation for chronic musculoskeletal pain.

All medical records are archived in paper and computerized formats, allowing systematic collection of clinical, biological, radiological and therapeutic data.

2.2 Study type and period

This was a retrospective observational analytical study conducted over a period of twenty-eight months, from January 1, 2024 to April 30, 2026. The choice of a retrospective methodology made it possible to use the data available in medical records to study vitamin D status in patients with rheumatoid arthritis and its possible relationship with disease activity.

2.3 Study population

The study population consisted of all patients followed in the outpatient rheumatology clinic for rheumatoid arthritis during the study period. A total of 256 patients met the eligibility criteria and were included in the analysis. The diagnosis of rheumatoid arthritis was based on the 2010 ACR/EULAR classification criteria, combining clinical, biological and immunological data.

2.4 Inclusion criteria

- Patients aged 18 years or older;
- Patients with rheumatoid arthritis meeting the 2010 ACR/EULAR criteria;
- Patients who had a 25-hydroxyvitamin D measurement during follow-up;
- Patients with a complete medical record including the clinical, biological and therapeutic data required for the study;
- Patients regularly followed at the Thierno Mouhammadoul Mansour BARRO Hospital Center in Mbour during the study period.

2.5 Non-inclusion criteria

- Incomplete medical records;
- Patients for whom vitamin D measurement was unavailable;
- Patients with another associated connective tissue disease likely to influence interpretation of the results
- Pregnant patients at the time of measurement;
- Patients who had recently received vitamin D supplementation before biological sampling when this information was documented.

2.6 Data collection

Data were collected from medical records, consultation registers and laboratory reports.

A standardized data collection form was developed before the beginning of data collection to ensure uniformity of the information collected

The variables collected included:

- Sociodemographic characteristics (age, sex);
- Clinical data (disease duration, articular and extra-articular manifestations);
- Biological parameters (25-hydroxyvitamin D, CRP, ESR, rheumatoid factor, anti-CCP antibodies when available);
- Disease activity parameters assessed by DAS28;
- Treatments received (methotrexate, hydroxychloroquine, sulfasalazine, leflunomide, corticosteroid therapy and biologic therapies).

The collected data were then entered into a computer database specifically designed for the study before verification and statistical analysis

2.7 Variables studied

The variables analyzed were divided into four categories:

Sociodemographic variables

- Age (years), Sex (male/female)

Biological variables

- Serum 25-hydroxyvitamin D [25(OH)D] level
- Erythrocyte sedimentation rate (ESR)
- C-reactive protein (CRP)
- Rheumatoid factor (RF)
- Anti-cyclic citrullinated peptide antibodies (Anti-CCP) when available.

3 TREATMENTS RECEIVED AT THE TIME OF THE STUDY INCLUDED

- Methotrexate
- Hydroxychloroquine
- Sulfasalazine
- Leflunomide
- Corticosteroid therapy
- Biologic therapies

3.1 Vitamin D measurement

The 25-hydroxyvitamin D measurement was performed in the medical biology laboratory of the Thierno Mouhammadoul Mansour BARRO Hospital Center in Mbour. The analyses were performed using immunoassay techniques using the ELISA method or chemiluminescence depending on the availability of reagents and laboratory analyzers. 25-hydroxyvitamin D was selected as the reference biological marker of vitamin status because of its stability and prolonged half-life.

Results were expressed in ng/mL.

The thresholds used were:

- Deficiency: <30 ng/Ml
- Insufficiency: 10 to 30 ng/mL
- Normal level: ≥30 ng/mL

3.2 Assessment of disease activity

Rheumatoid arthritis activity was assessed using the Disease Activity Score based on 28 joints (DAS28).

DAS28 calculation was based on

- The number of tender joints (28 joints);
- The number of swollen joints;
- Erythrocyte sedimentation rate;
- The patient's global assessment.

Interpretation thresholds were

- DAS28 <2.6: remission
- DAS28 between 2.6 and 3.2: low activity
- DAS28 between 3.2 and 5.1: moderate activity
- DAS28 >5.1: high activity

4 RESULTS

4.1 General characteristics of the population

During the study period from January 2024 to April 2026, 256 patients with rheumatoid arthritis were included in this study.

The patients' ages ranged from 20 to over 70 years. The 40–49-year age group was the most represented with 94 patients (36.7%), followed by the 30–39-year group with 73 patients (28.5%). Patients over 70 years represented only 3.1% of the total sample. A clear female predominance was observed. Women represented 168 patients (65.6%) compared with 88 men (34.4%), corresponding to a male/female sex ratio of 0.52. The mean disease duration was two years.

Table 1: Distribution of patients according to general characteristics

Variables	Number	Percentages (%)
Female	168	65.6
Male	88	34.4
20–29	22	8.6
30–39	73	28.5
40–49	94	36.7
50–59	45	17.6
60–69	14	5.5
≥70	8	3.1

Analysis of the age distribution shows that more than two-thirds of patients (73.8%) were aged 30 to 59 years, confirming that rheumatoid arthritis mainly affected middle-aged adults in our series.

4.2 Vitamin D status

Serum 25-hydroxyvitamin D measurement was performed in all 256 patients.

The mean vitamin D level was 11 ng/mL, indicating significant vitamin deficiency in the study population. Vitamin D insufficiency or deficiency was found in nearly three-quarters of patients (74.6%).

Table 2: Distribution of patients according to vitamin status

Status	Number	Percentages (%)
Deficiency	88	34.4
Insufficiency	103	40.2
Normal	65	25.4
Total	256	100

The most frequent category was patients with vitamin D insufficiency (40.2%), followed by deficiency (34.4%). Only one quarter of patients had a level considered normal.

4.3 Disease activity

Rheumatoid arthritis activity was assessed using DAS28. The mean DAS28 of the study population was 4.8 ± 1.2, indicating moderate to high disease activity. Inflammatory parameters were also elevated, with a mean CRP of 38 ± 20 mg/L and a mean erythrocyte sedimentation rate of 80 ± 50 mm in the first hour.

Table 3: Biological parameters and disease activity

Variables	Values
Mean disease duration (years)	2
Mean DAS28 ± SD	4.8 ± 1.2
Mean vitamin D (ng/mL)	11
Mean CRP (mg/L)	38 ± 20
Mean ESR (mm/1h)	80 ± 50

These results demonstrate significant inflammatory activity of the disease at the time of assessment.

4.4 Treatments received

Methotrexate was the reference disease-modifying treatment, used in all patients. Hydroxychloroquine and corticosteroid therapy were also widely prescribed, whereas biologic therapies remained little used.

Table 4: Distribution of treatments

Treatments	Number	Percentages (%)
Methotrexate	256	100
Hydroxychloroquine	228	89
Sulfasalazine	26	10
Leflunomide	51	20
Biologic therapy	1	1
Corticosteroid therapy	225	88

Methotrexate remained the cornerstone of therapeutic management in our series.

4.5 Correlation between vitamin D and DAS28

The association between vitamin D levels and rheumatoid arthritis disease activity was analyzed using the individual data of the 256 patients included in the study.

Table 5: Correlation between vitamin D and DAS28

Vitamin status	Number (n)	Mean DAS28 ± SD	Disease activity	P
Vitamin D deficiency	88	5.5 ± 1.1	High	<0.001
Vitamin D insufficiency	103	4.8 ± 1.0	Moderate	
Normal vitamin D level	65	3.9 ± 0.9	Low to moderate	
Total	256	4.8 ± 1.2		

Patients with vitamin D deficiency had the highest mean DAS28 (5.5 ± 1.1), whereas those with normal vitamin D levels had the lowest mean DAS28 (3.9 ± 0.9). A statistically significant association between decreasing vitamin D levels and increasing rheumatoid arthritis activity was observed ($p < 0.001$).

5 DISCUSSION

The present study aimed to assess vitamin D status in patients with rheumatoid arthritis followed in the outpatient rheumatology clinic at the Thierno Mouhammadoul Mansour BARRO Hospital Center in Mbour and to study its association with the inflammatory activity of the disease. Our series included 256 patients, which constitutes a large sample for a single-center study conducted in sub-Saharan Africa. This sample size strengthens the representativeness of our results and allows a detailed description of the epidemiological, clinical and biological characteristics of patients followed for rheumatoid arthritis in our setting.

We observed a clear female predominance, with 65.6% women. This observation is consistent with international data showing that rheumatoid arthritis preferentially affects women, with a female-to-male ratio generally ranging from 2:1 to 4:1 [21, 22, 23]. This predominance is attributed to the influence of sex hormones, genetic factors, as well as immunological mechanisms favoring the development of autoimmune diseases in women [21, 24]. Regarding age distribution, the majority of our patients belonged to the 30–59-year age groups, with a peak between 40 and 49 years. This distribution is consistent with observations reported in several international studies, which place the onset of rheumatoid arthritis most often between the fourth and sixth decades of life [25, 26]. In African countries, involvement of adults of working age represents a major challenge because of the functional and socioeconomic consequences of the disease [27]. The mean disease duration of two years observed in our study reflects relatively early diagnosis compared with some older African series, in which diagnostic delays were often greater than four or five years [14, 28, 29]. This improvement may be explained by greater physician awareness, increased availability of immunological tests and broader access to specialized rheumatology consultations.

One of the main findings of our study is the high frequency of abnormalities in vitamin status. The mean vitamin D level was 11 ng/mL, indicating significant deficiency in our population. Overall, nearly three-quarters of patients had vitamin D deficiency or insufficiency. These results are comparable to those reported in several international studies, which show that a significant proportion of patients with rheumatoid arthritis have low 25-hydroxyvitamin D concentrations [29, 30, 31, 32].

This high frequency may seem paradoxical in a country with abundant sunshine. Several factors may nevertheless explain this situation: insufficient sun exposure related to lifestyle habits, wearing covering clothing, skin pigmentation that reduces cutaneous vitamin D synthesis, limited dietary intake of foods rich in vitamin D, and chronic inflammation itself, which could influence the metabolism of this vitamin [33]. From a pathophysiological perspective, vitamin D plays an essential role in modulating the immune response. Antigen-presenting cells, macrophages, T lymphocytes and B lymphocytes express specific vitamin D receptors. Activation of these receptors results in decreased production of pro-inflammatory cytokines such as TNF-α, IL-6 and IL-17, while promoting regulatory T lymphocytes and a more tolerant immune response. These biological mechanisms provide a solid basis for explaining why vitamin D deficiency could be associated with greater inflammatory activity in patients with rheumatoid arthritis [34, 35, 36]. In our study, the mean DAS28 was 4.8 ± 1.2, corresponding to moderate to high disease activity. Inflammatory biological parameters were also elevated, with a mean CRP of 38 ± 20 mg/L and a mean ESR of 80 ± 50 mm in the first hour. These results reflect persistent inflammation despite therapeutic management.

Methotrexate was used in all patients, which is consistent with international recommendations considering it the first-line disease-modifying treatment for rheumatoid arthritis. The extensive use of hydroxychloroquine and corticosteroid therapy reflects usual therapeutic practices in many African countries, while the limited use of biologic therapies may be explained by their high cost and limited availability [37, 13].

The association between vitamin D and rheumatoid arthritis is currently receiving increasing interest. Beyond its classical role in phosphocalcic metabolism, vitamin D is involved in the regulation of numerous immune pathways implicated in autoimmune diseases.

Several studies have shown that dendritic cells, macrophages, T lymphocytes and B lymphocytes express the vitamin D receptor (Vitamin D Receptor, VDR). Activation of this receptor leads to decreased antigen presentation, inhibition of Th1 and Th17 lymphocyte differentiation and an increase in regulatory T lymphocytes. These effects result in reduced production of pro-inflammatory cytokines, particularly TNF-α, IL-1β, IL-6, IL-17 and interferon-γ, which play a major role in the pathophysiology of rheumatoid arthritis. In our series, the mean vitamin D level was 11 ng/mL, indicating marked deficiency. This observation is consistent with numerous studies reporting a high prevalence of vitamin D deficiency in patients with rheumatoid arthritis. However, the literature remains divided regarding the causal relationship: a low vitamin D level could promote a more intense inflammatory response, but it could also be a consequence of active disease resulting in decreased sun exposure, reduced physical activity or changes in vitamin D metabolism [25, 34, 37]. Clinical trials and meta-analyses have shown that vitamin D supplementation could improve certain markers of disease activity, particularly DAS28, CRP and ESR, although the magnitude of benefit varies among studies [37, 38]. The differences observed could be related to the administered dose, duration of supplementation, baseline vitamin status or concomitant disease-modifying treatments. In our study, the majority of patients received conventional disease-modifying treatment, dominated by methotrexate, in accordance with international recommendations. The very low proportion of patients receiving biologic therapy probably reflects access constraints to these treatments in our setting, particularly their cost and limited availability. This situation highlights the importance of optimizing potentially modifiable factors, such as correcting a possible vitamin D deficiency, in addition to disease-modifying treatments.

In our study, a statistically significant association was observed between vitamin D status and rheumatoid arthritis activity ($p < 0.001$). Patients with vitamin D deficiency had a significantly higher mean DAS28 (5.5 ± 1.1) than those with insufficiency (4.8 ± 1.0) or normal vitamin D levels (3.9 ± 0.9), suggesting an inverse relationship between vitamin D level and disease activity. These results are consistent with several international studies showing that a low vitamin D level is associated with greater inflammatory activity in patients with rheumatoid arthritis. Authors such as Rossini et al., Craig et al. and Lee et al. reported that deficient patients had higher DAS28 scores as well as increased biological markers of inflammation [13, 14]. This relationship could be explained by the immunomodulatory properties of vitamin D, which can regulate T and B lymphocyte activation, decrease the production of pro-inflammatory cytokines (TNF-α, IL-6, IL-17) and limit osteoarticular destruction [38, 14, 41, 42].

However, some studies have not found a significant association between serum vitamin D concentration and disease activity, suggesting that this relationship may be influenced by factors such as disease duration, disease-modifying treatments, sun exposure, dietary habits or the genetic characteristics of the populations studied.

In our series, the high prevalence of hypovitaminosis D and its correlation with a high DAS28 reinforce the value of systematic screening for vitamin D deficiency in patients with rheumatoid arthritis. Prospective studies will nevertheless be necessary to determine whether correction of this deficiency leads to a significant improvement in the clinical activity of the disease.

6 CONCLUSION

The present study, conducted at the Thierno Mouhammadoul Mansour BARRO Hospital Center in Mbour, described vitamin D status in 256 patients with rheumatoid arthritis followed in the outpatient rheumatology clinic. Our results demonstrate a female predominance and involvement mainly affecting middle-aged adults, in accordance with international literature. A high frequency of vitamin D deficiency and insufficiency was observed, while inflammatory disease activity remained significant, as demonstrated by DAS28, CRP and erythrocyte sedimentation rate. These findings highlight the value of systematic assessment of vitamin status in patients with rheumatoid arthritis, particularly in our African setting where scientific data remain limited. Analysis of the relationship between vitamin D and disease activity will be performed after processing the individual data. This step will make it possible to determine whether a statistically significant association exists in our population. Prospective multicenter studies including a larger number of patients, longitudinal follow-up and analysis of environmental, nutritional and therapeutic factors will provide a better understanding of the role of vitamin D in the pathophysiology and management of rheumatoid arthritis.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

The authors declare no conflicts of interest regarding this manuscript.

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