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ORIGINAL ARTICLE

Impact of Body Mass Index on Disease Severity in Rheumatoid Arthritis Patients

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Abstract

Background: Rheumatoid Arthritis (RA) is a chronic autoimmune disease characterized by joint inflammation and systemic manifestations, significantly impacting patients' quality of life. **Objective:** This study investigates the association of Body Mass Index (BMI) with disease severity in RA patients, focusing on inflammatory markers and clinical parameters. **Materials and Method:** A cross-sectional design was employed, enrolling RA patients from a rheumatology clinic who met specific inclusion criteria. Participants (n=90) were categorized into four BMI groups: normal, overweight, pre-obese, and obese. Clinical assessments included tender joint count (TJ28), swollen joint count (SJ28), and Disease Activity Score (DAS28-ESR), alongside biochemical markers such as Erythrocyte Sedimentation Rate (ESR), Rheumatoid Factor (RF), and Anti-Cyclic Citrullinated Peptide (ACCP). **Results**: Statistical analysis revealed that a higher BMI correlates with increased disease activity; notably, the obese group exhibited significantly elevated levels of ESR ($p = 0.026$*), TJ28 ($p = 0.014$*), SJ28 ($p = 0.030$*), and DAS28-ESR ($p = 0.024$*) compared to the other groups. The pre-obese group also showed higher ESR levels than those with normal BMI. These findings suggest that obesity exacerbates inflammation in RA patients, potentially due to adipose tissue secreting pro-inflammatory cytokines. Despite no significant difference in RF and ACCP in the BMI categories, the results highlight the direct effect of an increase in BMI on the disease severity in RA. Clinical outcomes in RA can be improved by weight management. Further research is required to elucidate the mechanistic role of obesity in enhancing the disease severity in RA. **Conclusion:** High BMI is significantly associated with an increase in the severity of rheumatoid arthritis. RA patients with obesity show an increase in inflammation and disease activity.

Keywords: Rheumatoid Factor; Erythrocyte Sedimentation Rate; Anti-Cyclic Citrullinated Peptide; Swollen Joint Count; Disease Activity Score.

INTRODUCTION

Rheumatoid Arthritis (RA), an autoimmune disease, exhibits systemic manifestations, including pain, swelling, and restricted mobility of joints [(1)]. The characteristics of RA include the positive serum autoantibodies like rheumatoid factor (RF) and anti-cyclic citrullinated peptide (ACCP) [(2)]. These antibodies produce joint deformity by destroying synovium and connective tissue associated with it.

The prognosis of RA can be assessed by the markers of inflammation, including C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) [(3)]. It has been seen that an increase in these inflammatory markers is associated with increased BMI in RA [(4)]. Hence, obesity causes aggravation of inflammation of joints in RA[(4, 5)]. An increase in disease severity and a decrease in treatment response has been reported in obese RA patients. Several factors are responsible for the effects of obesity on RA. An increase in adipose tissue leads to the release of pro-inflammatory cytokines, including IL-6 and TNF-α, which aggravates the chronic inflammation in RA. This increase in inflammation, along with dysregulation of the immune system caused by obesity, causes an increase in autoimmune reactions and more significant joint damage. In addition to this,

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obesity alters the effectiveness of RA treatments due to alterations in the pharmacokinetics of RA medicines. This includes a decrease in effectiveness and an increase in side effects of RA treatment [6]. The incidence of comorbid conditions, including diabetes and cardiovascular disease, along with obesity, additionally contributes to the complications in treatment and worsening of disease management, leading to a decrease in overall consequences for obese RA patients[7]. Body mass index (BMI) is a standard health assessment tool for determining obesity. However, it is not practical to assess the distribution of fat in particular areas of the body [8]. Changes in BMI or weight could be associated with a high risk of developing RA [9]. A previous study found that obesity plays a role in the rising prevalence of RA [10]. Raised BMI has been related to various metabolic abnormalities and systemic diseases. The possibility of comorbidities in RA, like cardiovascular diseases, type-2 Diabetes, and chronic pulmonary diseases, is fostered by obesity, thus reducing the quality of life in these patients[11]. Long-standing weight gain is related to an amplified risk of RA[11]. Since changes in BMI may provide insight into alterations in body composition [12]. Therefore, the present study aims to assess the association between BMI and disease activity in RA patients. By analyzing biochemical variables and disease activity scores across different BMI categories, this study aimed to provide further insights into whether higher BMI is associated with more severe RA symptoms, including elevated erythrocyte sedimentation rate (ESR), tender joint count (TJC28), swollen joint count (SJC28), and Disease Activity Score (DAS28-ESR). This understanding could have consequences for managing RA, accentuating the importance of weight management as part of the complete treatment approach.

MATERIAL AND METHODOLOGY

This cross-sectional study explored the association between BMI and disease severity in patients diagnosed with RA. The focus was on considering how BMI influences disease activity, including various inflammatory markers and clinical parameters of disease severity. Ethical approval was taken from Ziauddin University. The study included RA patients attending a rheumatology outpatient clinic or hospitalized for their RA-related symptoms. Informed written consent was obtained from the study participants. A total of 90 patients, aged between 18 and 80 years, diagnosed with RA, were included in this study. The patients of RA with Pregnancy or breastfeeding, chronic infections, or any serious comorbid conditions, such as malignancy or acute illness, and with a BMI outside the accepted range (i.e., underweight or morbidly obese, BMI <18.5 or >40) were excluded. Patients were grouped based on their BMI. The BMI was calculated for each participant using the formula: BMI = Weight (kg) / Height² (m^2). Participants were then classified into the following BMI groups: Normal BMI (18.5–22.9 kg/m^2), Overweight (23 –24.9 kg/m^2), Pre-obese (25–29.9 kg/m^2), and Obese (≥30 kg/m^2). Clinical and biochemical data, including demographics and disease activity measures: tender Joint count of 28 joints (TJ28), swollen joint count of 28 joints (SJ28), disease activity score based on 28 joints, including ESR as a measure of systemic inflammation (DAS28-ESR), were collected at the time of recruitment. Biochemical parameters, including ESR (mm/hour), RF (IU/mL), and ACCP (IU/mL), were included as markers of RA. Descriptive statistics were used to review demographic and clinical data. The Kruskal-Wallis test was applied to compare variables across the four BMI groups, as the data were non-parametric. The significance level was set at $p \leq 0.05$ for all statistical analyses.

RESULTS

The biochemical variables for the four BMI categories in RA patients are presented in Table 1. A Kruskal-Wallis test was applied to analyze the differences across these categories. A significant difference (p-value < 0.026) was observed, with elevated ESR levels in the pre-obese group when compared to the normal, overweight, and obese groups. Additionally, the obese group exhibited significantly higher levels of tender joint count (p-value < 0.014) when associated with the normal, overweight, and pre-obese groups. Similarly, there was a significant increase in the swollen joint count in the obese group (p-value < 0.030) compared to the other three groups (normal, overweight, and pre-obese). There was also a significant increase in the DAS28-ESR score in the obese group (p-

value < 0.024) as compared to the normal, overweight, and pre-obese groups. Interestingly, no significant modification in age, RF, and ACCP values among the three BMI groups was seen, suggesting that BMI may not directly predispose to these factors.

TABLE 1: COMPARISON OF CLINICAL PARAMETERS IN GROUPS OF BMI

Variables	Normal BMI (18.5-22.9) N=46	Overweight (23-24.9) N=19	Pre-obese (25-29.9) N=15	Obese (>30) N=10	p-value
	M(IQR)	M(IQR)	M(IQR)	M(IQR)	
Age (years)	48(15.50)	40 (15.00)	47 (8.00)	51.5 (20.00)	2.35
ESR (mm/hr)	35 (116.0)	16 (9.00)	38.5 (38.35)	35 (25.00)	0.026 *
RF (U/mL)	18.5 (125)	60 (83.00)	16 (85)	11.5 (55.00)	0.418
ACCP (EU/ml)	74 (199.00)	76.9 (118.00)	47 (8.00)	51.5 (20.00)	0.386
TJ28	5 (4.00)	5.5 (6.5)	9 (5.00)	10 (9.00)	0.014 *
SJ28	2 (4.00)	4 (3.00)	3 (3.00)	5.5 (7.25)	0.030 *
DAS28-ESR	1.32 (1.72)	4.41 (2.21)	4.9 (0.62)	5.38 (1.47)	0.024 *

*≤ 0.05 p-value. **≤ 0.001 p-value
"BMI: body mass index; RF: rheumatoid factor; ACCP: anti-cyclic citrullinated peptide; TJ28: tender joint count of 28 joints; SJ28: swollen joint count of 28 joints; DAS28-ESR: disease activity score of 28 joints-erythrocyte sedimentation rate;"

The graphical representation in Figure 1 highlights the positive correlation between BMI and DAS28-ESR. The Spearman's rank correlation coefficient of 6.76, with a p-value of 0.001, further indicates a strong positive relationship. This supports the idea that BMI is associated with amplified disease activity in RA patients.

DISCUSSION

The findings of our study specify a significant relationship between BMI and disease severity in patients with RA. Explicitly, we observed that higher BMI categories, particularly the pre-obese and obese groups, were associated with elevated levels of inflammatory markers such as ESR, as well as increased clinical parameters indicative of disease activity, including TJ28, SJ28, and DAS28-ESR [9]. Our results align with previous research, which has recognized a link between obesity and heightened inflammation in RA patients. The elevated ESR levels observed in the pre-obese and obese groups suggest that adipose tissue may play a critical role in modulating inflammatory processes. Adipose tissue serves as

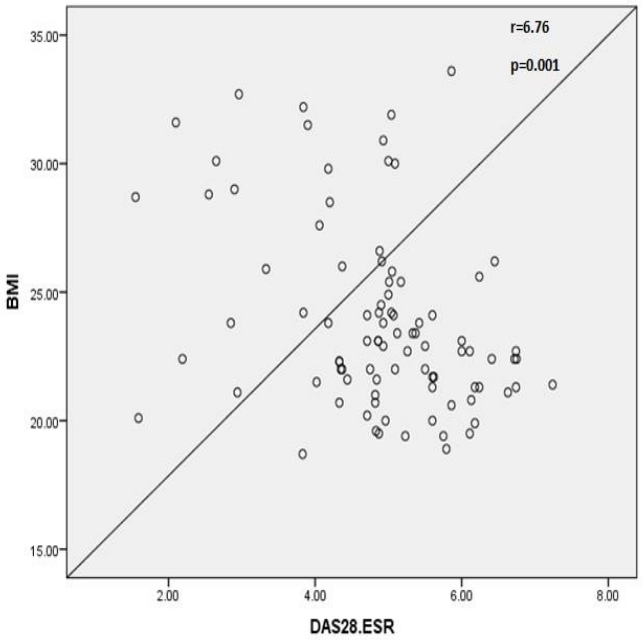

Figure 1: Correlation of BMI and DAS28-ESR in RA patients

a passive storage area for fat and actively produces various pro-inflammatory cytokines, known as adipokines. These substances can contribute to systemic inflammation, potentially exacerbating the autoimmune response seen in RA. This shows the mechanistic role of higher BMI in causing the severity of RA symptoms and disease activity. Additionally, an increase in the tenderness and number of joints involved in obese RA patients added to the concept that enhanced inflammatory responses are the contribution of obesity to joint tenderness. Inflammation leads to characteristic features of RA, including hyperplasia of synovium and an increase in pain sensitivity. Our study's findings are comparable with those of other studies, showing a correlation between obesity and an increase in the number of tender joints. This indicates that weight reduction is required in RA treatment [9]. A significant difference in swollen joint count has been seen among BMI groups, hence emphasizing the challenges faced by obese RA patients. Active inflammatory signs can be

irreversible if inadequate management is not implemented. This indicates that a decrease in RA effects can be achieved through early intervention and potential lifestyle modifications, including weight reduction [13]. Our study showed a significant association between BMI and clinical parameters of RA disease activity. However, no significant difference among BMI groups was found in RF or anti-cyclic citrullinated peptide (ACCP) levels. This proposes that obesity influences the severity of disease and inflammatory responses but does not essentially affect the production of autoantibody linked with RA. It signifies an intricate mechanism of the effect of obesity on clinical manifestations, with no impact on serological markers. Future research is required to learn more about the processes involved in this association. The study's limitation is its small sample size.

CONCLUSION

The research identified a notable link between elevated BMI and greater disease severity in RA patients, revealing that obese individuals exhibited higher inflammation and disease activity compared to normal or overweight BMI. While no notable correlation was found between RF and ACCP levels, the findings indicate that obesity might exacerbate RA outcomes. These results emphasize the importance of managing BMI in RA patients to improve disease management and quality of life.

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REFERENCES

1. Shrivastava AK, Pandey A. Inflammation and rheumatoid arthritis. Journal of physiology and biochemistry. 2013;69:335-47.
2. Sarkar R, Ghosh B, Lama M. Association of rheumatoid factor and anti-cyclic citrullinated peptide antibody with demographic, clinical, and inflammatory parameters in rheumatoid arthritis. Indian Journal of Health Sciences and Biomedical Research kleu. 2023;16(3):355-60.
3. Talotta R. The diagnostic laboratory tests in rheumatic diseases. Translational Autoimmunity: Elsevier; 2023. p. 113-48.
4. Mohan DFR, Jawad AT, Jaber AS. Review Article: Rheumatoid Arthritis and its Relationship with Vitamin D, ESR, and Obesity. International Journal of Toxins and Toxics. 2024;1(1):6-12p.
5. Yahya MZ, AL-Jarash RMN, Omran DG. Determination the Relationships between Body Mass Index and Incidence of Rheumatoid Arthritis. HIV Nursing. 2022;22(2):1824–32-–32.
6. Wang T, He C. Pro-inflammatory cytokines: The link between obesity and osteoarthritis. Cytokine & growth factor reviews. 2018;44:38-50.
7. Tsigalou C, Vallianou N, Dalamaga M. Autoantibody production in obesity: is there evidence for a link between obesity and autoimmunity? Current Obesity Reports. 2020;9:245-54.
8. Mohajan D, Mohajan HK. Body mass index (BMI) is a popular anthropometric tool to measure obesity among adults. Journal of Innovations in Medical Research. 2023;2(4):25-33.
9. Hollander Nd, Boeren AP, van der Helm-van Mil A, van Steenbergen H. Patients with obesity have more inflamed joints and higher CRP levels during the disease course in ACPA-positive RA but not in ACPA-negative RA. Arthritis Research & Therapy. 2024;26(1):42.
10. Shaikh SR, Beck MA, Alwarawrah Y, MacIver NJ. Emerging mechanisms of obesity-associated immune dysfunction. Nature Reviews Endocrinology. 2024;20(3):136-48.
11. Tournadre A, Beauger M. Weight loss affects disease activity and treatment response in inflammatory rheumatic diseases. Joint Bone Spine. 2024;91(3):105647.
12. de Carvalho Braga G, Simões JLB, Dos Santos YJT, Menta Filho JC, Bagatini MD. The impacts of obesity in rheumatoid arthritis and insights into therapeutic purinergic modulation. International Immunopharmacology. 2024;136:112357.
13. Meng CF, Lee Y, Schieir O, Valois MF, Butler M, Boire G, et al. Having More Tender Than Swollen Joints is Associated With Worse Function and Work Impairment in Patients With Early Rheumatoid Arthritis. ACR open rheumatology. 2024;6(6):347-55.