



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 result in clinical improvement.

Keywords: Disease activity; Obesity; Body mass index; PASI; 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, of lipid,

adipokine, and insulin sensitivity [2]. Patients complaining of RA 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, recognizing factors that impact RA's outcome is essential. Obesity is implicated in this poor outcome, but this fact is still uncertain [7]. Because of the inflammatory nature of these two conditions, it is hypothesized that disease severity

and activity are related to obesity and overweight [7]. Studies suggest that adipose tissue is not just a store for inert energy. It is an endocrine organ that interplays with the central nervous and immune system, with a range of essential functions, such as proteins and hormone production, that are involved in physiological and pathological processes, including immunity and inflammation [8]. Therefore, obesity can activate the pro-inflammatory pathways; thus, obese patients have more severe diseases. 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 present in high concentrations in patient serum and link between RA and obesity [9]. Studies evaluating the correlation between high body fat and RA development have revealed controversial results. Some studies reported that obese patients respond incompletely to treatment. These patients did not achieve disease control and were associated with increased structural and functional impairment [10-12]. Some authors declare that obesity could result in high disease activity [13, 14]. In contrast, obese RA patients showed less radiographic joint damage [12, 15]. Moreover, studies revealed that obesity might delay joint damage, particularly 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 secrete adipocytokines and inflammatory cytokines, including adiponectin, tumor necrosis factor, interleukin-6, CRP, and others [18]. Adipocytokines exert an immunomodulatory effect and impact inflammation [19]. This fact offers a wide area of research, as adipocytokines essential factors in the pathophysiology of rheumatic diseases, such as RA. We conducted this study to estimate the prevalence and how overweight and obesity affect patients with RA.

Materials 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 demographic data, clinical findings, disease activity (number of tender/swollen joints among 28 joints), drug history, and presence of concomitant

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

BMI: body mass index, DMARDs: disease modifying anti-rheumatic drugs.

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 informed consents were obtained from the participants before their recruitment for the study. The study was conducted following 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 and 70 (37.8%) of patients had normal weight, 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. Differences in VAS, ESR, CRP, and DAS28 were statistically significant between the two groups. 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.

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

Anti-CCP: anticyclic citrullinated peptide, RF: rheumatoid factor, VAS: visual analogue scale, ESR: erythrocyte sedimentation rate, CRP: C reactive protein, DAS 28: disease activity score using 28 joints.

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
DAS 28	4.6	4.8	0.154

Anti-CCP: anticyclic citrullinated peptide, RF: rheumatoid factor, VAS: visual analogue scale, ESR: erythrocyte sedimentation rate, CRP: C reactive protein, DAS 28: disease activity score using 28 joints.

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]. In a study comparing 349 incident cases of RA and 1457 controls, obese individuals are vulnerable to an increased risk of developing RA, specifically in women [24]. Similarly, in a prospective case-control study of 165 pairs including both genders, obese individuals were 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 a potential contributor to RA development [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 RA activity has been examined in several previous studies [29], although their conclusions are contradictory. The presence of adiposity in RA patients and its association with higher disease activity was found by some studies. Nevertheless,

other reports found no proven link between high fat in body mass and high disease activity in RA. Worldwide research showed that 18% of RA patients are obese, while a study from the UK found a prevalence of 31% [30]. In both studies, more than 60% of patients had BMI above the normal levels (>25kg/m²) 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 [31]. Other studies' results indicate that overweight and obesity are at least as prevalent even when assessed based on the general (WHO) BMI cut-offs. 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 [32], who reported that 26.9% of their patients were obese. Moreover, Hammouda et al. demonstrated that 32% of their patients were overweight, and 35% were obese [33]. In agreement with our results, Yacoub et al. [34] 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 [35]. 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. [36], who concluded that there was no significant statistical difference between RA patients with normal BMI and overweight RA patients regarding age, gender, and disease duration. 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, and other biologics [37]. 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 and found a significant difference in inflammatory markers and disease activity between different study 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. Hammuda et al. [33] 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 the serological status in RA patients. The findings of Gharbia et al. [36] agree with our study's results. However, other studies observed that obesity is significantly associated with increased development of negative anti-CCP [38, 39]. In contrast to our finding Hammuda et al and Yacoub et al. [33, 34] studies revealed a statistically significant higher prevalence of RF and anti- CCP seropositivity among overweight and obese patients and Ellabban et al. [40] reported nearly the same results.

Conclusion

Overweight and obesity were frequent among RA patients and associated with high disease activity. Therefore, weight reduction could improve the clinical outcome and disease activity control.

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Conflicts of interest

Authors declare that there is no conflict of interest.

Author's contributions

A.J.M., F.T.M., and A.B.A. designed the study. A.J.M. and F.T.M. drafted the manuscript. A.J.M., F.T.M., and A.B.A. contributed to the acquisition and analysis of data. A.J.M., F.T.M., and A.B.A. validated and reviewed the drafted manuscript. All authors approved the final manuscript.

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