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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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DIAGNOSTIC AND PROGNOSTIC VALUE OF ANTI-CYCLIC CITRULLINATED PEPTIDE AND RHEUMATOID FACTOR IN RHEUMATOID ARTHRITIS PATIENTS

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Abstract.

Objectives: This study aimed to assess the diagnostic and prognostic value of rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies in rheumatoid arthritis (RA) patients, focusing on early diagnosis and disease activity.

Methods: Dr. Mohammed Ali Saad Medical Center and Doctors Hospital in Port Sudan, red sea state in Sudan were the sites of an analytical case-control study was conducted, including 166 RA patients, 68 early RA patients, and 166 healthy controls. RF, anti-CCP, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) were measured. Statistical analyses included chi-square, Kruskal-Wallis, and receiver operating characteristic (ROC) curve studies.

Results: RF and anti-CCP antibody levels were higher in established RA patients than in early RA patients and healthy controls ($p < 0.001$). Anti-CCP demonstrated superior specificity (98%) compared to RF (79% specificity) for RA diagnosis. In established RA, anti-CCP showed higher sensitivity (79%) than RF (67%). However, the majority of early RA patients (54.5%) tested negative for both markers, indicating that inflammatory markers such as CRP and ESR may be more useful than autoantibodies for early RA detection. The combination of both tests enhanced diagnostic sensitivity in established RA.

Conclusion: It was discovered that anti-CCP antibodies were a very specific indicator of RA, especially when the disease was progressed. Improved diagnostic accuracy is achieved when RF and anti-CCP testing are combined, with anti-CCP testing showing greater sensitivity for early RA identification. This study emphasizes how useful both markers are in clinical practice for RA patient prognosis, disease activity evaluation, and early diagnosis.

Key words. Rheumatoid arthritis (RA), anti-cyclic citrullinated peptide (anti-CCP), Rheumatoid factor (RF), diagnosis, inflammatory markers, sensitivity and specificity.

Introduction.

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease that primarily affects synovial joints, leading to progressive joint degeneration, functional disability, and systemic complications. It affects approximately 0.5% to 1% of the global population, with a higher prevalence in women and individuals aged 40 to 60 years. A hallmark of RA is persistent synovial inflammation, which results in cartilage deterioration, bone erosion, and joint deformities. The pathophysiology of RA involves a complex interplay of genetic, environmental, and immunological factors. Genetic susceptibility, particularly the presence of HLA-DRB1 alleles, plays a significant role in disease vulnerability, while environmental triggers, such as infections and smoking, can initiate or exacerbate the autoimmune response [1-5].

Autoantibodies, particularly rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies, are crucial biomarkers for the diagnosis and prognosis of RA. RF is an autoantibody targeting the Fc portion of IgG, found in approximately 70–80% of RA patients. However, its diagnostic utility is limited due to its presence in other autoimmune diseases, chronic infections, and even in healthy individuals, particularly the elderly [6]. Anti-CCP antibodies are highly specific markers for RA, targeting citrullinated proteins generated through arginine modification. When combined with RF, they enhance diagnostic accuracy, as they can be detected early—often before clinical symptoms appear—and exhibit a 95% specificity with sensitivity comparable to RF [7].

The presence of anti-CCP antibodies is associated with increased inflammatory markers, more extensive joint damage, and progressive disability over time. Additionally, RA patients positive for both RF and anti-CCP antibodies tend to exhibit more severe disease manifestations and reduced responsiveness to conventional disease-modifying antirheumatic drugs (DMARDs) [8].

Recent studies emphasize the role of these autoantibodies in predicting treatment response and guiding therapeutic decisions. Patients with high anti-CCP titers often show suboptimal responses to certain biologic therapies, highlighting the necessity for personalized treatment strategies based on serological profiles [9]. Moreover, emerging evidence suggests that anti-CCP antibodies may actively contribute to RA pathogenesis by triggering complement pathways and immune complex formation, leading to prolonged synovial inflammation and joint destruction [10].

This study aims to comprehensively evaluate the diagnostic and prognostic significance of anti-CCP antibodies and RF in RA patients. By integrating recent advancements in immunopathology and clinical research, this work provides a detailed understanding of their roles in RA management, emphasizing their implications for early diagnosis, disease progression, and treatment strategies.

Materials and Methods.

Study design and Population:

An analytical case-control study was conducted at Doctor Hospital and Dr. Mohammed Ali Saad Medical Center in Port Sudan, Red Sea State, Sudan. The study population comprised

400 individuals, including 68 early rheumatoid arthritis (RA) patients, 166 diagnosed RA patients, and 166 healthy controls. Inclusion criteria required participants to be adults (≥18 years) diagnosed with RA based on the ACR/EULAR 2010 criteria. Early RA patients were included only if they had not received disease-modifying antirheumatic drugs (DMARDs) or biological therapy before sample collection. Early RA was defined as patients diagnosed with RA according to ACR/EULAR 2010 criteria within 2 years of symptom onset and before initiation of any disease-modifying antirheumatic drugs (DMARDs) or biologic therapy. This definition aligns with established criteria used in rheumatology research for identifying patients in the early stages of disease progression. Exclusion criteria included patients with other autoimmune diseases, chronic infections, malignancies, and pregnant or breastfeeding women.

Data Collection Methods:

Participants were selected using convenience sampling. Data collection involved face-to-face interviews and self-administered questionnaires, covering demographics and clinical characteristics such as age, sex, disease duration, morning stiffness, sore joints, and joint deformities. Laboratory analyses were conducted using semi-automated methods (Finecare Plus 114) for initial screening. RF levels were measured using the Rheumatoid Factor ELISA Kit (Euroimmun AG, Lübeck, Germany), with a diagnostic cutoff of >20 IU/ml considered positive according to manufacturer specifications. Anti-CCP antibodies were quantified using the Anti-CCP ELISA Kit (Euroimmun AG, Lübeck, Germany), with levels >5 U/ml considered positive per manufacturer recommendations. C-reactive protein (CRP) was measured using the high-sensitivity CRP turbidimetric immunoassay (Roche Diagnostics, Mannheim, Germany), with normal values <3.0 mg/L. Erythrocyte sedimentation rate (ESR) was measured using the Westergren method with age and gender-specific reference ranges (normal: <20 mm/h for men under 50 years, <30 mm/h for men over 50 years; <30 mm/h for women under 50 years, <40 mm/h for women over 50 years).

Statistical Analysis:

Data analysis was performed using SPSS version 26.0. Descriptive statistics were expressed as frequencies, percentages, means, and standard deviations. The chi-square test was used to evaluate associations between RA and control groups regarding RF and anti-CCP. Sensitivity and specificity were determined using the receiver operating characteristic (ROC) curve, while the Kruskal-Wallis test was employed to compare means between case and control groups.

Results.

This study comprised three groups: 166 established RA patients, 68 early RA patients, and 166 healthy controls. The majority of RA patients were female, had a mean age of 49 ± 12.8 years, had been suffering from the disease for 10 ± 8.5 years, and had 37.1 ± 6.8 minutes of morning stiffness, 5.3 ± 3.7 tender joint pain, 1.9 ± 0.5 swollen joints, and 29 (43.9%) rheumatoid hand deformity. Most early RA patients were also female, had a mean age of 31 ± 9.4, had a shorter disease duration of 1.7 ± 0.9 years, experienced morning stiffness for 35.1± 6.8 minutes, had 17 ± 5.6 tender joint pains, had 3.8± 2.1 swollen joints, and none had rheumatoid hand deformity. The average age of the control group was 50.5 ± 13.7 years (Table 1).

Table 1. *Characteristics of RA patients and early RA patients.*

Variables	RA patients (n=166)	Early RA patients (n=68)
Age (years)	49 ± 12.8	31 ± 9.4
Male/female patients	27/139	9/59
Duration of disease (years)	10 ± 8.5	1.7 ± 0.9
Morning stiffness (minutes)	37.1 ± 6.8	35.1 ± 6.8
Tender joint pain count (0-28)	5.3 ± 3.7	17 ± 5.6
Swollen joint count (0-28)	1.9 ± 0.5	3.8 ± 2.1
Presence of rheumatoid hand deformity	29 (43.9%)	0 (0.0%)

When compared to the early RA and control groups, patients with established RA diagnosis had the highest levels of RF and anti-CCP antibodies (p. value 0.000). With a p-value of 0.000, the inflammatory markers CRP and ESR were shown to be higher in the early RA group, RA, and control group (Table 2).

The majority of patients (n=73; 43.9%) were positive for both RF and anti-CCP antibody, followed by RF-negative/anti-CCP antibody negative (n=43; 25.9%), RF-positive/anti-CCP antibody negative (n=35; 21.0%), and RF-negative/anti-CCP antibody-positive (n=15; 9.0%) (Table 3).

Table 2. *Comparison mean of and RA laboratory variables between RA, early RA and control group.*

Variables	RA patients	Early RA patients	Control	p. value
RF (lU/ml)	22.5±12.2	16.6±7.4	7.9±2.1	0.000
Anti-CCP (U/ml)	10.9±6.6	8.4± 6.1	3.6±0.54	0.000
CRP (mg/dl)	11.7±7.4	16.2±12.5	4.3±2.3	0.000
ESR (mm/l h)	26.7±13.8	40.1±27.5	15.2±2.2	0.000

RF: Rheumatoid factor; CRP: C-reactive protein; Anti-CCP: Anti-cyclic citrullinated peptide; ESR: Erythrocyte sedimentation rate.

Table 3. *Association of anti-CCP antibody with RF in RA patients.*

RF	Anti CCP		p. value
	Positive	Negative	
Positive	73(43.9%)	35(21.0%)	0.002
Negative	15(9.0%)	43(25.9%)	

Anti-CCP: Anti-cyclic citrullinated peptide: RF: Rheumatoid factor.

Table 4. *Association of anti-CCP antibody with RF in early RA patients.*

RF	Anti CCP		p. value
	Positive	Negative	
Positive	13(19.6%)	11(16.6%)	0.000
Negative	7(9.0%)	37(54.5%)	

Anti-CCP: Anti-cyclic citrullinated peptide: RF: Rheumatoid factor.

The majority of patients (n=37; 54.5%) were negative for both RF and anti-CCP antibody, followed by RF-positive/ anti-CCP antibody positive (n=13;19.6%), RF-positive/anti-CCP antibody negative (n=11; 16.6%), and RF-negative/anti-CCP antibody-positive (n=7; 9.0%). This showed a significant

correlation of early RF and anti-CCP antibody co-occurrence (P=.000), (Table 4).

Testing for RF and anti-CCP in order to diagnose RA (Table 5). The sensitivity, specificity, PPV, NPV, LR+, LR-, and 93%, 79%, 37%, 93%, 3.12, and 0.42 for the RF test were as follows. The equivalent data for the anti-CCP test were 79%, 98%, 86%, 96%, 32.91, and 0.21, in that order.

Table 5. *Performance of RF and anti-CCPs in the diagnosis of RA.*

		RA	Non RA p. value	Performance
RF	Positive 0.000	108	19	Sensitivity = 67% (95% CI: 52–81)
				Specificity = 79% (95% CI: 73–84)
				PPV = 37% (95% CI: 26–48)
	Negative	58	147	NPV = 93% (95% CI: 89–96)
				LR+ = 3.12 (95% CI: 2.22–4.42)
				LR-= 0.42 (95% CI: 0.27–0.67)
Anti-CCP	Positive 0.000	88	14	Sensitivity = 79% (95% CI: 67–92)
				Specificity = 98% (95% CI: 95–100)
				PPV = 86% (95% CI: 75–97)
	Negative	78	152	NPV = 96% (95% CI: 94–99)
				LR+ = 32.91 (95% CI: 13.64–79.37)
				LR- = 0.21 (95% CI: 0.11–0.39

Anti-CCP: Anti-cyclic citrullinated peptide; NPV: Negative predictive value; LR-, Negative likelihood ratio; LR+: Positive likelihood ratio; PPV: Positive predictive values; RA: Rheumatoid arthritis; RF: Rheumatoid factor.

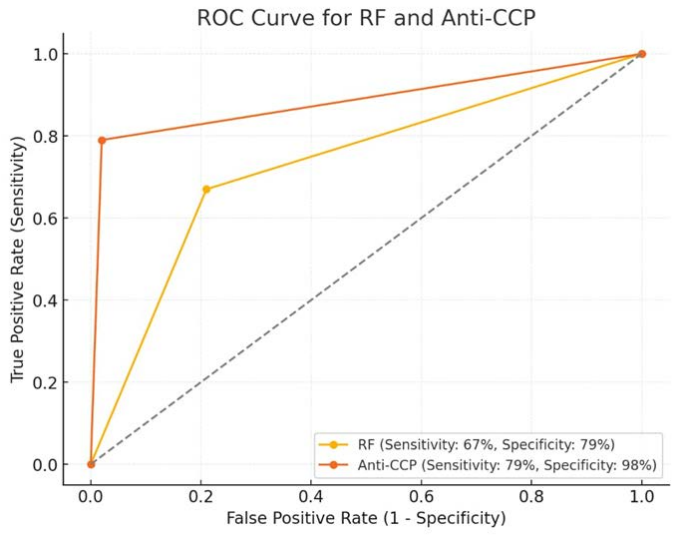

Figure 1. *RCO curve for sensitivity and specificity of RF and anti-CCP.*

The receiver operating characteristic (ROC) curve analysis further illustrated the superior diagnostic performance of anti-CCP compared to RF, with anti-CCP demonstrating both higher sensitivity and specificity in distinguishing RA patients from controls (Figure 1).

Discussion.

While numerous studies have examined the diagnostic utility of anti-CCP antibodies and RF in RA, this study provides several novel contributions to the existing literature. First, this is among the few studies to specifically examine these biomarkers in a Sudanese population, addressing a significant gap in the geographic representation of RA biomarker research. Second, our direct comparison of biomarker patterns between established RA, early RA, and healthy controls within the same population provides insights into the temporal evolution of autoantibody development. Third, our findings challenge the conventional emphasis on autoantibody testing in early RA by demonstrating that inflammatory markers may be more diagnostically relevant in this population subset.

It is challenging to forecast the prognosis of RA due to its unpredictable clinical course. The illness process is severe in many people, leading to gradual joint deterioration and significant disability [11]. Numerous research has examined the significance of anti-CCP in the diagnosis and prognosis of RA. The incidence of anti-CCP and its correlation with disease activity metrics in individuals with severe RA, however, are little understood [12,13].

According to this study, the number of tender joints and swollen joints was higher in early RA compared to RA, and the majority of early RA patients had normal RF and anti-CCP levels. On the other hand, RA patients had the highest levels of RF and anti-CCP compared to early RA and the control group, while early RA patients had the highest levels of ESR and CRP. These findings suggest that ESR and CRP are useful markers for diagnosing early RA with present joint pain more than RF and anti-CCP. While these markers lack specificity for RA and can be elevated in various inflammatory conditions, infections, and malignancies, their presence in the context of appropriate clinical symptoms may serve as important early indicators of inflammatory arthritis. The elevation of non-specific inflammatory markers preceding autoantibody development suggests that the inflammatory cascade initiating RA pathogenesis occurs before the generation of disease-specific autoimmune responses. However, clinicians must interpret elevated CRP and ESR in conjunction with clinical findings and exclude other inflammatory conditions through appropriate differential diagnosis. Our study demonstrated that RF was significantly associated with anti-CCP antibody positivity73(43.9%) with RA had both RF and anti-CCP antibody were positive. A notable limitation of our study is the significant age difference between the established RA group (mean age 49 ± 12.8 years) and early RA group (mean age 31 ± 9.4 years). This age disparity may represent a confounding factor, as older age has been associated with increased autoantibody production and altered inflammatory responses. The younger age in our early RA cohort may partially explain

the lower prevalence of RF and anti-CCP antibodies in this group, as autoantibody development often increases with disease duration and patient age. Future studies should include age-matched controls or perform age-adjusted analyses to better isolate the effects of disease stage from age-related factors, and this finding was supported by Chou et al. [14] where RF was found to be significantly co-occurred with anti-CCP antibody in a cohort of 155 Chinese RA patients. In the present study, 35(21.0%) patients were RF+ but tested negative for anti-CCP, and 15(9.0%) patients were RF negative but tested positive for anti-CCP. 43(25.9%) patients were negative for both RF and anti-CCP and this consistent with Sockalingam et al. and Abdul Wahab et al. previous studies [15,16].

Thus, some patients may present with established RA even in the absence of detectable anti-CCP and RF antibodies, representing seronegative rheumatoid arthritis. This cross-sectional analysis demonstrates that RA can occur without these autoantibodies, highlighting the existence of distinct phenotypic subtypes of the disease. RA is often difficult to differentiate from other inflammatory arthritis conditions and RF alone has low sensitivity in diagnosing early RA [17]. This is also confirmed by our findings in early RA patients, where we found that most patient had negative RF and negative anti-CCP antibody. The results of the present study show that anti-CCP had better sensitivity (79% vs. 67%) and better PPV (86% vs. 37%) than RF for the diagnosis of RA in our population. However, these two tests had similar NPVs (96% vs. 93%).In the present study, we found that the specificity of anti-CCP was better than RF (98% vs. 79%) and that anti-CCP had a much higher LR+ than RF (32.91 vs. 3.12).the anti-CCP test had higher sensitivity, specificity, PPV and LR+ in the detection of RA Use of the presence of either RF or anti-CCP had comparable diagnostic utility as anti-CCP alone, but these two tests were complementary in that they increased the sensitivity. In particular, the presence of either anti-CCP or RF had a sensitivity of 85%, and when they were both present, the specificity increased to 98%. The present study demonstrated that a positive anti-CCP test had an excellent LR+ of 32.91. This means that a positive anti-CCP test, alone or in combination with a positive RF test, performed better in the diagnosis of RA.

Conclusion.

In summary, our study demonstrates that patients can diagnosis with rheumatoid arthritis when RF and anti-CCP were negative where diagnostic based on number of tender joints and elevated inflammatory markers. We found that anti-CCP was a specific marker in advanced RA, Therefore, it might be suggested that anti-CCP might be useful in clinical practice in evaluation of both disease activity and therapeutic response in patients with advanced RA. Furthermore, use of the anti-CCP assay can significantly increase the sensitivity of diagnosis in RF negative patients with RA, as well as in the total RA population. Both anti-CCP and RF positivity are useful for the diagnosis of RA, and use of both tests together improves the diagnostic sensitivity. The RF and anti-CCP tests are complementary, and the co-detection of these antibodies can increase the detection rate and provide important clinical value in the diagnosis of RA.

Limitations.

Several limitations should be acknowledged in this study. The use of convenience sampling may have introduced selection bias and limits the generalizability of our findings to the broader Sudanese population and other ethnic groups. Patients presenting to the specific medical centers included in this study may not be representative of all RA patients in the region, potentially affecting the external validity of our results. Additionally, convenience sampling may have led to overrepresentation of patients with more severe disease who are more likely to seek medical care at specialized centres.

Ethics Approval.

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Dr. Mohammed Ali Saad Medical Center and Doctors Hospital in Port Sudan. All procedures performed involving human participants were in accordance with ethical standards.

Informed Consent.

Informed consent was obtained from all individual participants included in the study.

Data Availability.

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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Conflicts of Interest.

The authors declare that they have no conflict of interest.

Author Contributions.

S.A.O. conceived and designed the study, collected data, and drafted the manuscript. A.A.A. analyzed and interpreted the data and revised the manuscript. E.A.O. supervised the study, contributed to data interpretation, and critically revised the manuscript for important intellectual content. All authors reviewed and approved the final version of the manuscript.

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