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Original Article

Correlation of Body Mass Index with Inflammatory Markers in Rheumatoid Arthritis Patients

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ABSTRACT

Objective: To study the correlation of body mass index with inflammatory markers among rheumatoid arthritis patients.
Study Design: Comparative cross-sectional study.
Place and Duration of Study: Department of Biochemistry and Molecular Biology, Army Medical College, Rawalpindi Pakistan, in collaboration with the Rheumatology Department and laboratory of Pak Arab Emirates Military Hospital (PEMH), Rawalpindi Pakistan from Jan 2020 to Jan 2021.
Methodology: The study sample was sixty in number and was divided into two groups. Diagnosed Rheumatoid Arthritis (RA) patients on modifying rheumatic Drugs (DMARDs) therapy constituted Group-I. At the same time, Group-II consisted of 30 healthy individuals. BMI, C reactive proteins (CRP) and erythrocyte sedimentation rate (ESR) of both groups were assessed and compared. The correlation of BMI with inflammatory markers was also assessed in both groups.
Results: Sixty subjects with a mean age of 44.90±10 years were distributed evenly among two groups. Mean inflammatory markers for ESR and CRP, were 30.70±16.46 and 11.65±12.97, respectively, of Group-I. There was a significant difference in CRP and ESR ($p \leq 0.05$) among the two groups. The mean BMI was 25.20±4.65, which was also raised for Group-I. BMI was positively correlated with inflammatory markers in both groups. Group-I showed a more positive correlation of BMI with ESR (r=0.23) than Group-II (r= 0.143).
Conclusion: BMI is positively correlated with inflammatory status among RA patients.

Keywords: Body mass index (BMI), Erythrocyte sedimentation Rate (ESR), C reactive protein (CRP), Rheumatoid arthritis.

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INTRODUCTION

Rheumatoid Arthritis (RA) is a systemic inflammatory and autoimmune disease of joints that presents with inflammation, pain and decreased mobility of joints, and it also has systemic manifestations as well.[1] The regional prevalence of RA for countries of poor or moderate socio-economic status is 0.40%.[2] 0.142 % prevalence with female predominance from Karachi, Pakistan, was documented, along with 26.9% point prevalence in Karachi by the year 2015.[3]

Inflammatory markers like Erythrocyte Sedimentation Rate (ESR) and C-reactive protein (CRP) are habitually used as diagnostic and prognostic markers of RA.[4,5] CRP and ESR are acute-phase proteins, which are glycoproteins that are produced in the body in response to stimuli like inflammation or trauma. The amount of acute phase proteins corresponds to the severity of the stimulus. ESR is largely a measure of fibrinogen, whereas CRP is sensitive to the rheumatoid factor (RF) and immunoglobulin.[6,7] ESR provides information about the severity of the disease. CRP plays a regulatory role in inflammation and atherosclerosis.[8]

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Elevated BMI has been associated with various diseases and metabolic abnormalities, many of which have high mortality and morbidity. The risk of comorbidities in RA, like Type-2 Diabetes, cardiovascular diseases and chronic pulmonary diseases, is increased by obesity, thus decreasing the quality of life of RA patients.[9] On the contrary, it has also been observed that lean patients have elevated inflammatory markers in their blood and tend to show more radiographic joint damage.[10]

The rationale of this study is that it will emphasise inflammation as a biochemical basis of an autoimmune disease like RA. Moreover, it will link the effect of adipose tissue in the context of Body Mass Index (BMI) to RA in Pakistani cohorts. The objective of the study was to evaluate associations between inflammatory markers and BMI in RA patients.

METHODOLOGY

The comparative cross sectional study was conducted at the Department of Biochemistry and Molecular Biology, Army Medical College, Rawalpindi after formal approval from the Ethical Review Committee (Certificate number: ERC/ID/77). Patients were enrolled from the Rheumatology Department of Pak Arab Emirates Military Hospital (PEMH), Rawalpindi,

from January 2020 to January 2021. The sample size was calculated by using a correlation sample size calculator with parameters, expected correlation coefficient (r) to be 0.41.[10] Non-probability convenient sampling was done for sixty subjects.

Inclusion Criteria: Patients aged 30-60 years, of either gender, diagnosed with RA (disease duration: 8 to 10 years) and who had been on DMARD therapy for five years were enrolled in the study as Group-I. Healthy age and gender matched controls were enrolled in Group-II.

Exclusion Criteria: Patients of other chronic illnesses, malignancies, infections, pregnancy, patients of any other type of arthritis, and patients of RA not on DMARD therapy were excluded.

Thirty diagnosed patients with RA on DMARD therapy for five years were included as Group-I. Group-I individuals were in the period of remission and were advised to continue treatment in their follow-up visits. 30 healthy controls were enrolled in Group-II. The health status of the enrolled subjects was assessed by history and general physical examination. Enrolled healthy subjects were paramedical staff of PEMH. Individuals with normal blood pressure, pulse rate and body temperature were included as healthy subjects.

Written informed consent was taken from each subject. Biochemical parameters, i.e. inflammatory markers (ESR and CRP) of 60 subjects, were assessed. A detailed history of 60 subjects was taken. The history Performa included a record of the age, ethnicity, socio-economic status, weight and height of subjects. BMI is calculated by dividing weight in kg by height in square meters.[11] WHO criteria classify BMI into underweight (<18 kg/m_2), normal (18.5-24.9 kg/m_2), overweight (25-29.9 kg/m_2) and obese (>30kg/m_2) category.[12] In this study, the correlation of inflammatory markers was assessed with BMI among RA and controls.

Data was analysed using Statistical Package Social Sciences (SPSS) version 22. Quantitative variables were expressed as mean±SD and qualitative variables were expressed as frequency and percentages. Independent sample t-test was applied to explore the inferential statistics. Variables were correlated through Pearson's correlation. The *p*-value of ≤0.05 was considered statistically significant.

RESULTS

A total of 60 subjects aged 40-60 years were enrolled in the study. The mean age of the participants was 44.90±10.50 years, out of which 56.7% (34/60) were males. The average BMI of the participants was 24.85±3.97 kg/m_2, with a minimum BMI of 17.93 kg/m_2 and a maximum BMI of 42.90 kg/m_2. The mean ESR, CRP and BMI among patients and controls are given in Table-I.

Table-I: Comparison parameters between the Study Groups (n=60)

Variables	Group-I (Rheumatoid Arthritis) (Mean±SD)	Group-II (Controls) (Mean±SD)	*p*-value
Body Mass Index (kg/m_2)	25.20±4.65	24.51±3.21	0.507
Erythrocyte Sedimentation Rate (mm/hour)	30.70±16.46	17.8±9.29	0.050
C-Reactive Protein (CRP) (mg/L)	11.65±12.97	2.96±3.94	0.003

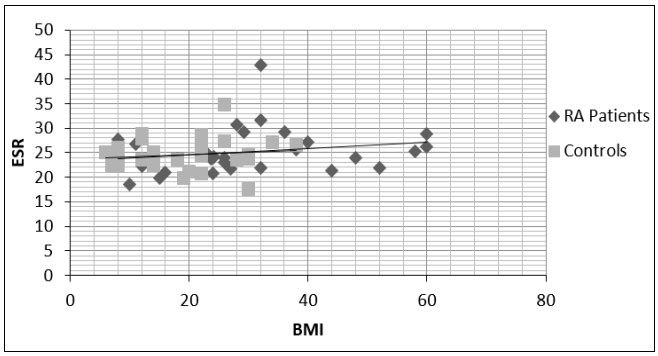

Figure -1: Scatter plot showing positive Correlation of ESR with BMI in both Groups

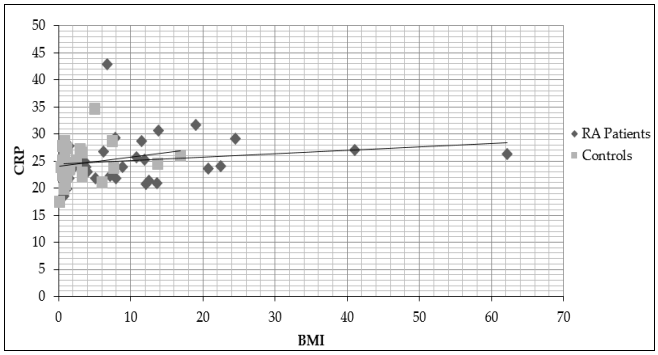

Figure-2: Scatter plot showing positive Correlation of CRP with BMI in both Groups

The mean values of ESR and CRP were significantly elevated in Group-I patients (RA Group) with a *p*-value of <0.05. At the same time, the mean values of BMI in the RA Group were higher than controls. Figure-1 shows that , ESR was markedly raised in RA patients, which is positively correlated with BMI (r=

0.23, p=0.001) in the RA Group. Whereas ESR, though positively correlated in controls, this correlation is statistically insignificant (r=0.143, p=0.452). Similarly, positive correlations are seen between BMI and CRP in the RA group (r=0.180,p=0.34) and in Controls (r= 0.215, p=0.124), respectively. However, CRP correlation with BMI was statistically insignificant in both groups, as shown in Figure-2.

DISCUSSION

Decreased health-related quality of life and depression are linked to obesity in various chronic illnesses, but this is less studied in RA patients. Obesity in the context of BMI, when studied across the globe, suggested that 42.9% of RA patients had a BMI ≥25kg/m_2 (overweight), which supports our findings.[13] The mean BMI of RA patients were 25.20 kg/m_2 (≥ 25kg/m_2, Obese) in our study. A higher BMI was seen in our RA Group. It has been seen that obesity is linked to higher systemic inflammation among RA, and obese RA patients have inferior response to treatment.[14] In a study conducted in Germany that involved over fifteen thousand RA patients, obesity in the context of BMI was 23.4 % more predominant among RA than among healthy controls, and higher figures have been stated (31.6%) in Mexican RA cohorts.[15] It was also seen in a study that among RA patients, females showed more mean BMI than males.[16] Obesity modulates inflammation and increases the risk of joint damage and following inflammation due to joint loading. Pain and inflammation then will again reduce physical activity in RA patients.[17,18]

The main focus of our study was to analyse the contribution of inflammation in autoimmune diseases like RA. ESR and CRP were significantly raised in the RA Group. Our results coincide with Pakistani studies that also showed significantly higher levels of ESR and CRP in the RA group.[19] CRP levels in the first year of RA correlate with the severity of clinical and radiological joint damage.[20]

The most central aspect of our study was the correlation of BMI with the inflammatory markers in our study. CRP and ESR showed an increasing trend with BMI in RA patients as well as controls. Similar results were seen in a study conducted by Simeons *et al*. They concluded that BMI became significantly associated with both inflammatory markers (CRP and ESR) at later stages of the disease. It has been advocated that higher secretion of IL-6 has been linked with being overweight, which ultimately is responsible for higher acute phase reactants.[11]

There is a positive correlation between CRP and ESR with RA, indicating that inflammatory processes may be an underlying mechanism of an autoimmune disease like RA. It also suggests that inflammatory markers are prognostic markers for RA. Moreover, the direct relationship between BMI and Inflammatory markers indicates the influence of weight gain in the development and progression of the disease.

LIMITATION OF STUDY

BMI does not reflect adipose tissue changes over time, so it's not an ideal measure of obesity and cachexia in chronic conditions like RA.

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CONCLUSION

The findings suggest that inflammatory markers are positively correlated with BMI in RA patients. It explains that obesity does not have a protective role in RA. Results also emphasise that 'inflammation' is a biochemical basis of an autoimmune disease like RA, as inflammatory markers were significantly raised in the RA group. Moreover, the study has also linked the effect of adipose tissue in the context of Body Mass Index (BMI) to RA in Pakistani individuals.

Conflict of Interest: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

YT & AR: Conception, study design, drafting the manuscript, approval of the final version to be published.

MJY & AM: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

AM: Critical review, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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