"PROJECT REPORT (MFNP-12)"

CORRELATION BETWEEN VITAMIN D DEFICIENCY AND DAS28 SCORE IN RHEUMATOID ARTHRITIS

Submitted in partial Fulfilment of the requirements for the Award of the

Degree of

MASTER OF SCIENCE IN DIETETICS AND FOOD SERVICE MANAGEMENT (MSCDFSM)

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CERTIFICATE

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To the best of my knowledge and belief, the work embodied in the dissertation has not been submitted previously, either in part or full, for the award of any degree, diploma, or other academic qualification of any university or institution.

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DECLARATION

I hereby declare that the dissertation entitled **"Correlation Between Vitamin D Deficiency and DAS28 Score in Rheumatoid Arthritis"**, submitted to the **Indira Gandhi National Open University (IGNOU)** in partial fulfillment of the requirements for the award of the Degree of **Master of Science in Dietetics and Food Service Management** is Bonafide record of original work carried out by me .

I further declare that this dissertation has not been submitted previously, either wholly or partly, for the award of any degree, diploma, or other academic qualification of any university or institution.

The information and data presented in this dissertation are true and correct to the best of my knowledge.

Place: Hyderabad

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LIST OF ABBREVIATIONS :

- **ACR :** American College of Rheumatology
- **Anti-CCP :** Anti-Cyclic Citrullinated Peptide
- **BMI :** Body Mass Index
- **CRP :** C-Reactive Protein
- **DAS28 :** Disease Activity Score in 28 Joints
- **DMARD :** Disease Modifying Anti-Rheumatic Drug
- **ELISA :** Enzyme-Linked Immunosorbent Assay
- **ESR :** Erythrocyte Sedimentation Rate
- **FFQ :** Food Frequency Questionnaire
- **IU :** International Unit
- **RA :** Rheumatoid Arthritis
- **RF :** Rheumatoid Factor
- **SD :** Standard Deviation
- **TNF-α :** Tumor Necrosis Factor Alpha
- **VAS :** Visual Analog Scale
- **VDR :** Vitamin D Receptor
- **WHO :** World Health Organization
- **25(OH)D :** 25-Hydroxy Vitamin D
- **TJC28 :** 28-Joint Tender Joint Count
- **SJC28 :** 28-Joint Swollen Joint Count

ABSTRACT :

Background : Rheumatoid Arthritis (RA) is a chronic autoimmune inflammatory disease in which vitamin D may influence immune regulation. The relationship between serum vitamin D status and RA disease activity remains an area of clinical interest.

Aim : To determine the Correlation between Serum 25-Hydroxyvitamin D levels and DAS28 score among patients with Rheumatoid Arthritis.

Methodology : A cross-sectional analytical study was conducted among **160 patients** with Rheumatoid Arthritis. Demographic, clinical and nutritional data were collected, serum 25(OH)D levels were recorded, and disease activity was assessed using DAS28 score. Data were analyzed using descriptive statistics and Pearson's and Spearman's correlation tests.

Results : The mean age was **54.01 ± 6.34 years**, and **76.9%** of participants were female. The mean serum 25(OH)D concentration was **22.29 ± 6.77ng/mL**, while the mean DAS28 score was **4.62 ± 0.82**. Vitamin D insufficiency was present in **46.4%** of participants and deficiency in **36.8%**. A statistically significant inverse correlation was observed between serum vitamin D levels and DAS28 (**Pearson r = -0.442, p = 5.02 x 10^{-9}**).

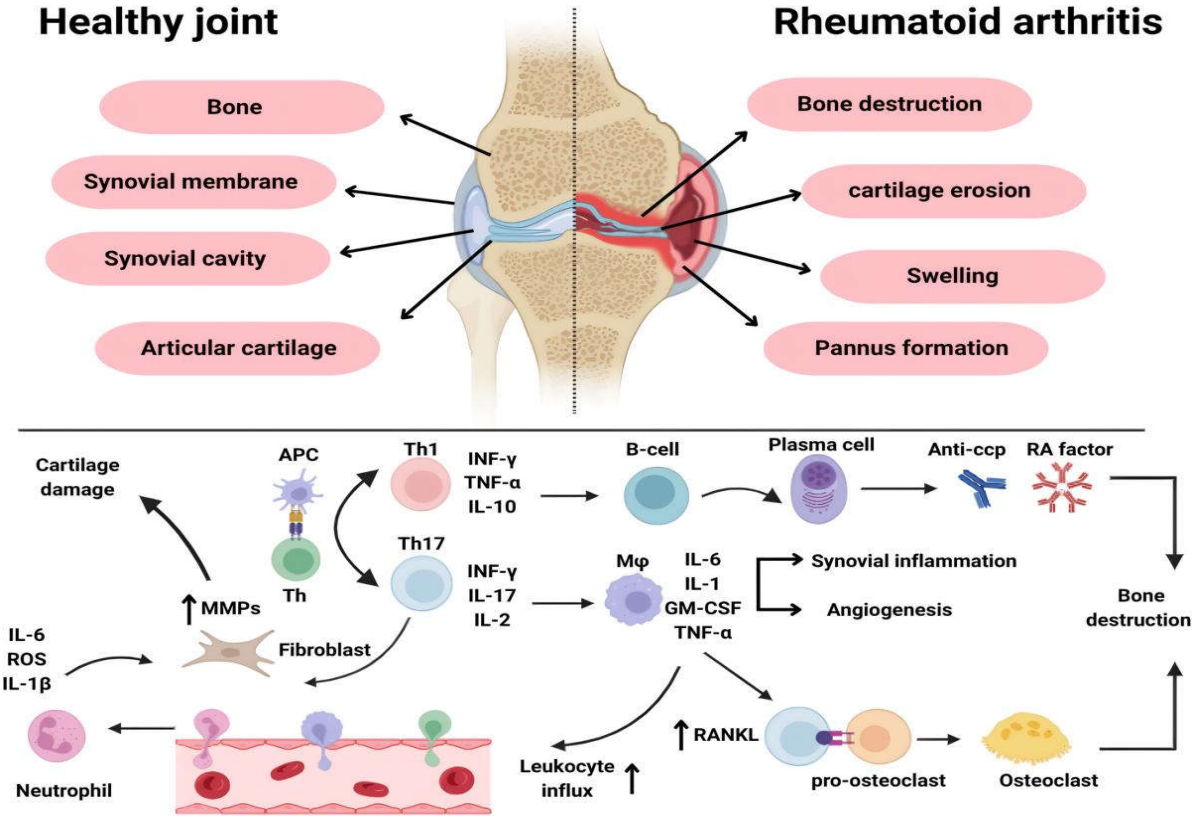
Conclusion : Lower serum vitamin D levels were associated with higher rheumatoid arthritis disease activity. Because the study is cross-sectional, the findings indicate an association rather than causation.

Keywords : Rheumatoid Arthritis, Vitamin D, DAS28, Disease Activity, Cross-sectional study.

CHAPTER 1
INTRODUCTION

1.1 Rheumatoid Arthritis: Pathophysiology

Rheumatoid arthritis is a chronic autoimmune inflammatory disorder in which the immune system contributes to inflammation of the synovial tissues. Persistent inflammation may lead to cartilage destruction, bone erosion, joint deformity and functional disability.



RA develops when genetic susceptibility interacts with environmental triggers, resulting in immune system activation.

The disease process includes:

- Activation of T lymphocytes
- Activation of B lymphocytes
- Production of rheumatoid factor (RF)
- Formation of anti-CCP antibodies
- Release of inflammatory cytokines
- Synovial inflammation
- Cartilage destruction

- Bone erosion

Major inflammatory mediators include:

- TNF-alpha
- IL-1
- IL-6
- IL-17

These cytokines contribute to pain, swelling, and progressive joint damage.

RA commonly affects the small joints of the hands and feet, although larger joints and other organs may also be involved. Common symptoms include:

- Joint pain
- Joint swelling
- Morning stiffness
- Reduced range of movement
- Fatigue
- Weakness
- Reduced physical activity
- Functional limitations

The disease can have important nutritional implications because chronic inflammation, reduced physical activity, altered dietary intake and medication-related factors may influence nutritional status.

RA affects multiple aspects of health.

Physical impact

- Chronic pain
- Joint deformities
- Reduced mobility
- Muscle weakness

Psychological impact

- Depression
- Anxiety
- Social isolation

Economic impact

- Loss of employment
- Increased medical expenses
- Long-term disability

Because RA is lifelong, identifying modifiable factors that may reduce disease activity has become an important area of research.

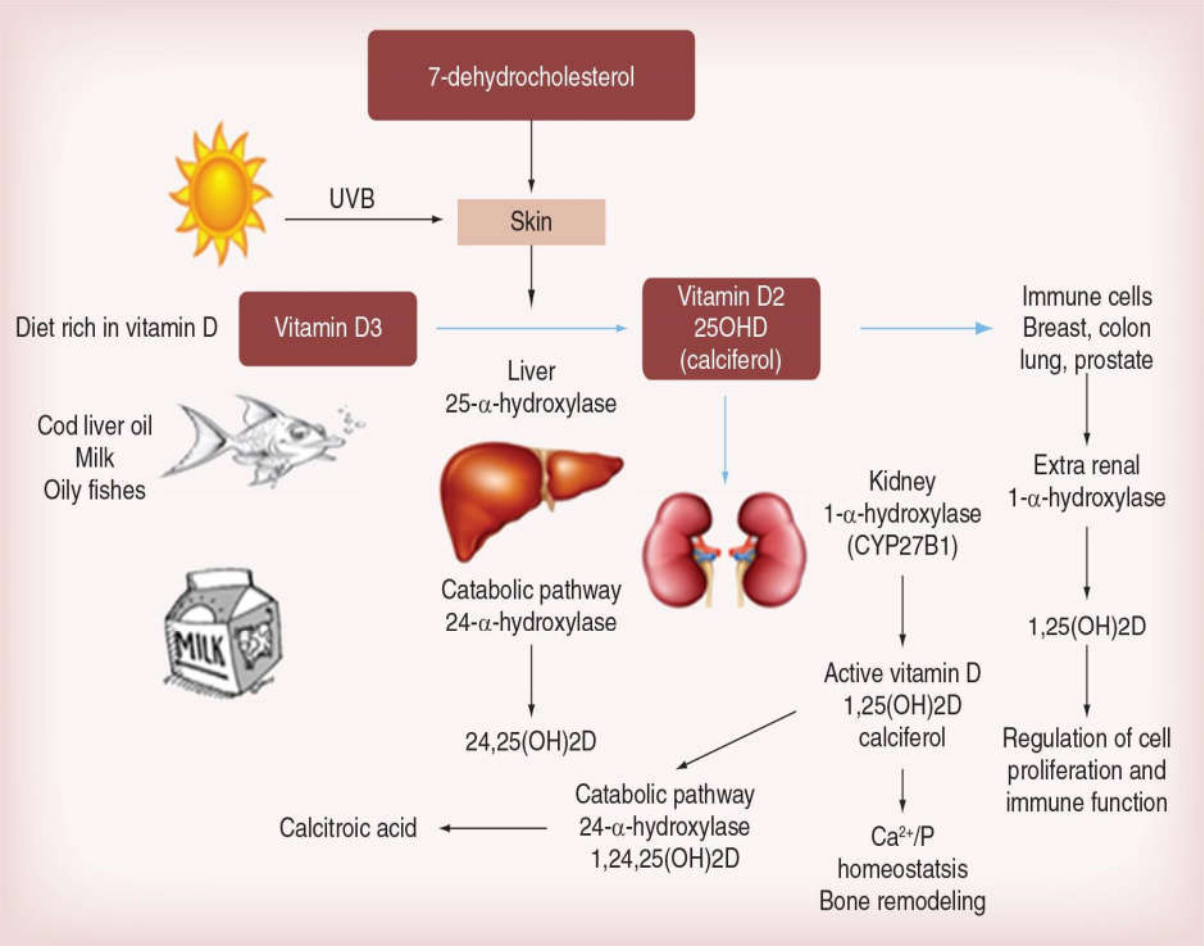
1.2 Vitamin D: Overview

Vitamin D is a fat-soluble vitamin involved in calcium and phosphorus homeostasis and skeletal health. Vitamin D can be obtained through cutaneous synthesis following exposure to ultraviolet-B radiation, dietary sources and supplements.

It exists in two major forms:

- Vitamin D2 (Ergocalciferol)
- Vitamin D3 (Cholecalciferol)

The body synthesizes Vitamin D3 in the skin after exposure to ultraviolet-B (UVB) sunlight.



Vitamin D metabolism

1. Sunlight converts 7-dehydrocholesterol into Vitamin D3.
2. Liver converts Vitamin D into 25-hydroxy Vitamin D [25(OH)D].
3. Kidney converts it into active 1,25-dihydroxy Vitamin D.

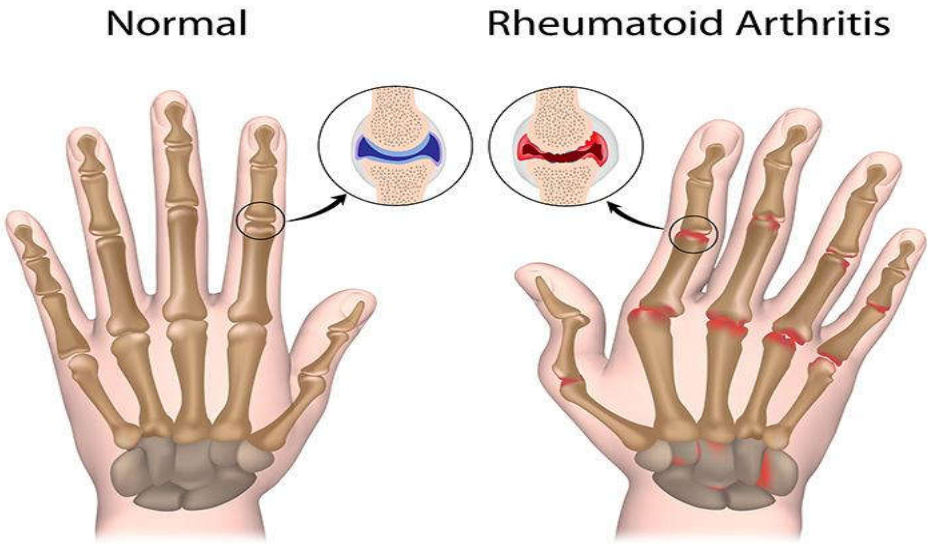
Serum 25(OH) Vitamin D is considered the best indicator of Vitamin D status because it reflects both dietary intake and sunlight exposure.

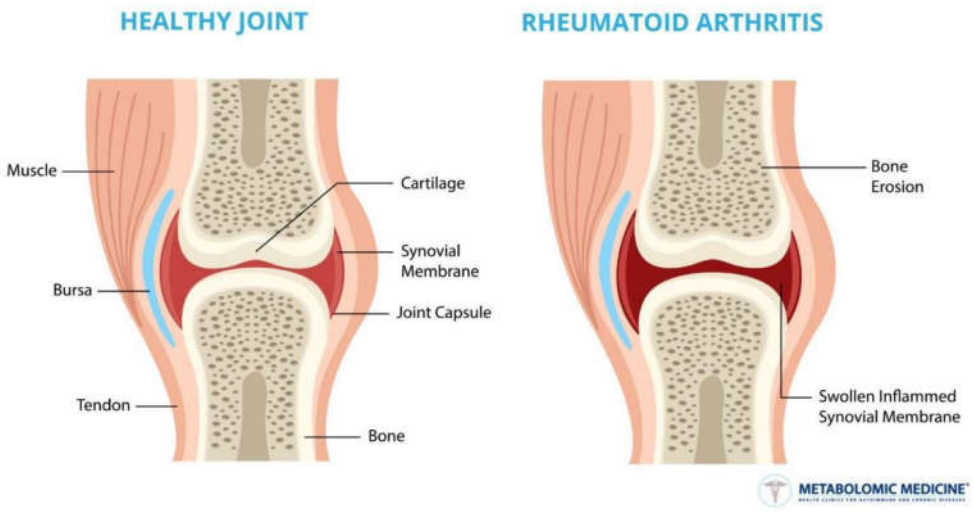
Vitamin D Status Classification

Serum 25(OH)D	**Interpretation**
Less than 20ng/mL	Deficient
20-29ng/mL	Insufficient
30ng/mL	Sufficient

1.3 Background :

Rheumatoid arthritis is a chronic systemic autoimmune inflammatory disorder in which immune-mediated inflammation primarily affects synovial joints. Persistent inflammation can result in pain, stiffness, swelling, impaired physical function and structural joint damage. Modern RA management therefore emphasizes early diagnosis, disease-modifying antirheumatic drugs and repeated measurement of disease activity rather than relying on symptoms alone. The 2010 ACR/EULAR classification criteria were developed to improve classification of patients with inflammatory synovitis, particularly earlier in the disease course [2].





DAS28 is a composite disease-activity measure incorporating tender joint count, swollen joint count, an inflammatory marker such as ESR or CRP, and a patient global assessment. The development and subsequent clinical application of DAS/DAS28 established the importance of combining several disease dimensions into a standardized index [36,35].

Vitamin D is a fat-soluble secosteroid hormone involved in calcium-phosphate homeostasis and skeletal health. Its active form also affects immune-cell function. Vitamin D receptor expression in immune cells and local vitamin D metabolism provide biological plausibility for investigating vitamin D in inflammatory and autoimmune disorders [6,16,19].

A number of observational studies have reported lower serum 25(OH)D concentrations in RA and inverse associations with disease activity. Sharma et al. reported a significant inverse correlation between vitamin D and DAS28 in an Indian RA cohort [28]. Meta-analyses by Lin et al. and Lee and Bae similarly reported inverse relationships, although the pooled effect sizes differed [23,22]. Indian evidence has also included a meta-analysis reporting a high prevalence of low vitamin D among RA patients [4].

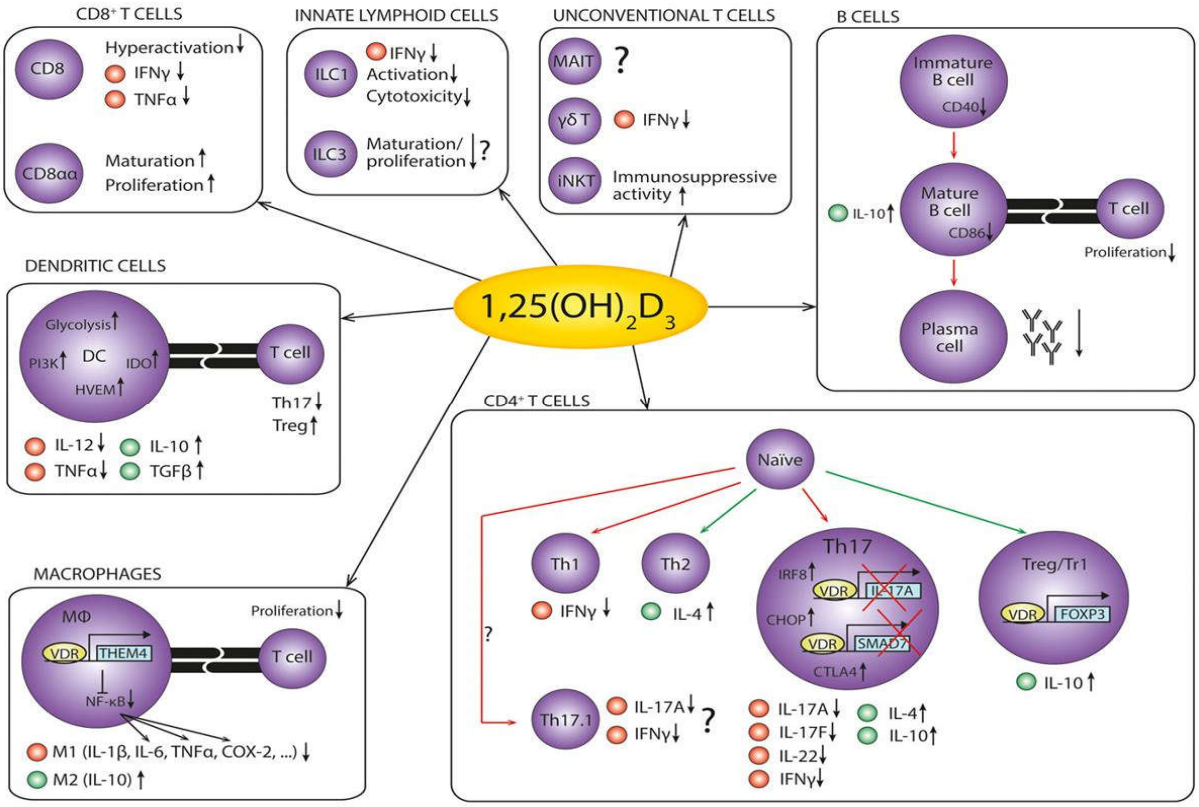
At the same time, evidence from intervention studies is not completely consistent. Recent systematic reviews and meta-analyses of vitamin D supplementation in RA have reported differing results concerning DAS28 and inflammatory markers [14]. Differences in baseline vitamin D status, dose, duration of supplementation, medications, sun exposure and other factors may contribute to this heterogeneity.

Therefore, assessment of the association between serum 25(OH)D and disease activity remains relevant. A study incorporating biochemical assessment, disease activity measurement and relevant nutritional and lifestyle factors may contribute useful information.

The present study proposes to assess the correlation between serum 25(OH)D concentration and DAS28 among patients with rheumatoid arthritis.

1.4 Vitamin D and the Immune System:

Vitamin D has functions beyond bone metabolism. The vitamin D receptor is expressed in various immune cells, and vitamin D-related pathways can influence immune-cell activity.



Research has shown that Vitamin D acts as an immune-modulating hormone rather than simply a vitamin.

Vitamin D receptors (VDR) are present on:

- T lymphocytes
- B lymphocytes
- Macrophages
- Dendritic cells

Vitamin D helps regulate immune responses by:

- suppressing excessive inflammatory reactions,
- reducing pro-inflammatory cytokines,
- increasing regulatory T cells,
- limiting autoimmune activity.

These biological mechanisms provide a strong theoretical basis for studying Vitamin D in RA.

Vitamin D Deficiency in India

Despite abundant sunlight, Vitamin D deficiency is highly prevalent in India because of:

- indoor lifestyle,
- limited sun exposure,
- darker skin pigmentation,
- inadequate dietary intake,
- obesity,
- urbanization.

Studies have reported Vitamin D deficiency across various age groups, making it an important nutritional concern.

1.5 Disease Activity Assessment in Rheumatoid Arthritis:

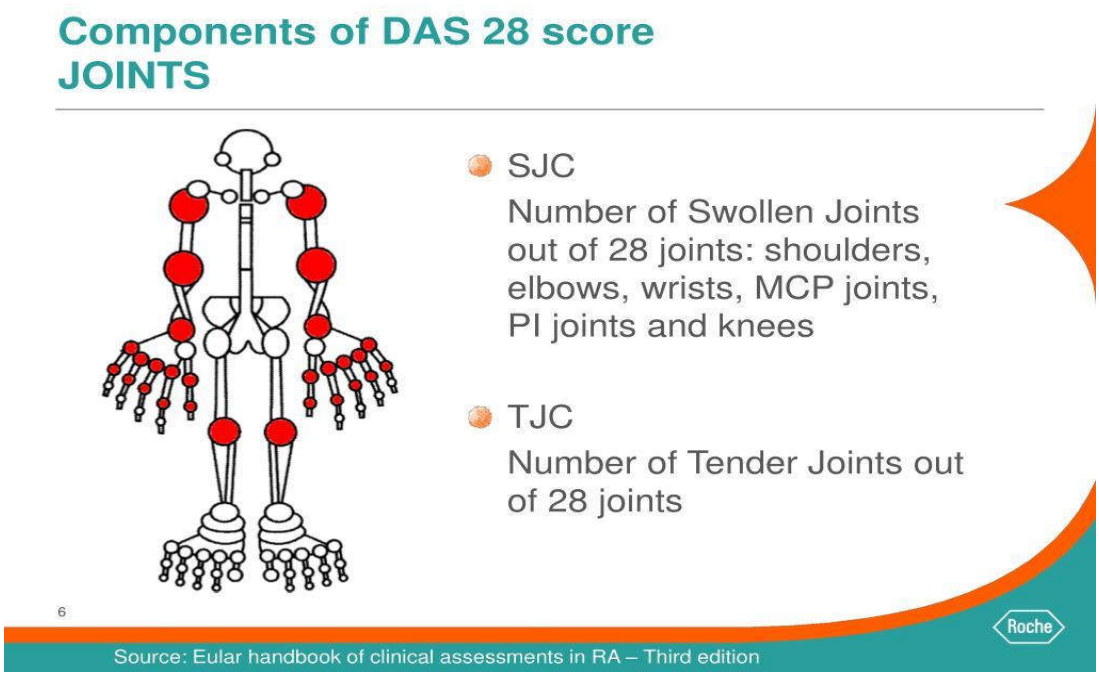
Disease activity refers to the degree of active inflammatory disease at a particular point in time. Accurate assessment of disease activity is important for evaluating disease severity and monitoring treatment response.

Several measures are available for assessing RA disease activity. DAS28 is one of the commonly used composite measures.

DAS28 can be calculated using:

1. Tender joint count based on 28 joints
2. Swollen joint count based on 28 joints
3. ESR or CRP
4. Patient's global assessment of health/disease activity

The resulting score provides a quantitative estimate of disease activity.



Broadly, DAS28 values are interpreted as:

DAS28 score	**General Interpretation**
<2.6	Remission
2.6-3.2	Low Disease Activity
>3.2-5.1	Moderate Disease Activity
>5.1	High Disease Activity

The exact DAS28 version used in the research should be specified in the methodology. The study should use the same version consistently for all 160 participants.

1.6 Vitamin D and Rheumatoid Arthritis:

A substantial body of observational literature has investigated vitamin D status in RA. The findings generally suggest that low vitamin D status is common among people with RA and that lower vitamin D concentrations may be associated with greater disease activity.

A meta-analysis found that vitamin D deficiency was significantly more prevalent in RA patients than in controls and also demonstrated an inverse relationship between vitamin D concentration and DAS28 [22].

Another meta-analysis reported a negative association between serum 25(OH)D and RA disease activity, although the authors emphasized the need for more strictly controlled studies.

More recent evidence concerning vitamin D supplementation has been heterogeneous. Some systematic reviews have reported improvements in DAS28 following supplementation, whereas other analyses have found no significant overall effect, highlighting the influence of study design and clinical heterogeneity [1,10].

This inconsistency provides a rationale for further investigation of the relationship between naturally measured serum vitamin D status and RA disease activity.

1.7 Nutritional Factors Relevant to Vitamin D Status:

Vitamin D status may be influenced by several nutritional and lifestyle factors, including:

- Dietary vitamin D intake
- Dietary calcium intake
- Intake of fortified foods
- Vitamin D supplementation
- Sunlight exposure
- Physical activity
- Body mass index
- Age
- Skin pigmentation
- Clothing habits
- Season

Therefore, these factors should be considered when interpreting the relationship between vitamin D and DAS28.

1.8 Rationale for the Present Study:

Although several studies have examined vitamin D and RA disease activity, the strength of the association has not been uniformed across populations.

The relationship may be influenced by demographic, clinical, nutritional and lifestyle characteristics. In addition, supplementation and medication use may influence both vitamin D status and disease activity.

A cross-sectional analytical study assessing serum 25(OH)D together with DAS28 among 160 patients can provide data regarding whether an association exists in the selected study population.

From a nutrition and dietetics perspective, the study is particularly relevant because vitamin D is an important nutritional factor and vitamin D status can potentially be assessed alongside dietary intake, supplementation and sunlight exposure.

1.9 Need for the Study:

Vitamin D deficiency is a potentially important nutritional problem among individuals with rheumatoid arthritis. Since RA is a chronic inflammatory condition, identifying nutritional factors associated with disease activity may be useful for nutritional assessment and counselling.

Evidence concerning vitamin D supplementation is not uniform. Guan et al. reported improvement in DAS28 in a meta-analysis of six studies, whereas other systematic reviews have emphasized heterogeneity and inconsistent effects [1,14]. A later 2025 meta-analysis also reported improvements in several outcomes but noted uncertainty regarding optimal dose and duration [10]. These differences justify careful observational analysis and appropriately designed longitudinal or randomized studies.

Therefore, the present study is designed to assess the relationship between serum 25(OH)D levels and DAS28 among patients with rheumatoid arthritis.

1.10 Hypothesis:

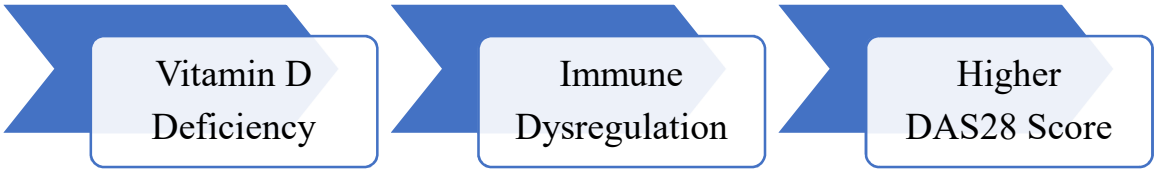
Null Hypothesis (H_0):

There is no significant correlation between serum 25-hydroxyvitamin D levels and DAS28 score among patients with rheumatoid arthritis.

Alternative Hypothesis (H_1):

There is a significant inverse correlation between serum 25-hydroxyvitamin D levels and DAS28 score among patients with rheumatoid arthritis.

1.11 Conceptual Framework:



The proposed framework suggests that lower Vitamin D levels may contribute to immune dysregulation, increased inflammation, and higher disease activity as measured by DAS28.

CHAPTER II

AIMS AND OBJECTIVES

2.1 Aim:

To assess the correlation between serum 25-hydroxyvitamin D levels and Disease Activity Score-28 (DAS28) among patients with rheumatoid arthritis.

2.2 Objectives:

- To assess selected demographic and anthropometric characteristics of participants.
- To assess serum 25(OH)D concentration and vitamin D status.
- To assess RA disease activity using DAS28.
- To determine the correlation between serum 25(OH)D and DAS28.
- To compare DAS28 across vitamin D status categories.
- To document selected dietary, sunlight-exposure and vitamin D supplementation characteristics.

CHAPTER 3
REVIEW OF LITERATURE

The literature was reviewed chronologically to examine biological rationale, observational evidence, Indian studies and intervention evidence.

- **Vitamin D Supplementation Meta-analysis – 2025**

A systematic review and meta-analysis published in **2025** evaluated the effects of vitamin D supplementation among patients with rheumatoid arthritis. The analysis included **11 studies**.

The pooled results demonstrated a significant improvement in DAS28 following vitamin D supplementation, with a weighted mean difference of approximately **−0.83 (95% CI −1.38 to −0.28; p < 0.001)**. Improvements were also reported for CRP, ESR and serum vitamin D levels. However, no significant effects were observed for the Health Assessment Questionnaire or VAS-pain outcomes [10].

- **Recent Indian Evidence (2025)**

A recent cross-sectional study among **50 Indian patients with rheumatoid arthritis** examined the relationship between serum 25(OH)D concentration and DAS28.

The mean DAS28 score was approximately **4.11 ± 1.50**, while the mean serum 25(OH)D concentration was approximately **26.84 ± 3.96 ng/mL**. Multiple linear regression analysis demonstrated a statistically significant inverse relationship between serum 25(OH)D and DAS28. Serum 25(OH)D was an independent inverse determinant of disease severity in the study model.

Conclusion

The researchers concluded that low vitamin D status was associated with greater disease activity among the Indian RA patients studied. They suggested that vitamin D status may be useful to consider alongside conventional disease activity measures. Because the study was cross-sectional and involved a relatively small sample, the findings should be interpreted as an association rather than proof of causation. **(Recent Indian cross-sectional study).**

- **Eastern India study (2024)**

A single-centre study from Eastern India investigated the relationship between serum vitamin D and disease activity in rheumatoid arthritis. The study included 80 newly diagnosed RA patients.

The researchers measured serum vitamin D and calculated the DAS28-ESR score. Approximately 72.5% of participants were female, and 47.5% had vitamin D deficiency. The mean serum vitamin D concentration was approximately 22.99 ± 10.01 ng/mL, while the mean DAS28-ESR was approximately 3.81 ± 1.19.

A statistically significant inverse correlation was identified between vitamin D concentration and DAS28-ESR ($p = 0.0003$).

Conclusion

The researchers concluded that vitamin D deficiency was common among newly diagnosed RA patients and that lower vitamin D levels were associated with greater disease activity. The study provides particularly relevant evidence from an Indian population and supports further evaluation of vitamin D status in RA patients. (Eastern India study, 2024) [7].

- **Al-Saoodi et al. and Subsequent Evidence (2024)**

The evidence available from randomized trials illustrates an important difference between association studies and intervention studies. Observational studies frequently report that patients with lower vitamin D levels have higher RA disease activity. However, supplementation trials do not always demonstrate a consistent reduction in disease activity.

This distinction is important for interpreting the present dissertation. A significant correlation between vitamin D and DAS28 does not by itself prove that vitamin D deficiency causes increased disease activity. Vitamin D status may be influenced by multiple factors, including sunlight exposure, dietary intake, physical activity, obesity, age, disease duration, inflammation and medication use.

Therefore, the literature supports investigation of vitamin D status as a potentially relevant factor in RA while recognizing that causality requires further longitudinal and intervention research [1].

- **Al-Saoodi et al. (2024)**

Al-Saoodi and colleagues conducted a systematic review and dose-response meta-analysis of randomized controlled trials to investigate whether vitamin D supplementation affected inflammatory and clinical outcomes in rheumatoid arthritis.

The review included 11 randomized trials involving 3,049 patients. The researchers evaluated outcomes including CRP, ESR, DAS28 and Health Assessment Questionnaire scores.

The findings did not demonstrate a statistically significant overall reduction in CRP, ESR, DAS28 or HAQ scores following vitamin D supplementation. Importantly, the researchers reported substantial heterogeneity between studies, indicating that the effects of supplementation were not consistent across all trials.

Conclusion

Al-Saoodi et al. concluded that the available randomized-trial evidence was heterogeneous and did not establish a consistent overall benefit of vitamin D supplementation on inflammatory or disease-activity outcomes in RA. This study is important because it demonstrates that the evidence from intervention studies is less consistent than some observational evidence. (Al-Saoodi et al., 2024) [1].

- **Bose et al. (2023)**

Bose and colleagues conducted an important Indian **single-arm meta-analysis** entitled **"Vitamin D deficiency in rheumatoid arthritis patients of India – a single-arm meta-analysis."**

The researchers identified and analyzed **15 studies** involving Indian RA patients. The objective was to estimate the prevalence of vitamin D deficiency in Indian RA patients and evaluate its association with disease activity.

The pooled mean serum vitamin D concentration was approximately **19.99 ng/mL**. The pooled proportion with low vitamin D levels was approximately **80%**, while vitamin D deficiency was estimated at approximately **56%** and vitamin D insufficiency at approximately **20%** using the random-effects model.

The researchers also identified a significant association between serum 25(OH)D concentration and disease activity. Lower vitamin D concentrations were observed among patients with higher disease activity scores.

Conclusion

Bose et al. concluded that low vitamin D status was highly prevalent among Indian patients with rheumatoid arthritis and that serum vitamin D levels showed an inverse relationship with disease activity. However, they emphasized that larger studies and randomized controlled trials were needed before vitamin D could be considered a disease-modifying treatment for RA. **(Bose et al., 2023)** [4]**.**

- **Guan et al. Vitamin D Supplementation Evidence (2020-Meta-analysis)**

A systematic review and meta-analysis published in **2020** evaluated the effects of vitamin D supplementation in patients with rheumatoid arthritis.

The researchers included **six studies involving 438 participants**. The outcomes included DAS28, ESR, CRP, tender joint count, swollen joint count, pain and serum vitamin D.

The pooled results demonstrated a statistically significant improvement in **DAS28**, with a weighted mean difference of approximately **−0.41**. Significant improvements were also reported for ESR and tender joint count, although not all evaluated outcomes showed significant changes.

Conclusion

The authors concluded that vitamin D supplementation might improve certain indicators of rheumatoid arthritis activity, particularly DAS28, ESR and tender joint count. However, the relatively small number of studies and variation between interventions indicated the need for additional well-designed randomized controlled trials. **(2020 systematic review and meta-analysis)** [14]**.**

- **Lee and Bae (2016)**

Lee and Bae conducted another important meta-analysis examining vitamin D levels in rheumatoid arthritis and their relationship with disease activity.

The analysis included **15 studies involving 1,143 patients with RA and 963 controls**. Serum vitamin D levels were significantly lower among RA patients than controls. The prevalence of vitamin D deficiency was also significantly higher in RA patients.

Importantly, **13 studies involving 924 RA patients** evaluated the relationship between vitamin D concentration and DAS28. The pooled analysis demonstrated a statistically significant inverse correlation between serum vitamin D and DAS28, with a correlation coefficient of approximately **−0.278**.

Conclusion

Lee and Bae concluded that vitamin D deficiency was more prevalent among RA patients and that serum vitamin D levels were inversely associated with RA disease activity. Their findings provided stronger evidence through pooled analysis that lower vitamin D concentrations may be associated with higher disease activity. **(Lee & Bae, 2016)** [22]**.**

- **Lin et al. (2016)**

Lin, Liu, Davies and Chen conducted a systematic review and meta-analysis titled **"Serum Vitamin D Level and Rheumatoid Arthritis Disease Activity: Review and Meta-Analysis."**

The researchers identified **24 reports involving 3,489 patients**. The analysis compared vitamin D levels between patients with rheumatoid arthritis and healthy controls and examined the correlation between serum 25(OH)D concentration and disease activity.

RA patients had lower serum vitamin D levels than healthy controls, with a pooled mean difference of **−16.52 nmol/L**. A significant negative relationship was identified between serum 25(OH)D and DAS28, with a pooled correlation coefficient of approximately **r = −0.13**.

The authors also reported that the inverse relationship appeared stronger in low-latitude regions and in developing countries [23].

- **Chandrashekara and Patted (2015)**

Chandrashekara and Patted conducted an exploratory study in India entitled **"Role of vitamin D supplementation in improving disease activity in rheumatoid arthritis."**

The investigators initially screened **150 RA patients**. Patients who had active disease and vitamin D deficiency were selected for supplementation. Among the eligible patients, 59 completed the 12-week intervention.

The study reported improvement in disease activity following vitamin D supplementation. The mean DAS28-CRP decreased from approximately **3.68 ± 0.93 to 3.08 ± 1.11**, while serum vitamin D concentration increased substantially during the intervention.

Conclusion

Chandrashekara and Patted concluded that correction of vitamin D deficiency was associated with an improvement in disease activity in the studied RA patients. The authors considered vitamin D supplementation potentially useful as an adjunct to conventional treatment, while recognizing the exploratory nature of the study. The article was first published online in 2015 and appeared in the journal issue in 2015. **(Chandrashekara & Patted, 2015)** [5]**.**

- **Sharma et al. (2014)**

Sharma and colleagues conducted a study titled **"Estimation of vitamin D levels in rheumatoid arthritis patients and its correlation with the disease activity."** The study included **80 patients with rheumatoid arthritis and 80 healthy controls**.

Serum 25-hydroxyvitamin D levels were measured, and disease activity was assessed using the **DAS28 score**. The researchers found that **90% of RA patients were either vitamin D deficient or insufficient**, compared with 70% of healthy controls. This difference was statistically significant (**p = 0.007**).

The study directly examined the relationship between vitamin D status and RA disease activity and therefore has particular relevance to the present dissertation.

Conclusion

Sharma et al. concluded that vitamin D deficiency or insufficiency was highly prevalent among patients with rheumatoid arthritis and that vitamin D status was related to disease activity. Their findings supported further investigation of vitamin D status in RA patients and its possible relationship with DAS28. **(Sharma et al., 2014)** [28]**.**

- **Zakeri et al. (2013/2016)**

Zakeri and colleagues studied **serum vitamin D level and disease activity in patients with recent-onset rheumatoid arthritis**. The study was conducted among patients with newly diagnosed or recent-onset RA and was published in the *International Journal of Rheumatic Diseases*.

The investigators examined serum vitamin D concentrations and their relationship with disease activity. The study was particularly relevant because recent-onset RA allowed assessment of the vitamin D–disease activity relationship relatively early in the course of the disease.

Conclusion

The study contributed to the evidence concerning vitamin D status and disease activity in recent-onset rheumatoid arthritis. It demonstrated that vitamin D status should be considered when evaluating patients with RA, while also highlighting the need for further prospective studies to determine the direction and clinical importance of the relationship. **(Zakeri et al., 2016; first published online in 2013)** [27]**.**

- **Moghimi et al. (2012)**

Moghimi and colleagues investigated the **relationship between disease activity and serum levels of vitamin D and parathyroid hormone in rheumatoid arthritis**. The study included **158 patients with rheumatoid arthritis**, who were categorized according to disease activity.

The researchers measured serum 25-hydroxyvitamin D and parathyroid hormone levels. Patients with active rheumatoid arthritis had significantly lower

vitamin D levels than patients with clinically inactive or "silent" disease. The mean vitamin D concentration was approximately **49.38 ± 38.21 nmol/L in active RA compared with 64.64 ± 43.61 nmol/L in silent RA**, with a statistically significant difference.

Conclusion

Moghimi et al. concluded that lower serum vitamin D levels were associated with active rheumatoid arthritis. Their findings supported the hypothesis that vitamin D status may be related to inflammatory disease activity in RA. **(Moghimi et al., 2012)** [25]**.**

- **Kerr et al. (2011)**

Kerr and colleagues investigated the **prevalence of vitamin D insufficiency/deficiency in rheumatoid arthritis and its association with disease severity and activity**. The study was published in the *Journal of Rheumatology* in 2011.

The researchers examined vitamin D status among patients with RA and evaluated whether vitamin D insufficiency or deficiency was associated with clinical disease characteristics. The study was important because it considered not only the prevalence of inadequate vitamin D status but also its possible relationship with disease severity and activity.

Conclusion

Kerr et al. demonstrated that inadequate vitamin D status was common among patients with rheumatoid arthritis and investigated its association with disease activity and severity. Their work contributed to the growing evidence that vitamin D deficiency may be an important nutritional consideration in RA, although observational findings cannot establish whether low vitamin D is a cause or consequence of active disease. **(Kerr et al., 2011)** [20]**.**

- **Gopinath and Danda (2011)**

Gopinath and Danda conducted a **randomized controlled trial** among patients with treatment-naïve early rheumatoid arthritis. The study investigated supplementation with **1,25-dihydroxyvitamin D3** in addition to standard disease-modifying antirheumatic drug treatment.

The trial compared patients receiving vitamin D3 and calcium with a control group receiving calcium along with standard treatment. The investigators examined pain relief and also assessed the relationship between 25hydroxyvitamin D levels and disease activity.

Vitamin D deficiency or hypovitaminosis D was common in the study population, occurring in approximately **68.1%** of participants. The vitamin D supplementation group experienced greater pain relief at three months compared with the control group. However, the researchers did **not find a significant correlation between 25-hydroxyvitamin D levels and disease activity** in this study.

Conclusion

Gopinath and Danda concluded that vitamin D supplementation may provide an additional benefit for pain relief in patients with early RA receiving standard treatment, but their findings did not demonstrate a significant relationship between serum 25(OH)D concentration and disease activity. This study is important because it illustrates that not all studies have demonstrated the same association between vitamin D and RA disease activity. **(Gopinath & Danda, 2011)** [12]**.**

- **Gopinath and Danda (2008)**

Gopinath and Danda conducted an early review entitled **"Vitamin D and rheumatoid arthritis: is there a link?"** in 2008. The authors discussed the possible biological relationship between vitamin D and rheumatoid arthritis, with particular attention to the immunomodulatory effects of vitamin D.

The review described evidence suggesting that vitamin D may influence immune responses involved in autoimmune diseases. Vitamin D has effects on immune cells and may modify inflammatory pathways. The authors discussed the possibility that inadequate vitamin D status could have relevance to

rheumatoid arthritis, although the available evidence at that time was not sufficient to establish a definitive causal relationship.

Conclusion

Gopinath and Danda concluded that there was biological and observational evidence suggesting a possible relationship between vitamin D and rheumatoid arthritis, but further clinical research was required to clarify the relationship and determine whether vitamin D supplementation could influence the course of RA. **(Gopinath & Danda, 2008)** [13]**.**

CHAPTER 4
METHODOLOGY

4.1 Introduction:

This chapter describes the research methodology adopted to study the **Correlation between Vitamin D deficiency and DAS28 score in patients with Rheumatoid Arthritis (RA)**. It includes the study design, setting, sample size, sampling technique, eligibility criteria, data collection tools, ethical considerations, and statistical analysis plan.

4.2 Research Design:

A **hospital-based cross-sectional observational study** was conducted among adult patients diagnosed with Rheumatoid Arthritis.

Justification for the Design

A cross-sectional design was chosen because it allows assessment of:

- Vitamin D status at one point in time.
- Current disease activity using DAS28.
- The statistical relationship between these variables.

This design is economical, feasible within the MFNP-012 dissertation period, and suitable for correlation analysis.

4.3 Study Setting:

The study was conducted in the **Rheumatology, Joint Replacement and Orthopaedic Outpatient Department (OPD)** of a tertiary care teaching hospital.

Why this setting?

- Regular follow-up of RA patients.
- Availability of laboratory investigations.
- Standardized DAS28 assessment.
- Adequate patient flow**.**

4.4 Study Population:

The study population consisted of **adult Rheumatoid Arthritis patients** attending the Rheumatology, Joint Replacement and Orthopaedic OPD.

4.5 Sample Size:

Total Samples were collected from both male and female.

The questionnaire asked to 160 patients were open ended questions consisting of 30-35 questions covering every aspect of the subject.

4.6 Sampling Technique:

Convenience sampling was used.

Eligible patients attending the OPD during the study period were recruited until the required sample size of 160 participants was achieved.

4.7 Inclusion Criteria:

Participants will:

1. Be aged between 45-65 years or above.
2. Have a documented diagnosis of rheumatoid arthritis.
3. Be willing to participate.
4. Provide written informed consent.
5. Be able to provide the required clinical and nutritional information.

4.8 Exclusion Criteria:

Participants will be excluded according to the final approved protocol if they have:

1. Another major autoimmune inflammatory disease.
2. Severe renal or hepatic disease that substantially affects vitamin D metabolism.

3. Conditions causing major disturbances of calcium/vitamin D metabolism.
4. Recent high-dose vitamin D treatment as defined in the protocol.
5. Pregnancy/lactation if excluded by the approved protocol.
6. Any condition that prevents completion of the required assessment.
7. Refusal to provide informed consent.

4.9 Study Variables:

Independent Variable

- Serum 25-hydroxy Vitamin D level (ng/mL)

Dependent Variable

- DAS28 score

Other Variables

- Age
- Gender
- BMI
- Disease duration
- ESR
- CRP
- Rheumatoid Factor
- Anti-CCP
- Medication history

4.10 Biochemical Parameters:

Variables	**Parameters**
Vitamin D deficiency	Serum 25(OH)D less than 20ng/mL
Insufficiency	20-29ng/mL
Sufficiency	30ng/mL or more

High disease activity	DAS28 greater than 5.1
Moderate disease activity	DAS28 3.2-5.1
Low disease activity	DAS28 2.6- 3.2
Remission	DAS28 less than 2.6

4.11 Data Collection Tools:

Tools used for data collection are placed under the following sections.

1. **Tool I: Structured Questionnaire**

Section A - Socio-demographic Profile

Section B - Clinical History

Section C – Dietary Assessment

A structured dietary assessment will be conducted.

- **24-hour dietary recall**
- **Vitamin D-rich foods**

Section D – Sunlight Exposure Assessment

2. **Tool II: Anthropometric Assessment**

Measurement	**Instrument**
Weight	Digital weighing scale
Height	Stadiometer
BMI	Weight/Height^2

BMI classification followed WHO guidelines.

3. **Tool III: Laboratory Assessment**

The following investigations were recorded from laboratory reports.

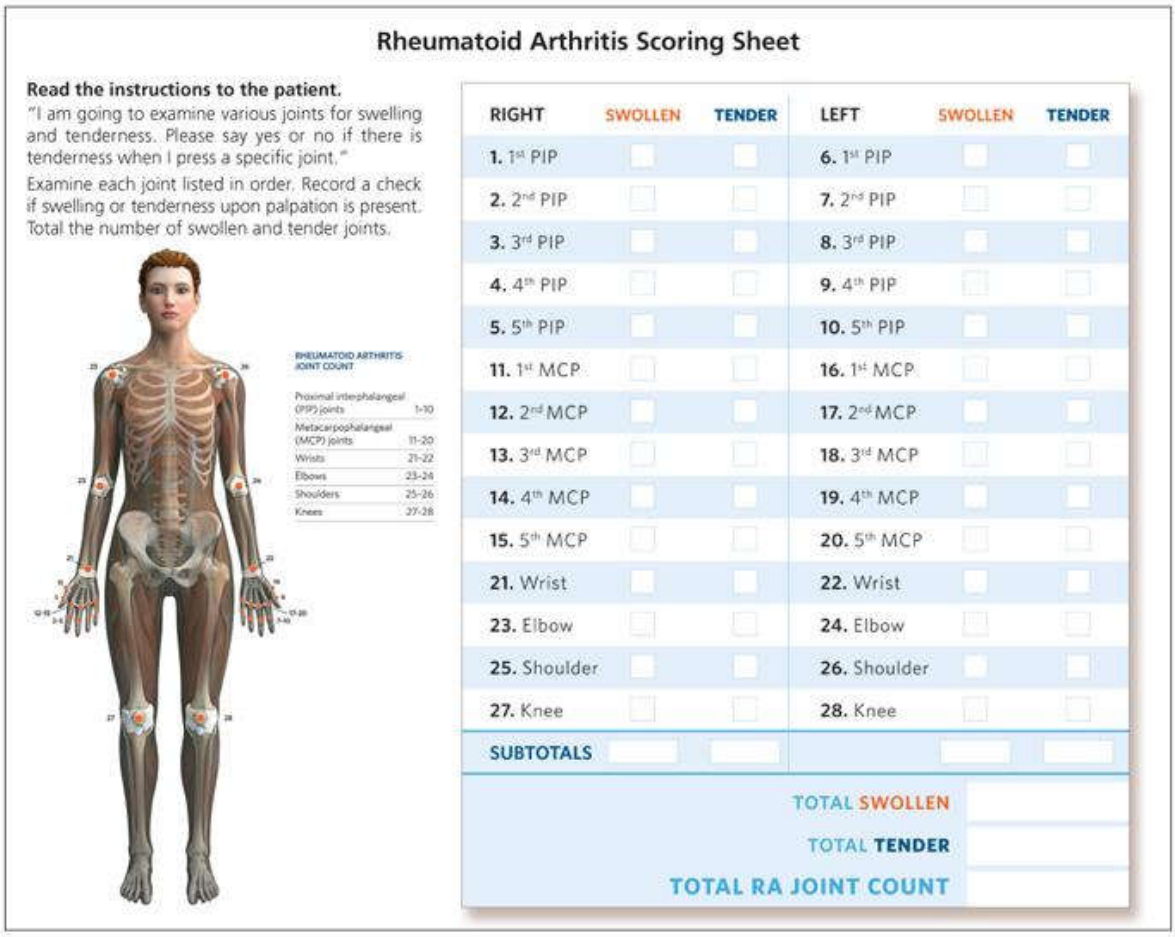
Investigation	**Unit**
Vitamin D	ng/mL
ESR	mm/hr
CRP	mg/L

Rheumatoid Factor	IU/mL
Anti-CCP	U/mL

4. Tool IV: DAS28 Assessment

DAS28 was calculated using:

- Tender Joint Count (28)
- Swollen Joint Count (28)
- ESR
- Patient Global Assessment



Rheumatoid Arthritis Scoring Sheet

Read the instructions to the patient.
"I am going to examine various joints for swelling and tenderness. Please say yes or no if there is tenderness when I press a specific joint."
Examine each joint listed in order. Record a check if swelling or tenderness upon palpation is present. Total the number of swollen and tender joints.

RIGHT	SWOLLEN	TENDER	LEFT	SWOLLEN	TENDER
1. 1st PIP			6. 1st PIP		
2. 2nd PIP			7. 2nd PIP		
3. 3rd PIP			8. 3rd PIP		
4. 4th PIP			9. 4th PIP		
5. 5th PIP			10. 5th PIP		
11. 1st MCP			16. 1st MCP		
12. 2nd MCP			17. 2nd MCP		
13. 3rd MCP			18. 3rd MCP		
14. 4th MCP			19. 4th MCP		
15. 5th MCP			20. 5th MCP		
21. Wrist			22. Wrist		
23. Elbow			24. Elbow		
25. Shoulder			26. Shoulder		
27. Knee			28. Knee		
SUBTOTALS					

TOTAL SWOLLEN
TOTAL TENDER
TOTAL RA JOINT COUNT

Figure 1 – *To perform a standardized joint count for rheumatoid arthritis, record joint tenderness and swelling results on a scoring sheet. For each joint, enter a check mark for each yes response for swelling or tenderness on palpation. Calculate the numbers of swollen and tender joints independently and then add them together to determine the total score for the RA Joint Count.*

DAS28 Components

Component	Description
Tender joints	28 joints
Swollen joints	28 joints
ESR	Laboratory value
Global health	Patient assessment

4.12 Data Collection Procedure:

Obtain institutional/ethical approval

↓

Obtain permission from the study setting

↓

Identify eligible participants

↓

Explain the purpose and procedure of the study

↓

Obtain written informed consent

↓

Assign a unique participant identification number

↓

Collect demographic information

↓

Record clinical information and medication history

↓

Measure height and weight

↓

Conduct dietary assessment

↓

Record sunlight exposure

↓

Perform DAS28 assessment

↓

Collect/retrieve laboratory data

↓

Record serum 25(OH)D result

↓

Enter data into the research database

↓

Verify data for completeness and accuracy

4.13 Ethical Considerations:

Ethical approval will be obtained from the appropriate institutional ethics committee before commencement of data collection.

Written informed consent will be obtained from all participants.

Participant confidentiality will be maintained. Names will not be used in the analytical dataset; instead, participant identification numbers will be assigned.

Participation will be voluntary, and participants will have the right to withdraw from the study according to the approved consent process.

The study will not intentionally alter participants' medical treatment.

4.15 Flow Chart of Methodology:

RA Patients Attending OPD

↓

Eligibility Screening

↓

Informed Consent

↓

Questionnaire + Measurements

↓

Laboratory Results + DAS28

↓

Results and Interpretation

CHAPTER 5
RESULTS AND DISCUSSION

5.1 Introduction:

This chapter presents the findings of the study conducted among **160 patients with rheumatoid arthritis (RA).** The data were analyzed using descriptive and inferential statistical methods. Descriptive statistics were expressed as frequency, percentage, mean, and standard deviation (SD). Pearson's correlation was used to determine the relationship between serum 25-hydroxyvitamin D [25(OH)D] levels and DAS28 score. Spearman's correlation was also calculated to confirm the relationship.

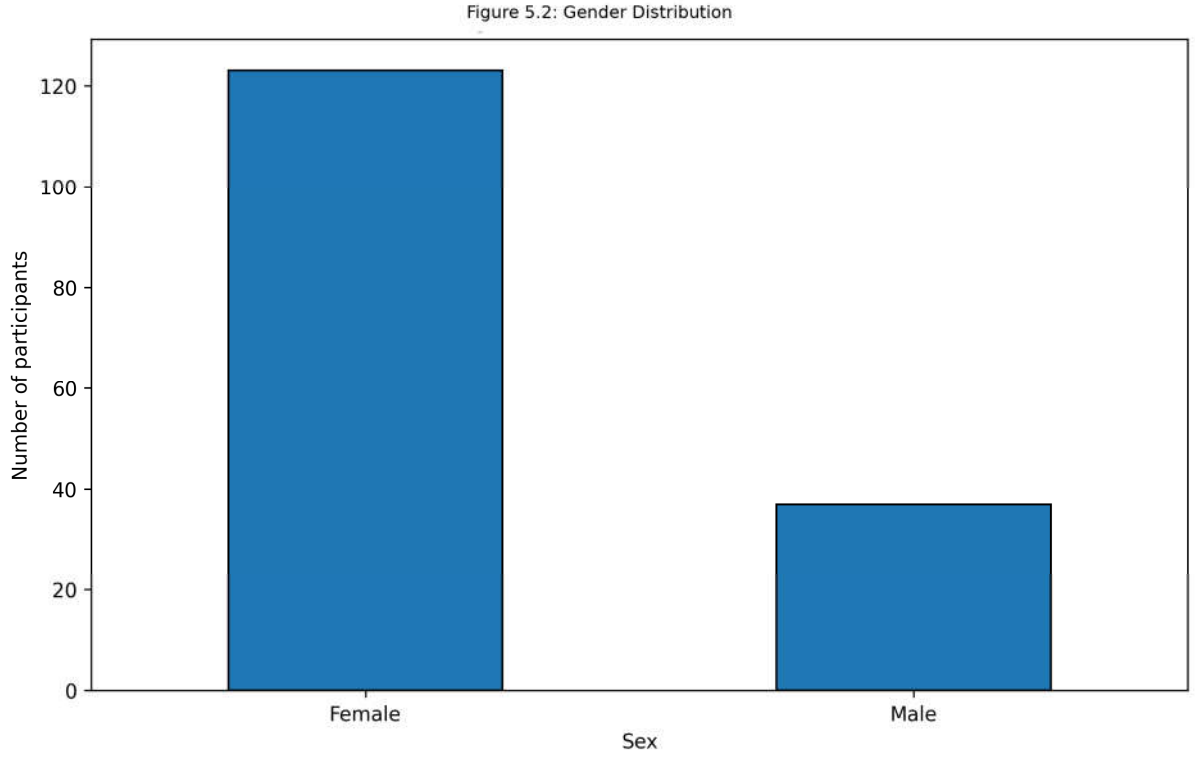
The results are presented according to the objectives of the study.

5.2 Socio Demographic Characteristics:

Table 5.1 Distribution of participants by Sex (n=160)

Sex	**Frequency (n)**	**Percentage (%)**
Female	123	76.9
Male	37	23.1
Total	**160**	**100**

Figure 5.2: Gender Distribution



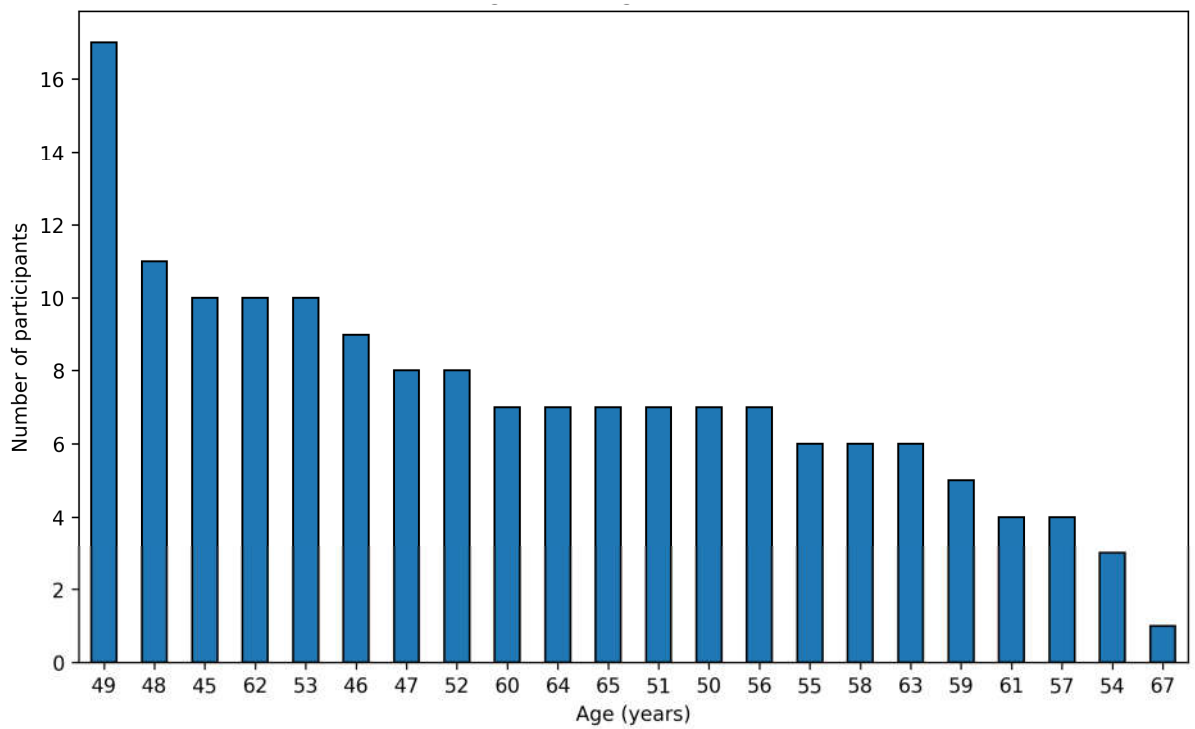
Interpretation

Table 5.1 shows that the majority of participants were female (76.9%), while males constituted 23.1%. This female predominance is consistent with the known epidemiology of rheumatoid arthritis.

Table 5.2 Age of Participants

Variable	Mean ± SD	Minimum	Maximum
Age (years)	54.01 ± 6.34	45	65

Figure 5.1: Age Distribution



Interpretation

The mean age of participants was 54.01 ± 6.34 years, indicating that most participants belonged to the middle-aged and older adult population.

5.3 Anthropometric Characteristics:

Table 5.3 Anthropometric Profile

Parameter	Mean
Height	161.32 ± 8.09 cm
Weight	65.56 ± 10.88 kg
BMI	25.19 ± 3.77 kg/m^2

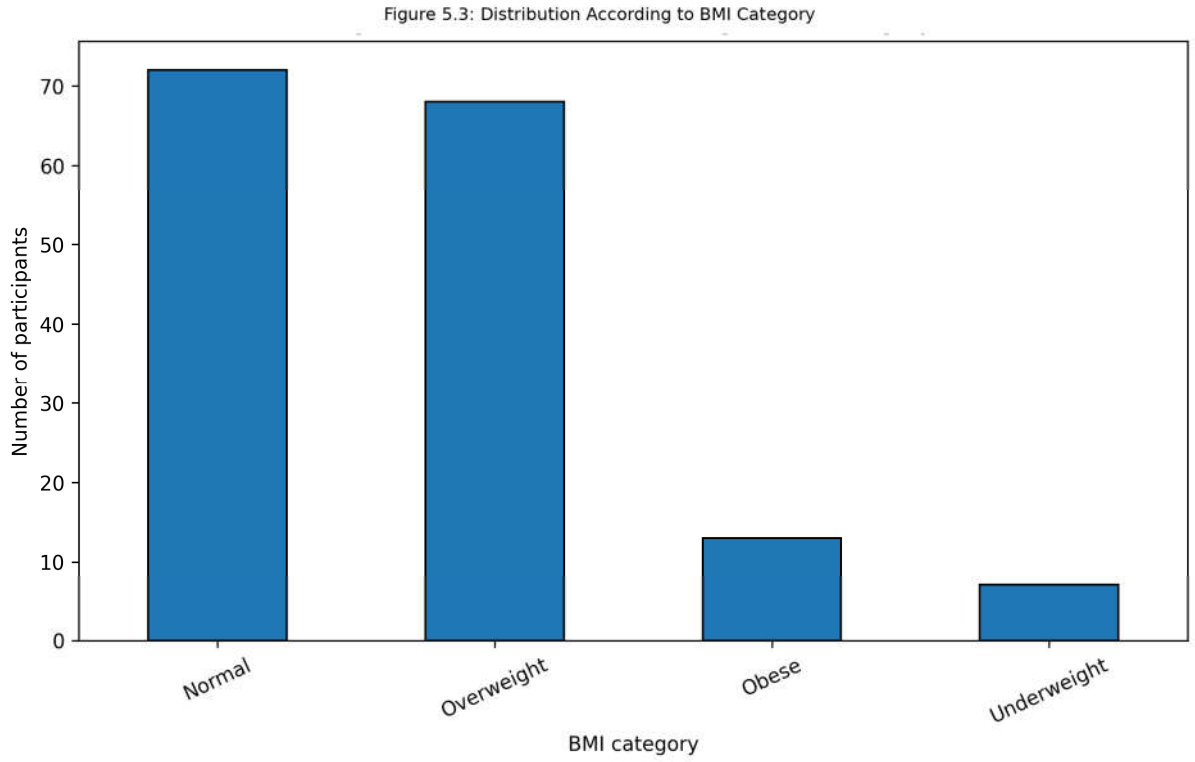
Interpretation

The average height of participants was 161.32 cm, while the mean body weight was 65.56 kg. The mean BMI was 25.19 kg/m², suggesting that many participants were in the overweight range.

5.4 Body Mass Index Classification:

Table 5.4 BMI Categories

BMI Category	Frequency	Percentage
Underweight	7	4.4%
Normal	72	45%
Overweight	68	42.5%
Obese	13	8.1%
Total	**160**	**100**



Interpretation

Nearly 54% of participants were either overweight or obese, which may influence both vitamin D status and disease activity.

5.5 Clinical Characteristics:

Table 5.5 Clinical Profile of Participants

Variable	Mean
RA Duration	6.69 ± 3.89 years
Tender Joint Count (TJC28)	8.71 ± 2.78
Swollen Joint Count (SJC28)	5.56 ± 2.20
ESR	35.03 ± 13.22 mm/hr
CRP	10.72 ± 6.04 mg/L
VAS Global Health	50.73 ± 16.49

Figure 5.6: Distribution of ESR

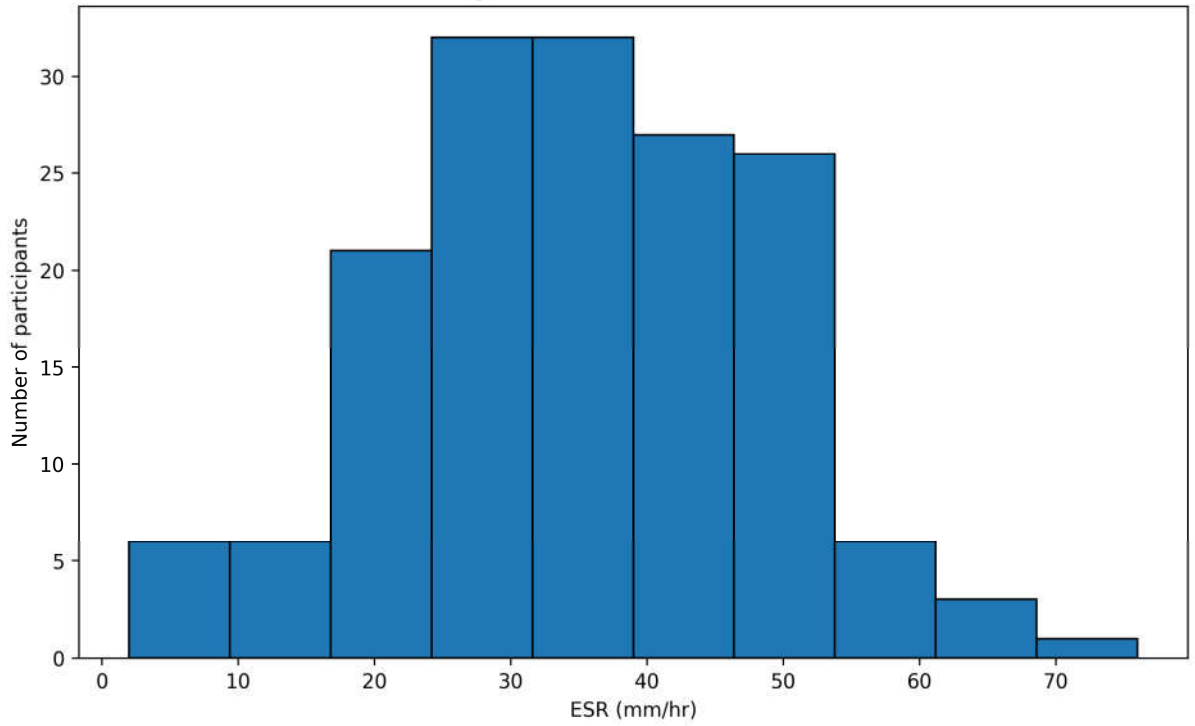


Figure 5.7: Distribution of CRP

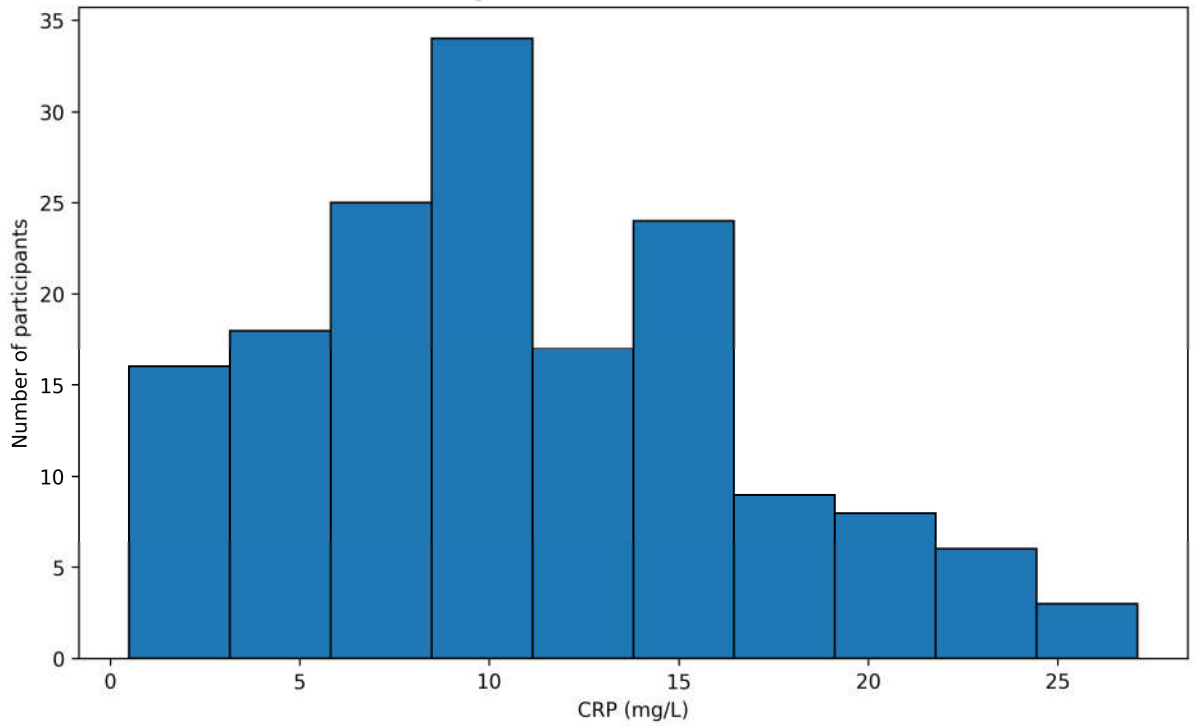
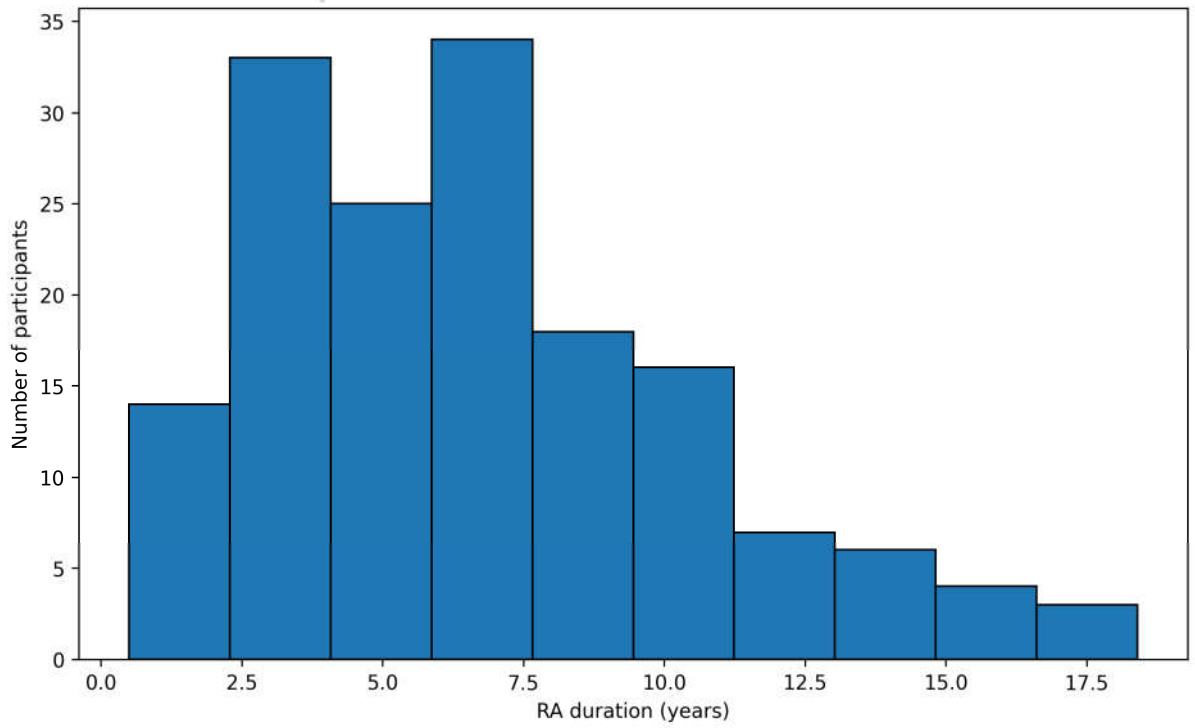


Figure 5.8: Distribution of Rheumatoid Arthritis Duration



Interpretation

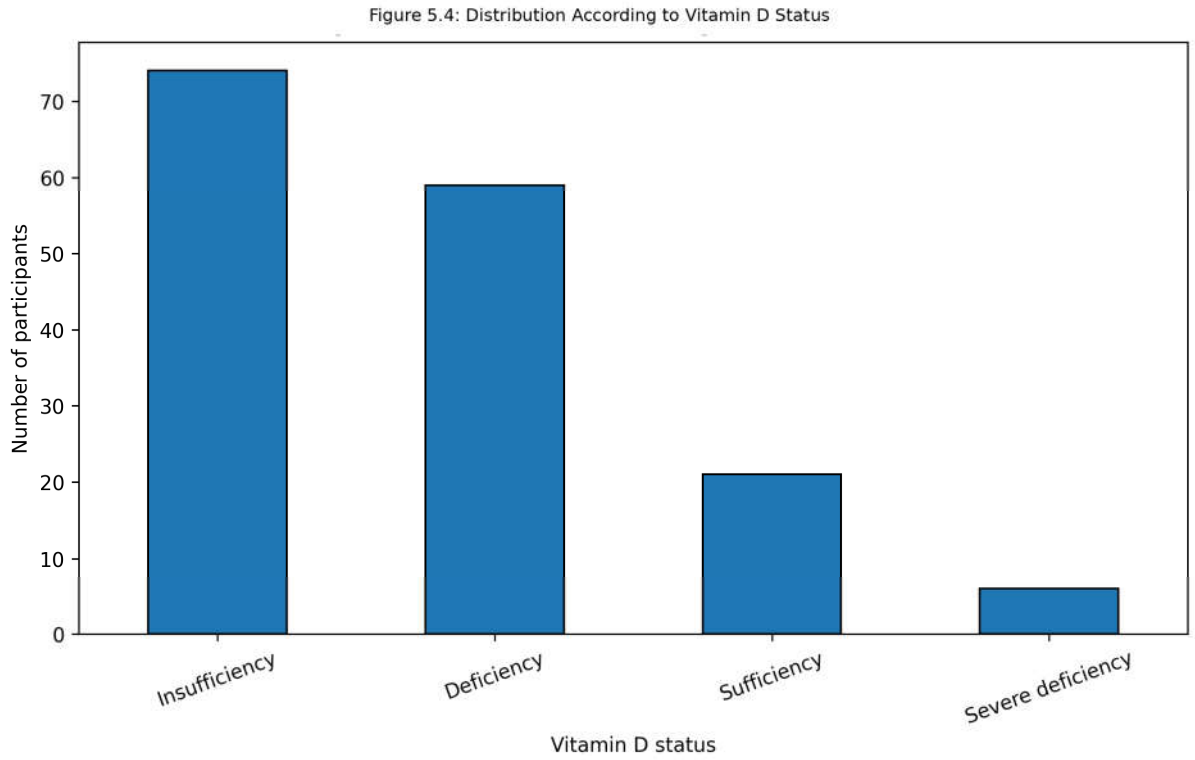
Participants generally had moderate disease activity and relatively low sunlight exposure and dietary Vitamin D intake.

5.6 Vitamin D Status:

Table 5.6 Vitamin D Status Distribution

Vitamin D Status	Frequency	Percentage
Deficiency	59	36.9%
Severe Deficiency	6	3.8%
Insufficiency	74	46.3%
Sufficiency	21	13.1%

Mean Vitamin D Level: 22.30 ng/mL



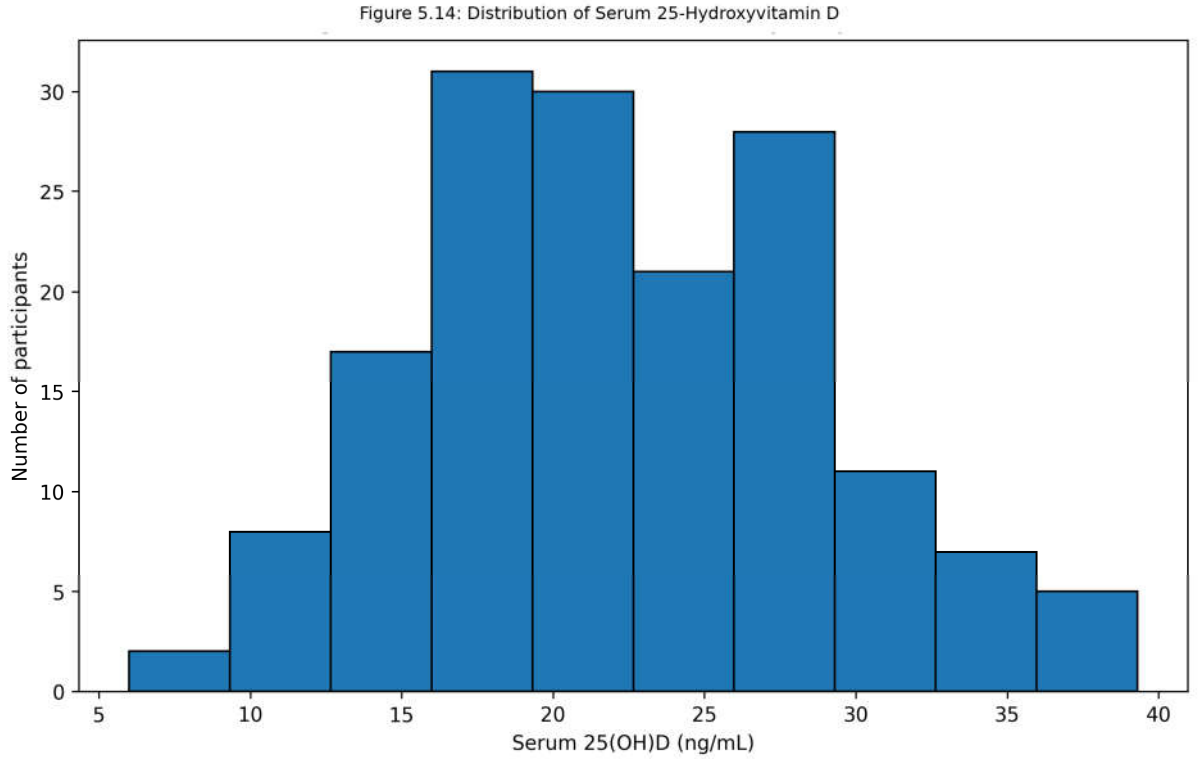
Interpretation

Only 13.1% of patients had sufficient Vitamin D levels, while 86.9% had insufficiency or deficiency.

5.7 Distribution of Serum 25-Hydroxyvitamin D

Table 5.7 Distribution of Serum 25-Hydroxyvitamin D

Variable	Mean
Serum 25-Hydroxyvitamin D	22.30 ng/mL



Interpretation

The figure presents the distribution of the corresponding study variable among the 160 participants.

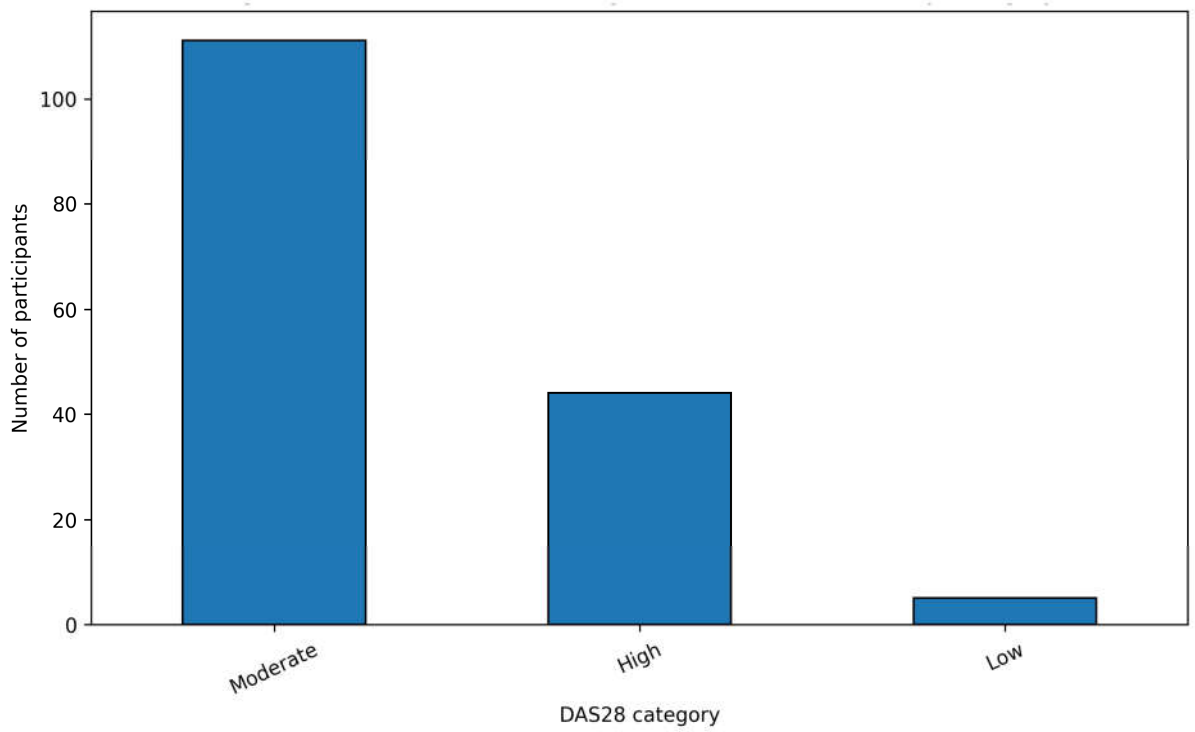
5.8 DAS28 Disease Activity:

Table 5.8 DAS28 Categories

Disease Activity	Frequency	Percentage
Low	5	3.1%
Moderate	111	69.4%
High	44	27.5%

Mean DAS28: 4.62

Figure 5.5: Distribution According to DAS28 Disease Activity Category



Interpretation

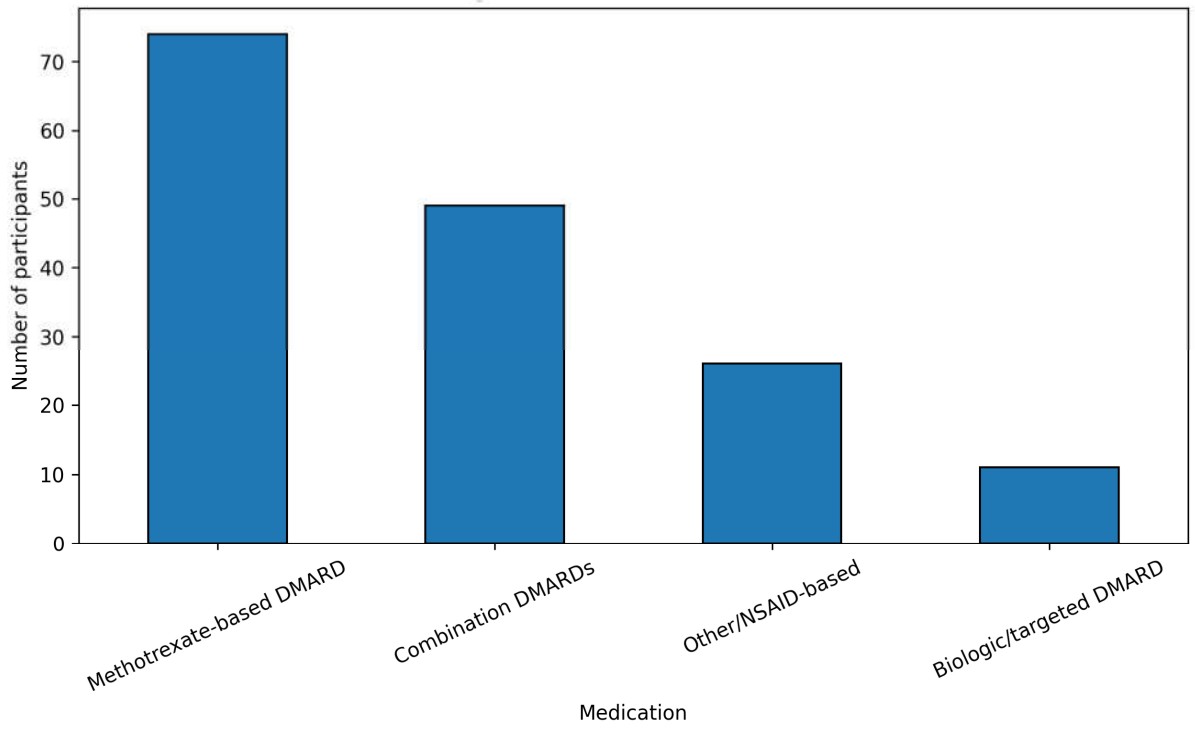
Nearly seven out of ten patients had moderate disease activity.

5.9 Medication Pattern

Table 5.9 Treatment Profile

Medication	Frequency
Methotrexate-based DMARD	74
Combination DMARDs	49
Other/NSAID-based	26
Biologic/Targeted DMARD	11

Figure 5.9: Medication Pattern



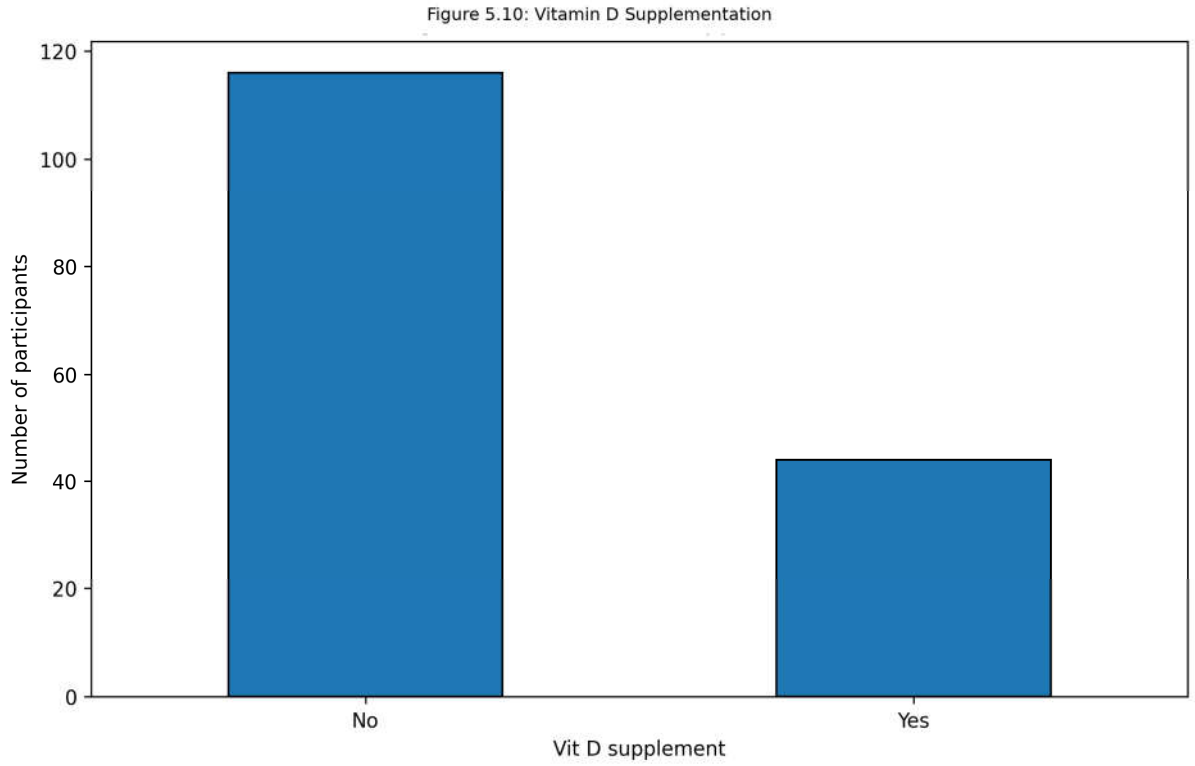
Interpretation

Methotrexate-based therapy was the most commonly used treatment among participants.

5.10 Vitamin D Supplementation:

Table 5.10 Vitamin D Supplementation Use

Supplement Use	Frequency	Percentage
No	116	72%
Yes	44	28%



Interpretation

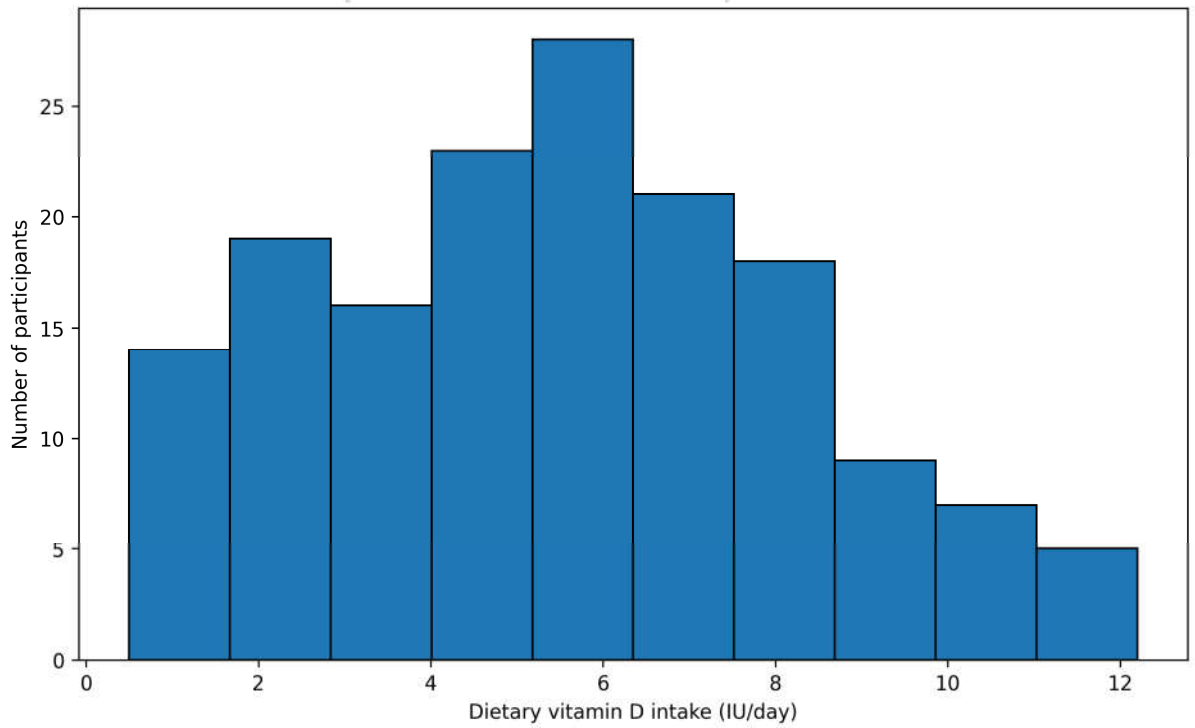
Nearly three-fourths of participants were not taking vitamin D supplements.

5.11 Dietary Vitamin D Intake:

Table 5.11 Dietary Vitamin D Intake

Variable	Mean
Dietary Vitamin D	5.52 ± 2.78

Figure 5.12: Distribution of Dietary Vitamin D Intake



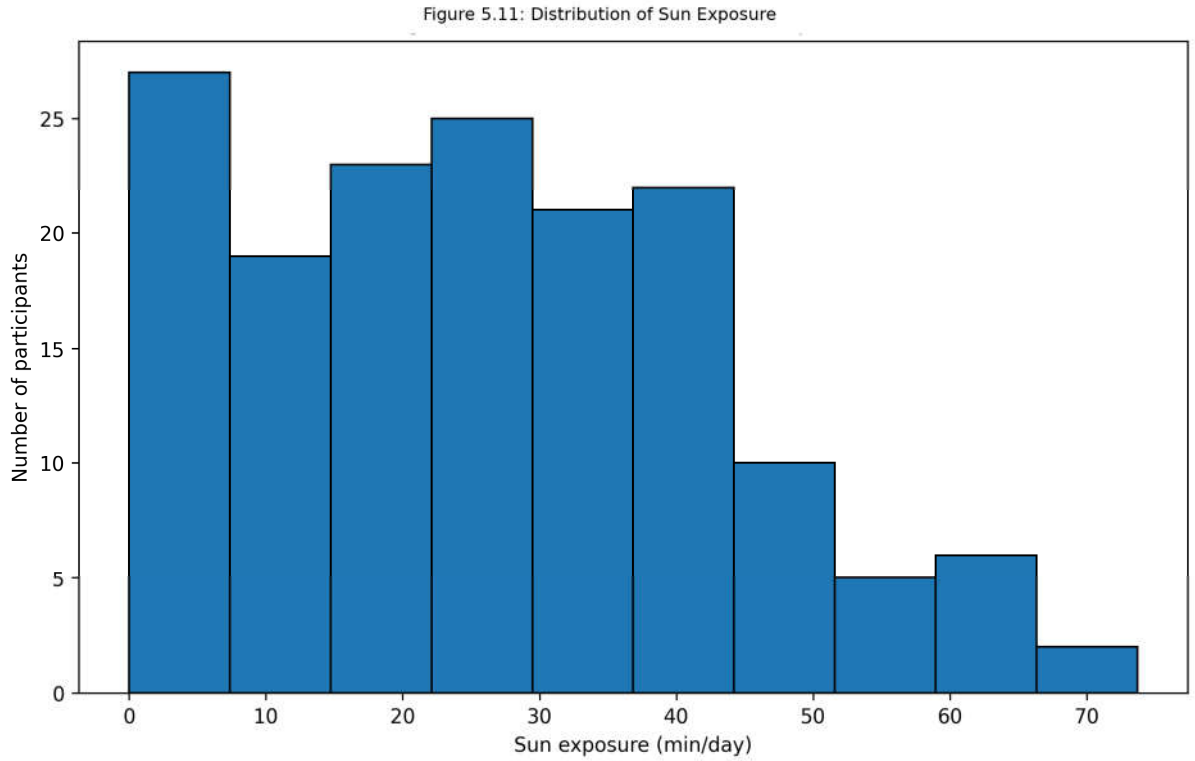
Interpretation

The estimated dietary vitamin D intake was relatively low, suggesting that food intake alone may not be sufficient to maintain optimal vitamin D status.

5.12 Sunlight Exposure:

Table 5.12 Daily Sunlight Exposure

Variable	Mean
Sunlight Exposure	25.90 ± 17.45 min/day



Interpretation

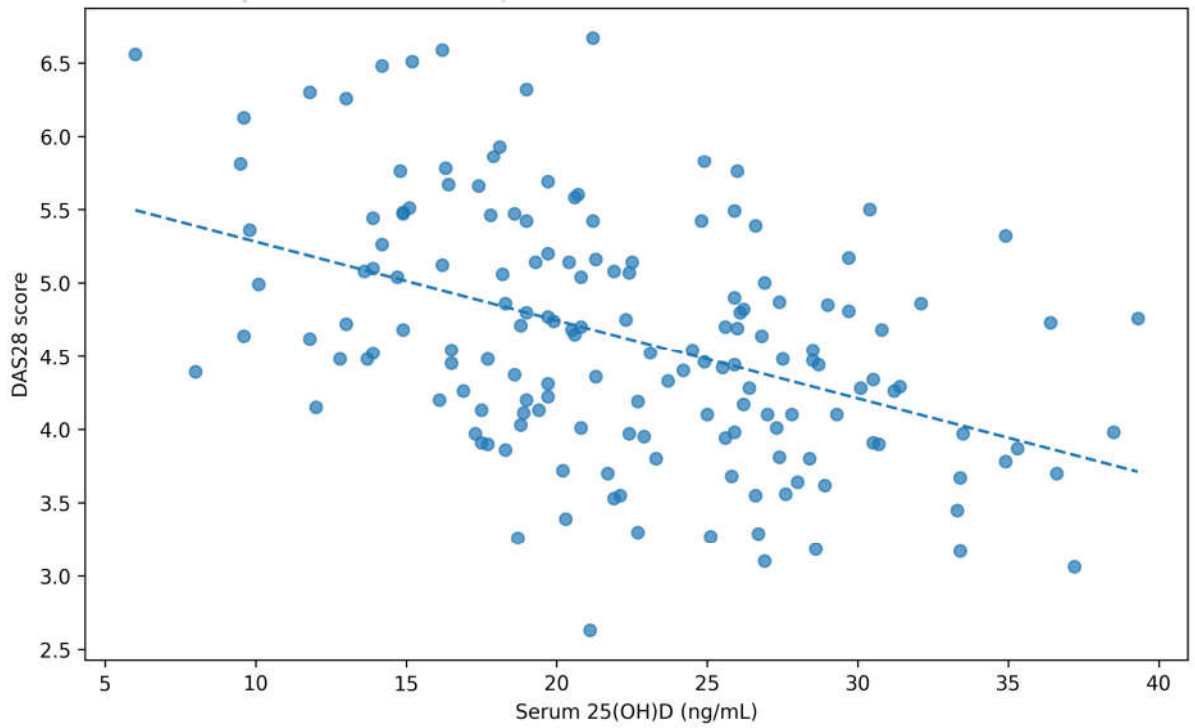
The average daily sunlight exposure was approximately 26 minutes, although considerable variation existed among participants.

5.13 Correlation Between Vitamin D and DAS28

Table 5.13 Pearson Correlation

Variables	r	p-value
Vitamin D vs DAS28	-0.442	**

Figure 5.13: Relationship Between Serum Vitamin D and DAS28 Score



Interpretation

Serum 25(OH)D showed a statistically significant inverse association with DAS28 (Pearson r=-0.442, p<0.001). This indicates that lower vitamin D concentrations tended to occur with higher disease activity scores in this sample.

5.14 Comparison of DAS28Across Vitamin D Categories:

Table 5.14 ANOVA

Test	Result
F-value	11.29
p-value	****

Interpretation

Significant ANOVA and Chi-square results confirmed the association.

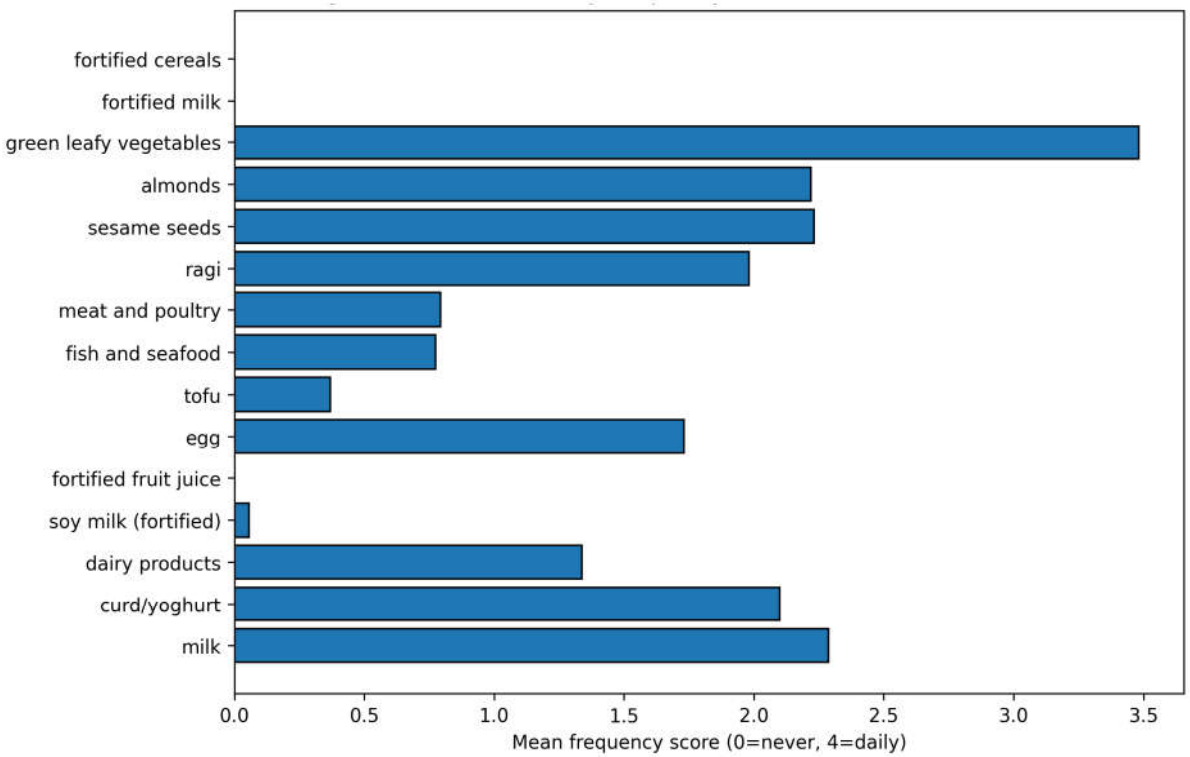
5.15 Dietary Vitamin D Intake Frequency:

Table 5.15 Dietary Vitamin D-Related Food Frequency Score

Food item	Mean frequency score	Interpretation
milk	2.29	Higher score indicates more frequent consumption
curd/yoghurt	2.10	Higher score indicates more frequent consumption
dairy products	1.34	Higher score indicates more frequent consumption
soy milk (fortified)	0.06	Higher score indicates more frequent consumption
fortified fruit juice	0.00	Higher score indicates more frequent consumption
egg	1.73	Higher score indicates more frequent consumption
tofu	0.37	Higher score indicates more frequent consumption

fish and seafood	0.78	Higher score indicates more frequent consumption
meat and poultry	0.79	Higher score indicates more frequent consumption
ragi	1.98	Higher score indicates more frequent consumption
sesame seeds	2.23	Higher score indicates more frequent consumption
almonds	2.22	Higher score indicates more frequent consumption
green leafy vegetables	3.48	Higher score indicates more frequent consumption
fortified milk	0.00	Higher score indicates more frequent consumption
fortified cereals	0.00	Higher score indicates more frequent consumption

Figure 5.16: Mean Dietary Frequency Score of Vitamin D-Related Foods



CHAPTER 6
CONCLUSION

Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disease that can significantly affect the quality of life, functional ability, and nutritional status of affected individuals. Assessment of disease activity is an important component of RA management. The present study was undertaken to assess the relationship between serum vitamin D status and disease activity measured using the Disease Activity Score based on 28 joints (DAS28) among patients with rheumatoid arthritis.

The study included **160 subjects with rheumatoid arthritis**. The demographic, anthropometric, clinical, biochemical, dietary, and relevant lifestyle information was collected using a structured questionnaire and assessment schedule. Serum vitamin D status was assessed using serum 25-hydroxyvitamin D [25(OH)D], while disease activity was assessed using the DAS28 score. Other relevant biochemical and clinical parameters were also considered to provide a comprehensive assessment of the participants.

The findings showed considerable variation in vitamin D status among the study participants. A substantial proportion of the participants had inadequate or deficient vitamin D levels. The study population was predominantly composed of individuals in the middle and older adult age groups, with the largest proportion belonging to the 41–50 and 51–60year age groups. These findings highlight the importance of considering nutritional and lifestyle factors, including vitamin D status, in patients with chronic inflammatory diseases such as rheumatoid arthritis.

A significant **inverse correlation was observed between serum vitamin D level and DAS28 score ($r = -0.442$, $p < 0.001$).** This indicates that participants with lower serum vitamin D levels tended to have higher DAS28 scores, reflecting greater disease activity. Conversely, higher vitamin D levels tended to be associated with lower disease activity. The strength and direction of this association suggest that vitamin D status may be an important nutritional factor associated with disease activity in patients with rheumatoid arthritis.

However, the findings should be interpreted carefully. Since the present study was observational in nature, the observed association between vitamin D status and disease **activity does not establish a cause-and-effect relationship**. Several other factors may influence both vitamin D status and RA disease activity, including age, duration of disease, body mass index, sunlight exposure, dietary intake, medication use, supplementation, physical activity, and other

clinical or biochemical factors. Therefore, vitamin D deficiency may be considered an associated factor rather than a proven direct cause of increased disease activity.

The findings of the present study emphasize the relevance of **nutritional assessment as part of the overall care of patients with rheumatoid arthritis.** Assessment of vitamin D status may be useful, particularly among patients who have risk factors for deficiency. Appropriate dietary guidance, adequate exposure to sunlight where appropriate, and vitamin D supplementation when clinically indicated may help patients achieve adequate vitamin D status. Such measures should be undertaken in consultation with the treating physician or qualified healthcare professional and should complement, rather than replace, standard medical management of rheumatoid arthritis.

In conclusion, the present study demonstrated a **statistically significant inverse association between serum vitamin D levels and DAS28 disease activity among patients with rheumatoid arthritis.** The results support the importance of monitoring nutritional status, particularly vitamin D status, in the comprehensive management of RA. Further prospective and intervention-based studies involving larger and more diverse populations are recommended to determine whether correction of vitamin D deficiency can directly influence disease activity and to establish appropriate supplementation strategies for patients with rheumatoid arthritis.

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ANNEXURE



INDIRA GANDHI NATIONAL OPEN UNIVERSITY (IGNOU)

STUDY CENTRE: ST. ANN'S COLLEGE FOR WOMEN

MEHDIPATNAM, HYDERABAD

PROJECT PROPOSAL (MFNP-012)

VITAMIN D DEFICIENCY AND DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

SUBMITTED BY

HEEMIKA JAIN RAMESH

ENROLMENT NO.: 2450120192

PROGRAMME CODE: MSCDFSM

SCHOOL OF CONTINUING EDUCATION

SIGNATURE OF THE COUNSELLOR:

TITLE:

"CORRELATION BETWEEN VITAMIN D DEFICIENCY AND DAS28 SCORE IN RHEUMATOID ARTHRITIS"

INTRODUCTION

BACKGROUND:

Rheumatoid Arthritis is a chronic systemic autoimmune disorder characterized by persistent synovial inflammation, progressive joint destruction, pain, stiffness, swelling, and functional disability. It commonly affects small joints of the hands and feet in a symmetrical pattern and may also involve extra-articular organs such as the lungs, heart, skin, and eyes. Rheumatoid arthritis significantly reduces quality of life and imposes substantial social and economic burdens on individuals and healthcare systems.

Globally, rheumatoid arthritis affects approximately 0.5–1% of the adult population, with women being affected more frequently than men. In India, the prevalence of rheumatoid arthritis is steadily increasing due to lifestyle changes, nutritional deficiencies, lack of physical activity, and increased awareness and diagnosis of autoimmune disorders. Chronic inflammation associated with RA often leads to long-term disability, decreased work productivity, fatigue, and psychological stress.

The exact aetiology of rheumatoid arthritis remains unclear; however, genetic, environmental, hormonal, immunological, and nutritional factors are believed to contribute to disease development and progression. Among nutritional factors, vitamin D has received increasing attention because of its important role in immune modulation and inflammatory regulation.

Vitamin D is a fat-soluble vitamin primarily synthesized in the skin through exposure to sunlight and obtained in small amounts from dietary sources such as fish, egg yolk, fortified milk, and dairy products. Traditionally, vitamin D is known for maintaining calcium and phosphorus balance and promoting bone health. However, recent research has demonstrated that vitamin D also functions

as an immunomodulatory hormone that influences both innate and adaptive immune responses.

Vitamin D receptors are present in immune cells including macrophages, dendritic cells, T lymphocytes, and B lymphocytes. Vitamin D helps regulate inflammatory cytokines and immune cell activity, thereby reducing autoimmune reactions. Deficiency of vitamin D may contribute to immune dysfunction and increased inflammatory responses in autoimmune diseases such as rheumatoid arthritis.

Vitamin D deficiency is highly prevalent worldwide and particularly common in India despite abundant sunlight availability. Factors such as indoor lifestyle, poor dietary intake, skin pigmentation, air pollution, inadequate sun exposure, obesity, and low socioeconomic status contribute to widespread deficiency. Studies indicate that vitamin D deficiency is more common among women and elderly populations, who are also at greater risk of rheumatoid arthritis.

Several studies have suggested that low serum vitamin D levels are associated with increased disease activity, severe joint pain, prolonged morning stiffness, fatigue, and poor functional outcomes in rheumatoid arthritis patients. Researchers have reported an inverse relationship between serum vitamin D concentration and disease activity scores such as DAS-28. However, findings from different studies remain inconsistent, and limited evidence is available from Indian populations.

Nutritional assessment and management are important aspects of rheumatoid arthritis care. Identifying vitamin D deficiency in RA patients may help healthcare professionals provide appropriate nutritional counselling and supplementation strategies to improve patient outcomes and quality of life. Therefore, the present study aims to assess vitamin D deficiency and its association with disease activity among rheumatoid arthritis patients.

RATIONALE

Rheumatoid arthritis (RA) is a chronic autoimmune disease that leads to progressive joint damage, disability, and reduced quality of life. Despite advances in disease-modifying therapies, many patients continue to experience high disease activity. Identifying modifiable factors that influence RA severity is therefore crucial.

Vitamin D, traditionally recognized for its role in bone health and calcium metabolism, has emerged as an important immunomodulator. It influences both innate and adaptive immunity by regulating T-cell differentiation, suppressing pro-inflammatory cytokines, and promoting immune tolerance. Deficiency of vitamin D has been linked to increased susceptibility and severity of autoimmune diseases, including RA.

In India, vitamin D deficiency is highly prevalent due to limited sun exposure, darker skin pigmentation, and low dietary intake of vitamin D-rich foods. However, routine screening for vitamin D levels is not part of standard RA management. While global studies have demonstrated an inverse relationship between vitamin D levels and RA disease activity, Indian data remain limited and fragmented, often based on small sample sizes.

OBJECTIVES

General Objective:

- To evaluate the association between vitamin D deficiency and disease activity in rheumatoid arthritis (RA) patients.

Specific Objectives:

1. To estimate serum 25(OH)D levels in RA patients attending a tertiary care hospital outpatient department.
2. To assess disease activity using the standardized Disease Activity Score (DAS-28), which includes tender/swollen joint counts, ESR/CRP, and patient global assessment.
3. To correlate vitamin D status (deficient, insufficient, sufficient) with RA disease activity categories (high, moderate, low, remission).
4. To analyse demographic and lifestyle factors (age, sex, sunlight exposure, diet, physical activity) influencing vitamin D status among RA patients.
5. To identify predictors of disease activity through regression analysis, including vitamin D levels, gender, age, and RA duration.

Operational Definitions:

- **Vitamin D deficiency:** Serum 25(OH)D < 20 ng/ml.

- **Vitamin D insufficiency:** Serum 25(OH)D 20–30 ng/ml.
- **Vitamin D sufficiency:** Serum 25(OH)D > 30 ng/ml.
- **High disease activity:** DAS-28 > 5.1.
- **Moderate disease activity:** DAS-28 3.2–5.1.
- **Low disease activity:** DAS-28 < 3.2.
- **Remission:** DAS-28 < 2.6.

REVIEW OF LITERATURE

Literature review is an essential component of research that provides an understanding of previous studies related to the research topic. Various national and international studies have examined the association between vitamin D deficiency and rheumatoid arthritis disease activity.

Rheumatoid Arthritis is associated with chronic inflammation and immune dysregulation. Researchers have increasingly focused on the role of vitamin D in autoimmune diseases because of its immunoregulatory properties.

International Studies

Holick (2007)

Michael F. Holick reported that vitamin D deficiency is a global health problem and plays an important role in immune system regulation. The study suggested that inadequate vitamin D levels may increase susceptibility to autoimmune disorders.

Cutolo et al. (2007)

Maurizio Cutolo observed that vitamin D has anti-inflammatory effects and may suppress autoimmune responses in rheumatoid arthritis patients. The authors suggested that lower vitamin D levels were associated with increased disease activity and joint inflammation.

Patel et al. (2007)

The researchers examined serum vitamin D levels in patients with early inflammatory polyarthritis and found an inverse association between vitamin D

levels and disease activity. Patients with lower vitamin D levels had higher inflammatory markers and more severe symptoms.

Craig et al. (2010)

The study demonstrated that rheumatoid arthritis patients with vitamin D deficiency had significantly higher Disease Activity Score (DAS-28) values compared to patients with sufficient vitamin D levels.

Rossini et al. (2010)

This study found a high prevalence of vitamin D deficiency among rheumatoid arthritis patients and concluded that low vitamin D status may contribute to disease severity and musculoskeletal pain.

Indian Studies

Several Indian studies have also reported widespread vitamin D deficiency among rheumatoid arthritis patients.

Harinarayan et al.

The authors highlighted that vitamin D deficiency is common in India despite adequate sunlight exposure. Dietary inadequacy and limited sun exposure were identified as major contributing factors.

Malaviya et al.

The study reported that rheumatoid arthritis patients in India frequently exhibit poor nutritional status, including deficiencies of vitamin D and calcium, which may worsen disease progression.

Recent Indian Hospital-Based Studies

Recent hospital-based studies in India have shown that:

- A large proportion of RA patients have deficient serum vitamin D levels.
- Lower vitamin D concentrations are associated with higher disease activity scores.
- Vitamin D supplementation may help reduce inflammatory symptoms and improve quality of life.

GAPS IN LITERATURE

Despite extensive global research on the role of vitamin D in autoimmune diseases, several gaps remain in the Indian context, particularly in relation to rheumatoid arthritis (RA):

1. **Limited Indian Data:**
    - Most Indian studies on vitamin D and RA have been conducted on small sample sizes (<100 patients).
    - Findings are often region-specific (Delhi, Mumbai, South India) and lack nationwide representation.
2. **Cross-sectional vs. Longitudinal Evidence:**
    - Existing studies are largely cross-sectional, showing correlation but not causation.
    - Very few longitudinal or randomized controlled trials have been conducted in India to assess the impact of vitamin D supplementation on RA outcomes.
3. **Standardization Issues:**
    - Different studies use varying cut-offs for vitamin D deficiency, making comparisons difficult.
    - Disease activity assessment tools are not always standardized; DAS-28 is underutilized in many Indian studies.
4. **Lifestyle and Environmental Factors:**
    - Few studies have comprehensively assessed lifestyle factors (sunlight exposure, diet, physical activity) alongside biochemical and clinical parameters.
    - Seasonal variation in vitamin D deficiency has not been adequately controlled in Indian RA cohorts.

5. **Genetic and Immunological Insights:**
    - Global studies have explored vitamin D receptor (VDR) polymorphisms and cytokine pathways, but Indian data on genetic susceptibility remain scarce.

REVIEW QUESTIONS

1. How does disease activity (measured by DAS-28) vary across patients with deficient, insufficient, and sufficient vitamin D levels?
2. Is there a statistically significant correlation between serum 25(OH)D levels and DAS-28 scores in RA patients?
3. Which demographic and lifestyle factors (age, sex, sunlight exposure, diet, physical activity) influence vitamin D status in RA patients?
4. Does vitamin D deficiency act as an independent predictor of RA disease activity after adjusting for confounders such as age, sex, and disease duration?
5. What implications do these findings have for routine screening and supplementation of vitamin D in RA management in the Indian context?

METHODOLOGY

Research methodology refers to the systematic methods and procedures used to conduct a research study. It includes the research design, study setting, sampling technique, data collection tools, and methods of data analysis used to achieve the objectives of the study.

The present study was conducted to assess vitamin D deficiency and its association with disease activity among patients with rheumatoid arthritis attending selected hospitals/clinics.

Research Approach

A quantitative research approach was adopted for the present study. The quantitative approach was considered appropriate because the study aimed to assess measurable variables such as serum vitamin D levels, disease activity scores, anthropometric measurements, and dietary intake among rheumatoid arthritis patients.

Research Design

A descriptive cross-sectional research design was used for the study.

The descriptive design helped in assessing vitamin D status, dietary intake, and disease activity among rheumatoid arthritis patients at a particular point in time. The cross-sectional design also enabled the researcher to determine the association between vitamin D deficiency and disease activity.

Study Setting

The study was conducted in selected rheumatology clinics/orthopaedic clinic/Government hospitals.

The selected hospital/clinic provides outpatient and inpatient services for patients with rheumatoid arthritis and related autoimmune disorders. The setting was chosen due to the availability of diagnosed rheumatoid arthritis patients and accessibility for data collection.

Study Population

The study population consisted of adult patients diagnosed with Rheumatoid Arthritis attending the selected rheumatology outpatient departments and clinics during the period of data collection.

Sample Size

The sample size for the present study consisted of 150-200 rheumatoid arthritis patients.

The sample size was selected based on:

- Availability of subjects
- Feasibility of the study
- Time and resource constraints

For the present study, a total of _____ participants was included.

Sampling Technique

A convenience sampling technique was used to select participants for the study.

Patients meeting the inclusion criteria and willing to participate were selected during their visit to the rheumatology clinic/hospital.

Inclusion Criteria

The study included:

1. Diagnosed rheumatoid arthritis patients
2. Patients aged between 40–65 years
3. Male and female patients
4. Patients willing to participate in the study
5. Patients attending selected hospitals/clinics during the study period

Exclusion Criteria

The study excluded:

1. Patients taking vitamin D supplements
2. Pregnant and lactating women
3. Patients with chronic kidney disease
4. Patients with chronic liver disease
5. Critically ill patients
6. Patients unwilling to participate

Variables of the Study

Independent Variable

- Serum vitamin D level

Dependent Variable

- Disease activity score (DAS-28)

Other Variables

- Age

- Gender
- Dietary intake
- Sun exposure
- BMI
- Duration of disease

Description of the Tool

Data were collected using a structured questionnaire and assessment schedule prepared by the researcher after reviewing relevant literature.

The tool consisted of the following sections:

Section A: Socio-demographic Information

Included:

- Age
- Gender
- Marital status
- Educational status
- Occupation
- Monthly income
- Residential area

Section B: Clinical Information

Included:

- Duration of rheumatoid arthritis
- Family history
- Symptoms
- Medication history
- Co-morbidities

Section C: Sun Exposure Assessment

Included:

- Daily duration of sun exposure
- Time of exposure
- Outdoor physical activity
- Use of sunscreen/body covering

Section D: Dietary Assessment

Dietary assessment was conducted using:

1. 24-hour dietary recall
2. Food frequency questionnaire

The dietary assessment evaluated intake of:

- Vitamin D-rich foods
- Calcium-rich foods
- Energy intake
- Protein intake

Section E: Anthropometric Measurements

Anthropometric assessment included:

- Height
- Weight
- Body Mass Index (BMI)

BMI Formula

BMI = Weight in kgs/ Height in m^2

BMI classification was interpreted according to standard WHO guidelines.

Section F: Biochemical Assessment

Biochemical parameters included:

- Serum 25-hydroxy vitamin D
- ESR (Erythrocyte Sedimentation Rate)

- CRP (C-reactive protein)
- Rheumatoid factor

Classification of Vitamin D Status

Serum Vitamin D levels	Interpretation
<20ng/mL	Deficient
20-30ng/mL	Insufficient
>30ng/mL	Sufficient

Section G: Disease Activity Assessment

Disease activity was assessed using DAS-28 (Disease Activity Score-28).

The DAS-28 score included:

- Tender joint count
- Swollen joint count
- ESR/CRP
- Patient global assessment

DAS-28 Interpretation

DAS28 Score	Disease Activity
<2.6	Remission
2.6-3.2	Low activity
3.2-5.1	Moderate activity
>5.1	High activity

Validity of the Tool

The research tool was validated by experts from the fields of:

- Clinical Nutrition
- Rheumatology
- Dietetics

- Community Medicine

Necessary modifications and corrections were made based on expert suggestions.

Reliability of the Tool

Reliability of the questionnaire was established through pilot testing among a small group of rheumatoid arthritis patients who were not included in the final study.

The tool was found suitable and reliable for data collection.

Pilot Study

A pilot study was conducted among _____ rheumatoid arthritis patients to assess:

- Feasibility of the study
- Clarity of the questionnaire
- Time required for data collection

Necessary modifications were made after the pilot study.

Data Collection Procedure

Prior permission was obtained from the hospital authorities before conducting the study.

The data collection procedure included the following steps:

1. Participants meeting the inclusion criteria were identified.
2. The purpose of the study was explained to participants.
3. Written informed consent was obtained.
4. Socio-demographic and clinical information were collected through interview.
5. Anthropometric measurements were recorded.
6. Dietary assessment was conducted using 24-hour recall and food frequency questionnaire.
7. Information regarding sunlight exposure was obtained.

8. Laboratory values were collected from hospital records/reports.
9. Disease activity was assessed using DAS-28 scoring.

The average duration of each interview was approximately _____ minutes.

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APPENDIX I

PARTICIPATION INFORMATION SHEET

Study Title

Correlation Between Vitamin D Deficiency and DAS28 Score in Patients with Rheumatoid Arthritis

Purpose

To study the relationship between Vitamin D levels and disease activity among RA patients.

Procedures

- Questionnaire
- Height and weight measurement
- Review of laboratory reports
- DAS28 assessment

Confidentiality

Participant identity will remain confidential.

Voluntary Participation

Participants may withdraw at any time without affecting their medical care.

APPENDIX II

INFORMED CONSENT FORM

Participant Name: _____

Age: _____

Gender: _____

I have read and understood the purpose of this study. I voluntarily agree to participate.

Participant Signature: _____

Researcher Signature: _____

Date: _____

APPENDIX III

PROPOSED QUESTIONNAIRE STRUCTURE

SECTION A: SOCIO-DEMOGRAPHIC DETAILS

(Please tick ✓ the appropriate answer)

1. Participant ID: _____
2. Age (in years): _____
3. Gender:
   ☐ Male
   ☐ Female
4. Marital Status:
   ☐ Married
   ☐ Unmarried
   ☐ Widow/Widower
5. Education Level:
   ☐ Illiterate
   ☐ Primary
   ☐ Secondary
   ☐ Graduate & above
6. Occupation:
   ☐ Housewife
   ☐ Farmer
   ☐ Service
   ☐ Self-employed
   ☐ Others _____
7. Monthly Family Income:
   ☐ < ₹10,000
   ☐ ₹10,000–20,000

☐ ₹20,000–40,000

☐ > ₹40,000

8. Type of Family:

☐ Nuclear

☐ Joint

9. Area of Residence:

☐ Rural

☐ Urban

SECTION B: CLINICAL HISTORY

10. Duration of Rheumatoid Arthritis:

☐ <1 year

☐ 1–5 years

☐ >5 years

11. Family history of RA:

☐ Yes

☐ No

12. Symptoms present (tick all that apply):

☐ Joint pain

☐ Swelling

☐ Morning stiffness

☐ Fatigue

☐ Restricted movement

13. Any other chronic illness:

☐ Diabetes

☐ Hypertension

☐ Thyroid disorder

☐ None

☐ Others _____

14. Current medication for RA:

- Methotrexate
- Combination DMARD
- Biologic
- Other

15. Are you taking Vitamin D supplements?

☐ Yes

☐ No

SECTION C: SUN EXPOSURE ASSESSMENT

16. Daily sunlight exposure:

☐ <15 minutes

☐ 15–30 minutes

☐ >30 minutes

17. Time of sun exposure:

☐ Morning (6–10 AM)

☐ Afternoon

☐ Evening

18. Do you use sunscreen or full body covering?

☐ Yes

☐ No

19. Outdoor physical activity:

☐ Regular

☐ Occasional

☐ Rare

SECTION D: DIETARY ASSESSMENT

24-Hour Diet Recall:

Time	Food Items	Quantity
Breakfast		
Mid-morning		
Lunch		
Evening snack		
Dinner		

Food Frequency Questionnaire:

Frequency Code	Meaning
Never	Never consumed
Monthly	1-3 times/month
Weekly	1-2 times/week
3-4/week	3-4 times/week
Daily	Once or more daily

1) Milk and Dairy Products

Food Item	Never	Monthly	Weekly	3-4/week	Daily
Milk					
Curd/Yoghurt					
Paneer					
Cheese					
Butter					

2) Eggs

Food Item	Never	Monthly	Weekly	3-4/week	Daily
Whole egg					
Egg yolk					

3) Fish and Seafood

Food Item	Never	Monthly	Weekly	3-4/week	Daily
Salmon					
Sardines					
Mackerel					
Tuna					

4) Meat and Poultry

Food Item	Never	Monthly	Weekly	3-4/week	Daily
Chicken					
Liver					

5) Fortified Foods

Food Item	Never	Monthly	Weekly	3-4/week	Daily
Fortified Milk					
Fortified cereals					
Fortified fruit juice					

6) Vegetarian Vitamin D Sources

Food Item	Never	Monthly	Weekly	3-4/week	Daily
Mushrooms					
Soy milk (fortified)					
Tofu					

7) Calcium-Rich Foods

Food Item	Never	Monthly	Weekly	3-4/week	Daily
Ragi					
Sesame seeds					
Almonds					
Green leafy vegetables					

SECTION E: ANTHROPOMETRIC DATA

26.Height: _____ cm

27.Weight: _____ kg

28.BMI (calculated): _____ kg/m²

BMI Classification:

☐ Underweight (<18.5)
☐ Normal (18.5–24.9)
☐ Overweight (25–29.9)
☐ Obese (≥30)

SECTION F: BIOCHEMICAL PARAMETERS

29.Serum Vitamin D (25-OH): _____ ng/ml

Interpretation:

☐ Deficient (<20 ng/ml)
☐ Insufficient (20–30 ng/ml)
☐ Sufficient (>30 ng/ml)

30.ESR: _____ mm/hr

31.CRP: _____ mg/L

32.Rheumatoid Factor (RF): _____

SECTION G: DISEASE ACTIVITY (DAS-28)

33.Tender Joint Count: _____

34.Swollen Joint Count: _____

35.ESR/CRP value: _____

36.Patient Global Health Score: _____

DAS-28 Interpretation:

☐ Remission (<2.6)
☐ Low Activity (2.6–3.2)
☐ Moderate Activity (3.2–5.1)
☐ High Activity (>5.1)

SECTION H: LIFESTYLE FACTORS

37.Smoking:
☐ Yes
☐ No

38.Alcohol consumption:
☐ Yes
☐ No

39.Physical activity level:

☐ Active

☐ Moderate

☐ Sedentary

APPENDIX IV

OPERATIONAL DEFINITIONS

Rheumatoid arthritis:

For the purpose of this study, rheumatoid arthritis refers to a clinically diagnosed RA condition documented by the treating physician/rheumatologist.

Vitamin D Status:

Vitamin D status refers to the serum concentration of 25-hydroxyvitamin D [25(OH)D] measured using the laboratory method adopted by the study centre.

Serum 25(OH)D:

Serum 25-hydroxyvitamin D is the biochemical indicator used in this study to assess circulating vitamin D status.

DAS28:

DAS28 refers to the Disease Activity Score based on assessment of 28 joints together with the specified inflammatory marker and patient assessment.

Disease Activity:

Disease Activity refers to the degree of active rheumatoid arthritis as represented by the DAS28 score.

Correlation:

Correlation refers to the statistical relationship between serum 25(OH)D concentration and DAS28 score.

APPENDIX V

INDIRA GANDHI NATIONAL OPEN UNIVERSITY

MSCDFSM, MFNP -12

FORMAT OF BIODATA FOR SUPERVISOR /GUIDE FOR MFNP-012

(Other than Academic Counsellors)

l. Name of the Supervisor/Guide (in Block Letter) : MRS. UROOJA BIRJIS FATIMA

2. Address: St. Ann's College for Women, Mehdipatnam, Hyderabad, Telangana

3. Contact No.: 9542815524

4. E-mail address: birjisurooja@gmail.com

5. Academic Qualifications (from Graduation upwards):

Sl. No.	**Qualification** (with subjects)	**University**	**Month/Year**	**Area of Specialization**
1	B.Ed.	Osmania University	2022	Biological Science
2	B.Sc.	Osmania University	2011	Applied Nutrition and Public Health
3	M.Sc.	OUCW	2014	Nutrition and Dietetics
4	UGC NET	UGC	2017	Home Science

6. Teaching Experience:

Sl. No.	**Job Position**	**Name of Organization**	**From**	**To**	**Total Experience**	**Subjects Taught**
1	Faculty	Shadam degree & PG College	2013	2015	2.5 years	Nutrition- All Semester Papers
2	Assistant Professor	St. Ann's College	2015	Till date	12+ years	PG Nutrition Subjects

7. Publication and Research (add more pages if required) : 20 publications

8.Any other relevant information:

Date:

Name:

Signature of the Guide/ Supervisor

APPENDIX VI

CONSENT LETTER OF SUPERVISOR/GUIDE

This is to certify that the Project titled **Correlation Between Vitamin D Deficiency and DAS28 Score in Rheumatoid Arthritis** for the partial fulfillment of MSCDFSM Program of IGNOU will be carried out by **Ms. Heemika Jain Ramesh** Enrollment No. **2450120192** under my guidance.

(Signature)

Name of the Supervisor: Mrs. Urooja Birjis Fatima

Designation: Assistant Professor

Address: St. Ann's College for Women

Date: