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Research Article

Prevalence and impact of obesity in patients with rheumatoid arthritis

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Abstract

Background: The impact of overweight and obesity on outcomes of patients with Rheumatoid Arthritis (RA) is still uncertain. This study aimed to evaluate the prevalence and influence of overweight and obesity on patients with RA.

Methods: Demographic and clinical data of 185 (38 male and 147 females) RA patients were recorded. According to BMI, patients were categorized into two groups; normal weight and overweight/obese. The two groups were evaluated for clinical, laboratory, radiographic damage and disease activity parameters.

Results: Out of 185 RA patients, 70 (37.8%) were normal weight, and 115 (62.2%) were overweight/ obese. There were no significant differences in joint erosion, RF, and Anti-CCP between normal weight and overweight/ obese groups. There were statistically significant differences between both average weight and overweight/ obese groups in VAS, ESR, CRP, and DAS28. Disease duration and older age were associated with high BMI. DAS28 was significantly lower in normal-weight (1.8) compared to the overweight/obese group (4.7).

Conclusion: Obesity was prevalent among patients with RA. Obese patients were associated with worse disease activity. Weight reduction may be associated with clinical improvement.

Keywords: Body mass index, Disease activity, Obesity, Rheumatoid arthritis

Introduction

Rheumatoid arthritis (RA) is chronic inflammatory arthritis characterized by the inflammation of multiple joints and significant joint destruction and disability. It is the most common form of inflammatory arthritis that affects synovial joints. In early disease, the wrists, proximal interphalangeal, metacarpophalangeal, interphalangeal joints of the thumbs, and metatarsophalangeal are the most commonly affected joints in the body [1]. Additionally, chronic inflammation secondary to RA can result in a tremendous risk of pulmonary and cardiovascular disease and changes in bone density [1]. RA has a significant effect on body composition, the levels of lipid, adipokine, and insulin sensitivity [2]. RA patients had a higher body fat mass and lowered lean mass than the healthy population [3]. Despite the significant therapeutic advances in the medical treatment of RA, a considerable proportion of RA patients shows an inadequate response to treatments and, therefore, are at high risk of different medical complications, disability, and low quality of life [4-6]. Consequently, it is essential to recognize factors that impact the outcome of RA. Obesity is implicated in this poor outcome, but this fact is still uncertain [7]. Owing to the inflammatory nature of these two conditions, it is hypothesized that obesity and overweight are associated with high disease activity and more disease severity in RA patients [7]. Studies suggest that adipose tissue is not just a store for inert energy, but it is an endocrine organ that interplays with the central nervous and immune system, with a range of essential functions, such as proteins and hormones production that are involved in physiological and pathological processes, including immunity and inflammation [8]. Therefore obesity is implicated in the activation of pro-inflammatory pathways; thus, obese RA patients have more active and severe disease. Adipose tissue is considered a dynamic organ that produces several molecules, including cytokines, adipokines, and interleukin (IL)-6. The pro-inflammatory activities of these molecules are responsible for chronic systemic inflammation. These molecules are abundant in the serum of

patients with RA and make the link between obesity and RA [9]. Studies investigating the impact of obesity on RA patients have revealed controversial results. Some studies show poor response to treatment in obese RA patients. These patients did not achieve disease control and were associated with increased structural and functional impairment [10-12]. Some studies showed that obesity is implicated in high disease activity [13,14]. In contrast, obesity was associated with more favorable radiographic outcomes [12,15]. Moreover, studies suggested that obesity may delay the progression of radiographic damage in the early phases of RA [16,17]. However, the mechanism by which obesity may be correlated to RA is still unknown. One mechanism is the association between obesity and chronic inflammation. Fatty tissue increases during weight gain, and adipocytes secret adipocytokines and inflammatory cytokines, including adiponectin, tumor necrosis factor, interleukin-6, CRP, and others [18]. The major adipocytokines have immunomodulatory properties and impact inflammation [19]. This fact offers an active area of research, and adipocytokines and inflammatory cytokines are essential factors in the pathophysiology of rheumatic diseases, such as RA. This study aimed to evaluate the prevalence and the influence of obesity on patients with RA.

Patients and Methods

This was a cross-sectional study carried out at the Department of Rheumatic outpatients and Basrah biologic center in Basrah Teaching Hospital from May 2021 till May 2022. A sample of 185(38 males and 147 females) patients with RA, diagnosed according to the 2010 ACR/ EULAR criteria for the classification of RA [20], were enrolled for the study. Data collection was done through an interview with the patients using a special questionnaire developed by the researchers. The researchers evaluated the clinical history and physical examination of all patients. The following parameters were recorded in all patients during the first examination; demographic data, clinical findings, disease activity (number of tender/swollen joints among 28 joints), drug history, presence of articular and extra-articular symptoms, presence of concomitant comorbid diseases, laboratory parameters including complete blood count, CRP, ESR, RF, anti-CCP antibody, and radiological changes detected on radiography by a rheumatologist and a radiologist. Patients diagnosed with other connective tissue diseases (overlap syndromes), except for secondary Sjögren syndrome, were excluded. Disease activity was scored using the DAS28 erythrocyte sedimentation rate (ESR) system. Scores was interpreted as follows: <2.6 (clinical remission), 2.6–3.1 (low), 3.2–5.0 (moderate), and ≥ 5.1 (high) [21]. Obesity was determined based on BMI, and the adopted BMI ranges were: normal (18.5–24.9), overweight (25–29.9), and obese (≥ 30) [22]. Normal ranges of laboratory parameters were described as follows: CRP (normal 0–5), ESR (normal 20 mm/h by Westergren method), RF (normal <5 by nephelometry method), and anti-CCP (normal <20 by ELISA method).

Ethical considerations

Written consent was obtained from all participants prior to their involvement. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statistical analysis

SPSS software version 25.0 was used for data analysis. Percentages and mean were used to present the data in tables. In addition, a comparison of study groups was carried out using a chi-square test for categorical data and Student's t-test for continuous data. A P-value of <0.05 was considered statistically significant.

Results

The demographic distributions of patients are shown in **Table 1**. From the total sample of 185 patients with RA, 38 (20.54%) were men, and 147 (79.46%) were women with mean age disease duration and BMI of 55 ± 7.4, 9.7 ± 6.2 years, and 26. 9 ± 7.2 for men respectively and 52 ± 6.4,10.8 ± 5.4 years, and 27. 9 ± 6.4 for women, respectively, the difference was statistically not significant (p>0.05). There were 115 (62.2%)) overweight/obese patients and 70 (37.8%) normal weight patients, the difference was statistically significant (p=0.015). There were no significant differences in structural joint damage, RF, and Anti-CCP between normal weight and overweight/obese groups, as shown in **Table 2**. There were statistically significant differences between normal weight and overweight/obese groups in VAS, ESR, CRP, and DAS28; P-values were 0.022, 0.031, 0.015, and 0.013, respectively, as shown in **Table 2**. There were no significant differences in clinical, laboratory, and disease activity between the overweight and obese patients, as shown in **Table 3**.

Discussion

Obesity is medically known as excess body fat that has accumulated to the extent that it may increase morbidity and mortality in obese individuals [23]. Obesity was found to associate with an increased risk of developing RA in a study comparing 349 incident cases of RA and 1457 controls, specifically in women [24]. Similarly, in a prospective case-control study of 165 pairs including both genders, obesity was associated with an almost 4-fold increase in the risk for developing RA; this association was again more pronounced in women [25] and, until recently, some authors still consider obesity as a potential contributor to the development of RA [26]. However, newer studies suggest that obesity is not a predisposing factor for RA [27,28]. The effect of body composition type on patients' clinical state and, more specifically, the degree of disease activity in RA has been examined in several previous studies [29-33], although their conclusions are

Table 1. Demographic and clinical data of the study population.

Char	Men 38 (20.54%)	Women 147 (79.46%)	p-value
Age (mean ± SD)	55 ± 7.4	52 ± 6.4	>0.05
Disease duration (mean ± SD)	9.8 ± 6.2	10.2 ± 5.4	>0.05
BMI (mean ± SD)	26.9 ± 7.2	27.9 ± 6.4	>0.05
DMARDs	38(100%)	147(100%)	>0.05
Biologics	36(94.7%)	140(95.2%)	>0.05

Table 2. Comparison between normal weight and overweight/obese RA patients with regard to clinical, laboratory, and disease activity.

Variable	Normal weight group	Overweight/ obese	P- value
Total (No. %)	70 (37.8%)	115 (62.2%)	0.015
Men (No. %)	12(6.5%)	26 (14%)	0.017
Women (No. %)	58 (31.3%)	89 (48.2%)	0.035
Age (mean±SD)	34 ± 5.1	56 ± 6.6	0.025
Disease duration (mean ± SD)	6.2 ± 5.5	11.2 ± 6.4	0.025
Joint erosion (No. %)	30 (42.8%)	51(44.3%)	0.188
Anti-CCP (No. %)	54 (77.1%)	89(77.4%)	0.192
RF (No. %)	57 (81.4%)	92 (80.0%)	0.187
VAS (mean ± SD)	3 ±1.1	7 ± 8.6	0.022
ESR (mean ± SD)	21 ±1.4	49 ± 8.8	0.031
CRP (mean ± SD)	2 ±7.2	7 ± 6.6	0.015
DAS 28	1.8	4.7	0.013

Table 3. Comparison between overweight and obese RA patient with regard to clinical, laboratory, and disease activity.

Variable	Overweight	Obese	P- value
Total (No. %) 185	65 (35.2%)	50 (27.0%)	0.145
Joint erosion (No. %)	20 (30.75%)	14 (28.0%)	
Anti-CCP (No. %)	50(76.9%)	38 (76.0%)	0.182
RF (No. %)	52 (80.0%)	41 (82.0%)	0.177
VAS (mean ± SD)	7 ± 1.3	7 ± 8.6	0.153
ESR (mean ± SD)	50 ± 2.4	49 ± 6.8	0.118
CRP (mean ± SD)	7 ± 7.1	7 ± 6.8	0.118

contradictory. Some reports found a significant association between higher disease activity and the presence of adiposity. Nevertheless, other reports found no proven association between the percentage of fat in body mass and the level of disease activity in RA. A worldwide study identified 18% of RA patients as obese, while a UK-based study found a higher prevalence of 31% [34]. However, in both studies, >60% of RA patients exhibited BMI above the desired levels (>25kg/m^2) and were overweight or obese. These results are comparable with those of the general population in the UK, where about 35% are overweight and about 25% obese [35]. Other studies' results indicate that overweight and obesity, even when assessed based on the general (WHO) BMI cut-offs, are at least as prevalent. In this study, overweight/obesity was highly prevalent, as defined by BMI (62.2%) of the study population; of them, 27% were obese. Moreover, it was found to be associated with high disease activity but not with joint erosion or serological positivity. These results are nearly similar to Guimaraes et al. findings [36], who reported that 26.9% of their patients were obese. Moreover, Hammoda et al. demonstrated that 32% of their patients were overweight, and 35% were obese [37]. In agreement with our results, Yacoub et al. [38] demonstrated that 30% of their patients were overweight, but 16.8% of their study population were obese, which is lower than our findings. One explanation of the increased prevalence of overweight and obesity in RA patients may be explained by reduced physical activity and long-term treatment of corticosteroids [39]. We found that overweight and obese patients were significantly older and had longer disease duration with statistically significant female predominance compared to the normal weight group. Voigt et al. [24] reported that obesity was prevalent in RA patients, in particular women. These results disagree with Gharbia et al. [40], who concluded that there was no significant statistical difference between RA patients with normal BMI and overweight RA patients regarding age, disease duration, and sex distribution. In this study, RA patients showed no significant difference in the clinical, laboratory, and activity indexes in terms of DAS-28 and VAS between overweight and obese subgroups. Vidal et al. found a protective effect of obesity against joint damage in their study population. Their results were explained by the association of obesity with seronegativity, which is known to be associated with a better structural prognosis or related to the more intensive therapy because of high DAS28 levels and/or high plasmatic drug concentrations for treatment with dosage adapted to the weight, such as infliximab, abatacept, and tocilizumab [41]. In contrast, we found no significant differences in radiological changes in a term of structural joint damage between overweight/obese and normal

weight patients. The result may be related to the lack of optimal treatment regimens, such as the shortage of biological agents in our locality. Our study showed a significant difference in activity indexes regarding DAS-28, VAS of pain, and inflammatory markers such as ESR and CRP. DAS-28, VAS, ESR, and CRP were all higher in overweight/obese patients than those normal-weight patients. This is in agreement with the findings of Stavropoulos-Kalinoglou et al. [14], who evaluated a total of 294 RA patients; based on BMI, patients were divided into four groups (underweight, normal weight, overweight, and obese) and found a significant difference in inflammatory markers and disease activity, between these groups: underweight or obese patients had significantly higher CRP, and poorer DAS-28 than those who had normal weight, which means that obese RA patients have more active disease on clinical, and laboratory levels. Hammoda et al. [37] also reported an increase in inflammatory markers such as (ESR and CRP) and disease activity indexes such as DAS-28 and VAS among overweight/obese compared to normal weight RA patients; results were consistent with ours. The current study found no significant associations between BMI and RF anti- CCP in RA patients. The findings of Gharbia et al. [40] agree with our study's results. However, other studies observed that obesity is significantly associated with increased development of negative anti-CCP [42,43]. In contrast to our finding Hammoda et al. and Yacoub et al. [37,38] studies revealed a statistically significant higher prevalence of RF and anti- CCP seropositivity among overweight and obese patients, and Ellabban et al. [44] reported nearly similar results.

Conclusion

Overweight and obesity were frequent among RA patients and associated with high disease activity. Therefore, weight reduction can help in the improvement of the clinical outcome and disease activity control.

Recommendation

More studies are required to investigate whether weight reduction can decrease the non-remission rate among obese RA patients.

Author's contributions

AM: Conceptualization, Methodology, Software, Data curation, Writing- Original draft preparation, approval of the final manuscript. FM: Visualization, Investigation, Software, Validation, approval of the final manuscript. AA: Writing- Reviewing and Editing, approval of the final manuscript.

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Conflicts of Interest

Authors declare that there is no conflict of interest.

References

1. Pons-Estel GJ, Alarcon GS, Scofield L, Reinlib L, Cooper GS. Understanding the epidemiology and progression of systemic lupus erythematosus. Semin Arthritis Rheum. 2010;39(4):257-68.
2. Kahlenberg JM, Fox DA. Advances in the medical treatment of rheumatoid arthritis. Hand Clinics. 2011;27(1):11–20.
3. Naidu GS, Bhilave N, Sharma K, Verma I, Sharma A. Prevalence of Metabolic Syndrome in Rheumatoid Arthritis Patients: A Case-Control Study from a Tertiary Care Centre in North India. The Journal of the Association of Physicians of India. 2019 Jul 1;67(7):22-4.
4. Son KM, Kang SH, Seo YI, Kim HA. Association of body composition with disease activity and disability in rheumatoid arthritis. The Korean Journal of Internal Medicine. 2021 Jan;36(1):214.
5. Neovius M, Simard JF, Klareskog L, Askling J; ARTIS Study Group. Sick leave and disability pension before and after initiation of antirheumatic therapies in clinical practice. Annals of the Rheumatic Disease. 2011 Aug;70(8):1407-14.
6. Eriksson JK, Neovius M, Bratt J, Petersson IF, van Vollenhoven RF, Geborek P, et al. Biological vs conventional combination treatment and work loss in early rheumatoid arthritis: a randomized trial. JAMA Internal Medicine. 2013 Aug 12;173(15):1407-14.
7. Cutolo M, Kitas GD, van Riel PL. Burden of disease in treated rheumatoid arthritis patients: going beyond the joint. Seminars in Arthritis and Rheumatism. 2014 Feb 43;(4):479-488.
8. AS OA, El-Karim A. Impact of obesity on rheumatoid arthritis: Relation with disease activity, joint damage, functional impairment and response to therapy. International Journal of Clinical Rheumatology. 2018;13(6).
9. Hotamisligil GS. Inflammation and metabolic disorders. Nature. 2006;444(7121):860-7.
10. Stavropoulos-Kalinoglou A, Metsios GS, Koutedakis Y, Kitas GD. Obesity in rheumatoid arthritis. Rheumatology. 2011 Mar 1;50(3):450-62.
11. Ellerby N, Mattey DL, Packham J, Dawes P, Hider SL. Obesity and comorbidity are independently associated with a failure to achieve remission in patients with established rheumatoid arthritis. Annals of the Rheumatic Diseases. 2014 Nov 1;73(11):e74.
12. Sandberg ME, Bengtsson C, Källberg H, Wesley A, Klareskog L, Alfredsson L, et al. Overweight decreases the chance of achieving good response and low disease activity in early rheumatoid arthritis. Annals of the Rheumatic Diseases. 2014 Nov 1;73(11):2029-33.
13. Vidal C, Barnetche T, Morel J, Combe B, Daïen C. Association of body mass index categories with disease activity and radiographic joint damage in rheumatoid arthritis: a systematic review and meta-analysis. The Journal of Rheumatology. 2015 Dec 1;42(12):2261-9.
14. García-Poma A, Segami MI, Mora CS, Ugarte MF, Terrazas HN, Rhor EA, et al. Obesity is independently associated with impaired quality of life in patients with rheumatoid arthritis. Clinical Rheumatology. 2007 Nov;26(11):1831-5.
15. Stavropoulos-Kalinoglou A, Metsios GS, Panoulas VF, Nevill AM, Jamurtas AZ, Koutedakis Y, et al. Underweight and obese states both associated with worse disease activity and physical function in patients with established rheumatoid arthritis. Clinical Rheumatology. 2009 Apr;28(4):439-44.
16. Baker JF, Østergaard M, George M, Shults J, Emery P, Baker DG, et al. Greater body mass independently predicts less radiographic progression on X-ray and MRI over 1–2 years. Annals of the Rheumatic Diseases. 2014 Nov 1;73(11):1923-8.
17. Westhoff G, Rau R, Zink A. Radiographic joint damage in early rheumatoid arthritis is highly dependent on body mass index. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology. 2007 Nov;56(11):3575-82.

18. Van Der Helm-van Mil AH, Van Der Kooij SM, Allaart CF, Toes RE, Huizinga TW. A high body mass index has a protective effect on the amount of joint destruction in small joints in early rheumatoid arthritis. Annals of the Rheumatic Diseases. 2008 Jun 1;67(6):769-74.

19. Fransson EI, Batty GD, Tabak AG, Brunner EJ, Kumari M, Shipley MJ, et al. Association between change in body composition and change in inflammatory markers: an 11-year follow-up in the Whitehall II Study. The Journal of Clinical Endocrinology & Metabolism. 2010 Dec 1;95(12):5370-4.

20. Derdemezis CS, Voulgari PV, Drosos AA, Kiortsis DN. Obesity, adipose tissue and rheumatoid arthritis: coincidence or more complex relationship. Clinical and Experimental Rheumatology. 2011 Jul 1;29(4):712-27.

21. Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, Bingham CO, et al. Rheumatoid arthritis classification criteria: an American College of Rheumatology/ European League Against Rheumatism collaborative initiative. Arthritis and Rheumatology. 2010;62:2569-81.

22. Aletaha D, Smolen J. The Simplified Disease Activity Index (SDAI) and the Clinical Disease Activity Index (CDAI): a review of their usefulness and validity in rheumatoid arthritis. Clinical and Experimental Rheumatology. 2005 Sep 1;23(5):S100.

23. Physical status: the use and interpretation of anthropometry. Report of a WHO expert committee. World Health Organ Tech Rep Ser 1995; 854:1–452.

24. Haslam D, James W. Obesity. Lancet 2005; 366:1197–1209.

25. Voigt LF, Koepsell TD, Nelson JL, Dugowson CE, Daling JR. Smoking, obesity, alcohol consumption, and the risk of rheumatoid arthritis. Epidemiology. 1994 Sep 1:525-32.

26. Symmons DP, Bankhead CR, Harrison BJ, Brennan P, Silman AJ, Barrett EM, et al. Blood transfusion, smoking, and obesity as risk factors for the development of rheumatoid arthritis. Results from a primary care-based incident case-control study in Norfolk, England. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology. 1997 Nov;40(11):1955-61.

27. Symmons DP. Looking back: rheumatoid arthritis—aetiology, occurrence, and mortality. Rheumatology. 2005 Dec 1;44(suppl_4):iv14-7.

28. Cerhan JR, Saag KG, Criswell LA, Merlino LA, Mikuls TR. Blood transfusion, alcohol use, and anthropometric risk factors for rheumatoid arthritis in older women. The Journal of Rheumatology. 2002 Feb 1;29(2):246-54.

29. Bartfai T, Waalen J, Buxbaum JN. Adipose tissue as a modulator of clinical inflammation: does obesity reduce the prevalence of rheumatoid arthritis?. The Journal of Rheumatology. 2007 Mar 1;34(3):488-92.

30. Giles JT, Bartlett SJ, Andersen RE, Fontaine KR, Bathon JM. Association of body composition with disability in rheumatoid arthritis: impact of appendicular fat and lean tissue mass. Arthritis Care and Research. 2008;59:1407-14.

31. Akar S, Sari I, Comlekci A, Birlik M, Onen F, Goktay Y, et al. Body composition in patients with rheumatoid arthritis is not different than healthy subjects. European Journal of Rheumatology. 2014;1:106-10.

32. Alvarez-Nemegyei J, Buenfil-Rello FA, Pacheco-Pantoja EL. Association between body composition and disease activity in rheumatoid arthritis. A systematic review. Rheumatol Clin. 2016;12:190–5.

33. Stavropoulos-Kalinoglou A, Metsios GS, Koutedakis Y, Nevill AM, Douglas KM, et al. Redefining overweight and obesity in rheumatoid arthritis patients. Annals of the Rheumatic Diseases. 2007 Oct 1;66(10):1316-21.

34. Rezuş E, Macovei LA, Burlui AM, Cardoneanu A, Rezuş C. Ischemic Heart Disease and Rheumatoid Arthritis—Two Conditions, the Same Background. Life. 2021 Oct 3;11(10):1042.

35. Naranjo A, Sokka T, Descalzo MA, Calvo-Alén J, Hørslev-Petersen K, Luukkainen RK, Combe B, Burmester GR, Devlin J, Ferraccioli G, Morelli A. Cardiovascular disease in patients with rheumatoid arthritis: results from the QUEST-RA study. Arthritis Research & Therapy. 2008 Apr;10(2):1-0.

36. Zaninotto P, Wardle H, Stamatakis E, Mindell J, Head J. Forecasting obesity to 2010. London: Department of Health. 2006.

37. Guimarães MF, Rodrigues CE, Gomes KW, Machado CJ, Brenol CV, Krampe SF, et al. High prevalence of obesity in rheumatoid arthritis patients: association with disease activity, hypertension, dyslipidemia and diabetes, a multi-center study. Advances in Rheumatology. 2019 Oct 28;59.

38. Hammoda RM, Moussa SG, Hassan RM. Prevalence of Obesity in A Cohort of Egyptian Rheumatoid Arthritis Patients and Its Implication on Disease Activity. The Egyptian Journal of Hospital Medicine. 2021 Jan 1;82(3):536-41.

39. Ibn Yacoub Y, Amine B, Laatiris A, Wafki F, Znat F, Hajjaj-Hassouni N. Prevalence of overweight in Moroccan patients with rheumatoid arthritis and its relationships with disease features. Clinical Rheumatology. 2012 Mar;31(3):479-82.

40. Abuhelwa AY, Hopkins AM, Sorich MJ, Proudman S, Foster DJ, Wiese MD. Association between obesity and remission in rheumatoid arthritis patients treated with disease-modifying anti-rheumatic drugs. Scientific Reports. 2020 Oct 29;10(1):1-9.

41. Ghrbia O, El-Bahnasawy A. Okasha A. Impact of obesity on rheumatoid arthritis: Relation with disease activity, joint damage, functional impairment and response to therapy. Internatonal Journal of Clinical Rheumatology. 2018;13(6).

42. Vidal C, Barnetche T, Morel J, Combe B, Daïen C. Association of body mass index categories with disease activity and radiographic joint damage in rheumatoid arthritis: a systematic review and metaanalysis. The Journal of Rheumatology. 2015 Dec 1;42(12):2261-9.

43. Pedersen M, Jacobsen S, Klarlund M, Pedersen BV, Wiik A, Wohlfahrt J, et al. Environmental risk factors differ between rheumatoid arthritis with and without auto-antibodies against cyclic citrullinated peptides. Arthritis Research & Therapy. 2006 Aug;8(4):1-5.

44. Wesley A, Bengtsson C, Elkan AC, Klareskog L, Alfredsson L, Wedrén S, et al. Association between body mass index and anti–citrullinated protein antibody–positive and anti–citrullinated protein antibody–negative rheumatoid arthritis: results from a population-based case–control study. Arthritis Care & Research. 2013 Jan;65(1):107-12.

45. Ellabban A, Abdelhakeem M, Hamdy M, Fathy I. Impact of obesity on functional and laboratory parameters in patients with rheumatoid arthritis. Egyptian Rheumatology and Rehabilitation. 2016 Jan;43(1):21-6.