

## The Association between Body Mass Index, Diagnostic Markers and Disease Activity Score with Progression of Rheumatoid Arthritis in a Sample of Iraqi Patients

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Received: 30/05/2023

Accepted: 20/07/2023

Online: 26/3/2024

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### ABSTRACT

**Background:** Rheumatoid arthritis (RA) is a widespread, chronic, systemically inflammatory disease that, if improperly treated, can cause deformed joints and functional disability. For best disease management, greater chances of recovery, and the avoidance of irreversible clinical and radiographic damage, RA must be diagnosed and treated as soon as possible. **Objectives:** The purpose of this study was to evaluate body mass index utilizing DAS and levels of diagnostic tests in rheumatoid arthritis patients. **Materials and methods:** 120 patients with rheumatoid arthritis (60 newly diagnosed untreated patients and 60 others under treatment) were collected from Al-Yarmouk Hospital in Baghdad and 60 control individuals. Equation and diagnostic tests measured body mass index (BMI), then vitamin D3 with the COPAS 111 device. **Results:** The prevalence of the disease in females was 91%, while males were 9%. Diagnostic tests recorded clear significance ( $p \leq 0.05$ ) differences between patients and healthy persons, and it increased with the severity of the disease. Additionally, patients' levels of vitamin D3 reduced significantly when compared to controls, and there was a significant disparity between patients' and healthy participants' sugar levels, and the BMI correlated with disease activity. **Conclusions:** The current study concluded that there is a relationship between weight gain and disease severity that diagnostic tests increased in patients and that vitamin D3 can be used as a diagnostic marker for rheumatoid arthritis.

Keywords: Body mass index (BMI), Disease activity score DAS-28, Diagnostic marker.

DOI: <https://doi.org/10.24126/jobrc.2024.18.1.708>

### 1-INTRODUCTION

Rheumatoid arthritis (RA), The most prevalent inflammatory arthritis forms an ongoing, systemic autoimmune disorder marked by difficult, symmetrical inflammation of numerous joints (1). Body mass index (BMI), which is determined by dividing an individual's body weight by kilograms with the square of their height in meters ( $\text{kg}/\text{m}^2$ ), is typically used to diagnose obesity and is defined as an increase in fat at a level high enough to have negative health effects (2). Overweight and obesity are pandemic public health issues in the Western world because they are linked to an elevated risk of chronic autoimmune and inflammatory disorders, such as type 2 diabetes and rheumatoid arthritis. This has an important effect on society and the economy (3).

A composite score has been established for assessing the RA's severity. To differentiate between individuals with differing degrees of disease activity, the Disease Activity Score 28- joint count (DAS28) was recommended in the clinical environment due to its usability and feasibility; Experts in the diagnosis of rheumatoid arthritis frequently refer to the DAS28 as the "gold standard." To calculate the DAS28 score, a rheumatologist will count the number of painful and swollen joints as well as estimate the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) values. The patient also answers questions on their "Global Assessment of Health" and rates it on a scale of 1 to 10 (4).

Diabetes is thought to arise as a result of inflammation. Some common Type 2 Diabetes Mellitus (T2DM) risk factors are also very common in patients with RA. As a result, diabetes may be more common in RA patients (4).

## **2- MATERIAL AND METHODS**

### **Patients**

A group of RA patients (n = 120) was diagnosed according to the criteria of the World Health Organization, which was based on signs, symptoms, clinical examination and routine tests: (CBC, ESR, CRP, RF, ACCP, Vitamin D) and then classified into two groups, the first includes patients under treatment (n=60) (8 males and 52 females) aged between (35- 85) The second group includes patients who did not undergo treatment (n=60) (9 male and 51 female) aged between (41-65). Samples were taken from healthy control (n = 60) aged between (24 -75) healthy individuals. In patients and controls, data on RA risk factors such as gender, age, smoking, family history, and diabetes mellitus were collected through the use of a structured questionnaire.

### **Blood Collection**

Blood samples totaling seven mL were taken from the median cubital by both patients and volunteers. For clotting, the blood was left to stand for 30 minutes. For additional examination, serum samples were taken after being centrifuged for 5 minutes at 10,000 rpm. The Ethics Committee of the Iraqi Ministry of Health, Al-Yarmouk Teaching Hospital in Baghdad, accepted the study's protocol. Each subject who took part in the study provided a signed written consent.

### **Diagnostics Parameters**

A variety of the following diagnostic tests were evaluated: rheumatoid factor (RF), C-reactive protein (CRP), anti-cyclic citrullin peptide (Anti-ccp), complete blood count (CBC), vitamin D3, FBS, HbA1c and Erythrocyte sedimentation rate (ESR).

### **Methods**

ESR is calculated using the technique developed by Westergren, and an auto hematology analyzer examines the complete blood count (CBC).

RF, CRP, Vit-D3, FBS and HbA1c were assessed by cobas C 111. Four main measurement methods—turbidimetry, fluorescence polarimetry, ion-selective electrode (ISE) potentiometry, and absorbance photometry—were the foundation of the Cobas analytical system. Testing for vitamin D3 must be finished in 30 minutes, while the rest of the tests must be finished in 15 minutes. The anti-cyclic peptide containing citrulline antibody in the sample and the antibody becoming immunoglobulin complexes by agglutination with latex reaction were used to determine anti-ccp using the Anti-CCP kit on a hipro analyzer.

The DAS-28 was developed for patients to categorize RA patients based on their DAS28-ESR towards mild, moderate, and severe by using the formula provided in the website (<https://www.mdcalc.com/disease-activity-score28-rheumatoid-arthritis-esr-das28-esr#evidence>).

if the score of DAS28-ESR is:

- < 2.6 Remission.
- $\geq 2.6$  - < 3.2 Low activity (Mild).
- $\geq 3.2$  -  $\leq 5.1$  Moderate activity (Moderate).
- > 5.1 High activity (Sever).

**Statistical analysis**

SPSS 20.0 was used to conduct the statistical analysis. Using a chi-square test, categorical variables were examined. Continuous normal distribution variables with a mean as well as a standard deviation were examined by samples that were independent ANOVA for between-group comparisons.

**3-RESULTS**

Results from the DAS were combined with BMI levels to produce this figure, and the findings revealed a definite significant relationship between the progression of the disease and an increase in BMI.

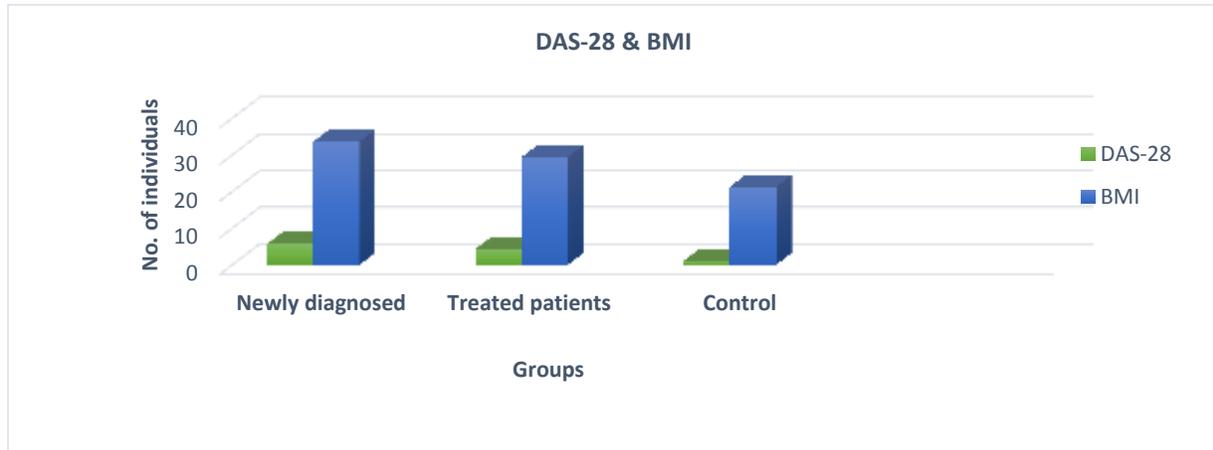


Figure (3-1): The comparison of body mass index with DAS-28

Due to the fact that the levels of the tests used for diagnosis were higher in the newly diagnosed patients, the findings of this figure's analysis revealed statistically significant differences between the diagnostic tests of the newly diagnosed patients and those of the patients who were already receiving treatment.

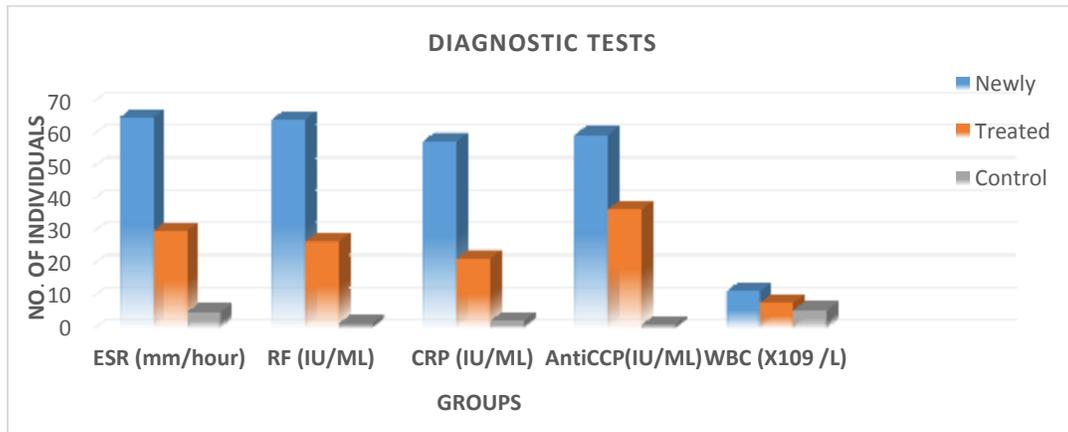


Figure (3-2): Levels of diagnostic markers between patients group and control.

The findings demonstrated in the following figure (3-3) that there were significant variations in the biochemical tests between the patient groups and the control, with significant variations in the levels of sugar and vitamin D3 and very low vitamin D3 levels in the patient groups compared to higher levels in the control groups.

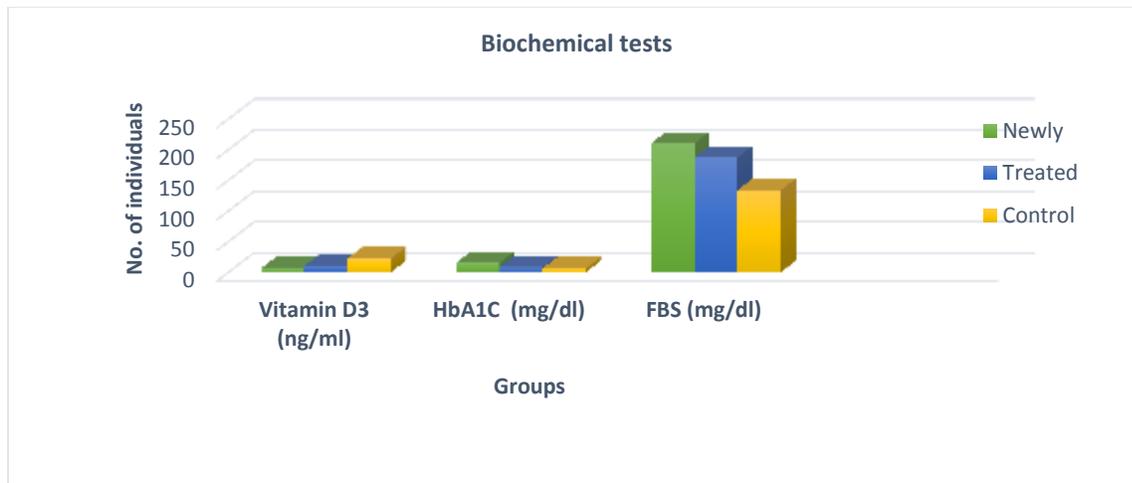


Figure (3-3): Levels of biochemical tests between patient groups and control.

#### 4- DISCUSSION

In rheumatoid arthritis, results of diagnostic tests and disease activity are highly correlated, Therefore, disease activity scores are frequently used to direct personal therapy and evaluate the effectiveness of medicines in clinical trials (5).

According to the results of the current study, RA risk is increased by obesity or a higher BMI. This result was in line with a Mendelian randomization study that showed a causal link between BMI and an elevated risk of RA (6). Inflammatory cytokines such as leptin, Tumor necrosis factor (TNF), IL-6, interleukin-1, and monocyte chemoattractant protein-1 (MCP-1) are secreted by the adipose tissue of obese people, People experience inflammation as a result of these adipokines (7). In people before the beginning of RA, prior investigations have found higher levels of these inflammatory markers, Concentrations of numerous sex hormones, including estrogen, estradiol, as well as free estradiol, are substantially correlated with obesity.

According to the findings of another investigation, Rheumatoid arthritis patients have a high prevalence of having high body mass. Additionally, the acute phase and lean mass are linearly related. (8) These findings agree with those of our most current research.

Rheumatoid Factors (RF) are autoantibodies that target immune globulin (Ig) Fc region. Up to 80% of people with RA have RF, although their specificity is limited by the fact that they can also develop from a variety of other inflammatory diseases that cause chronic antigenic stimulation (9).

An increased risk of developing RA is associated with RF positive and greater titers (10).

The focus of RA biomarker research has long been autoantibodies against citrullinated peptide epitopes. This process is a post-translational alteration of proteins that may outcome in the creation of novel epitopes that the immune system is intolerant to, which can then result in the development of fresh autoantibodies, The (anti-CCP2) assay for antibodies has strong diagnostic and prognostic value and is frequently used in clinical settings (11).

Both strong titer RF as well as anti-CCP2 antibodies enhance the likelihood of erosive joint injury, while anti-CCP2 antibodies may do so more so than RF (12).

When placed in a vertical tube, the rate at which erythrocytes pass through plasma is known as the ESR. ESR readings rise with age and are marginally greater in women than in men. Elevated ESR levels can be brought on by either systemic as well as local inflammation (13).

Based on a higher frequency of this condition among RA patients, our finding supports the idea that inflammation may play a role in increased disease activity and severity.

Increasing data suggested that inflammation is a major contributor to the development of diabetes. Generates a variety of cytokines and chemokines, such as IL-6, TNF- and IL-6 upregulation and production are two important mechanisms in the pathogenesis of RA. In animal studies, TNF- and IL-6 impair insulin sensitivity by blocking insulin signaling and consequently inducing insulin resistance, which is linked to T2DM (14)

The pentraxin protein relatives, which include pattern-recognition molecules implicated in the innate immune response, include the acute-phase response CRP, The elevated levels of cytokines that are pro-inflammatory in the RA synovium boost the liver's synthesis of CRP, making it a promising option as a disease activity biomarker, CRP occurs across both acute as well as chronic inflammatory disorders (15).

## 5-CONCLUSION

We concluded from this study that there is a relationship between weight gain and the severity of the disease, the more a patient weighs, the more severe the symptoms of the disease, that diagnostic tests increased in patients and that vitamin D3 can be used as a diagnostic marker for rheumatoid arthritis.

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### الارتباط بين مؤشر كتلة الجسم والعلامات التشخيصية ودرجة نشاط المرض مع تطور التهاب المفاصل الروماتويدي في عينة من المرضى العراقيين

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#### الخلاصة

**خلفية عن الموضوع:** التهاب المفاصل الروماتويدي هو مرض التهابي جهازي واسع الانتشار ومزمن ويمكن أن يسبب تشوه المفاصل وإعاقة وظيفية إذا تم علاجه بشكل غير صحيح. من أجل إدارة المرض بشكل أفضل ، وفرص أكبر للشفاء ، وتجنب الأضرار السريرية والشعاعية التي لا رجعة فيها ، يجب تشخيص التهاب المفاصل الروماتويدي وعلاجه في أسرع وقت ممكن. **الهدف:** الغرض من هذه الدراسة هو تقييم مؤشر كتلة الجسم باستخدام معايير ومستويات الاختبارات التشخيصية في مرضى التهاب المفاصل الروماتويدي. **المواد وطرق العمل:** تم جمع 120 مريضاً مصاباً بالتهاب المفاصل الروماتويدي (60 مريضاً تم تشخيصهم حديثاً ولم يتم علاجهم و 60 آخرين يخضعون للعلاج) من مستشفى اليرموك في بغداد و 60 شخصاً من مجموعة السيطرة، تم قياس مؤشر كتلة الجسم بالمعادلة ، ثم فيتامين د3 والاختبارات التشخيصية لتقييم المرض بجهاز متطور. **النتائج:** بلغت نسبة انتشار المرض بين الإناث 91% مقابل 9% بين الذكور. سجلت الاختبارات التشخيصية فروق معنوية واضحة بين المرضى والأصحاء وزادت مع شدة المرض بالإضافة الى ذلك انخفضت مستويات فيتامين د3 ( $p < 0.05$ ) لدى المرضى بشكل ملحوظ عند مقارنتها بالضوابط ، وكان هناك تفاوت كبير بين مستويات السكر لدى المرضى والمشاركين الأصحاء ، ومؤشر كتلة الجسم مرتبط بنشاط المرض. **الاستنتاج:** خلصت الدراسة الحالية إلى أن هناك علاقة بين زيادة الوزن وشدة المرض ، وأن الاختبارات التشخيصية تزداد عند المرضى ، وأن فيتامين د3 يمكن استخدامه كمؤشر تشخيصي لالتهاب المفاصل الروماتويدي.

**الكلمات المفتاحية:** مؤشر كتلة الجسم ، درجة نشاط المرض ، مؤشر التشخيص الحيوي.