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Association between Rheumatoid Arthritis Disease Activity and Comorbidities

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Abstract

Background and objectives: Rheumatoid arthritis is an autoimmune condition marked by chronic joint inflammation, frequently resulting in substantial impairment and diminished quality of life. However, rheumatoid arthritis rarely occurs in isolation, as individuals with this condition frequently present with comorbidities, such as cardiovascular disease, diabetes, and osteoporosis. Understanding the role of comorbidities in Rheumatoid Arthritis is critical for comprehensive patient care. The aim of this study was to investigate the impact of various comorbidities on disease activity of rheumatoid arthritis.

Methods: Patient data for this cross-sectional study was collected at rheumatology outpatient of Rizgary teaching hospital in Erbil city of Kurdistan-Iraq from August 2022 August 2023. Study participants included patients with rheumatoid arthritis with (n=60) and without (n=60) comorbidities and they were matched for age and sex.

Results: Our findings revealed that among patients with rheumatoid arthritis, hypertension is the most frequent comorbidity, affecting 27 patients (45%) of them. This is followed by the coexistence of hypertension and diabetes mellitus in 9 (15%) of cases, and hypothyroidism in 8 (13.3%) of cases. Furthermore, the study establishes a strong and statistically significant link between patient age and the presence of comorbidities ($p<0.001$). Additionally, it demonstrates a significant correlation between the high activity of RA disease and comorbidities ($p=0.03$).

Conclusions: This research is providing insights into the ways in which these accompanying medical conditions affect the activity of rheumatoid arthritis. The results of this current study have important implications for making treatment choices, assessing risks, and crafting customized approaches to managing this disease.

Keywords: BMI, Comorbidities, DAS28 Score, Rheumatoid Arthritis.

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Introduction

Rheumatoid arthritis (RA) is a common persistent autoimmune disorder that affects approximately 1% of the global population, largely women, and leads to joint inflammation, pain, and functional impairment.[1] The hallmark of RA is its long-term inflammation of the synovial joints, leading to cartilage degradation by the substantial infiltration of inflammatory cells into the synovial tissue, coupled with the excessive growth of synovial fibroblasts in individuals with RA, leads to the formation of an overgrown tissue known as hyperplastic pannus, which aggressively invades and kills underlying cartilage and causes bone erosion, and ultimately loss of joint.[2, 3] This process not only causes physical discomfort but also diminishes the overall quality of life for those living with the condition.[4, 5] The precise cause of RA remains obscure, though a combination of genetic predisposition and environmental triggers is believed to be a factor which is involved in disease development.[6, 7] The presence of ACPA, RF, and growing CRP levels in some patient years before the onset of clinical symptoms suggests that critical immunological responses for RA development begin extremely early. The shared epitope alleles, the most important genetic risk factor for RA development, is found in the MHC class II area.[6, 8, 9] RA often exhibits a progressive course, making early diagnosis and intervention critical for preventing irreversible joint damage and disability. Over the years, advancements in understanding of the disease have transformed the management of RA. Innovative therapies, ranging from conventional disease-modifying antirheumatic drugs (DMARDs) to biologics and targeted synthetic (DMARDS), have revolutionized treatment strategies, allowing for better disease control and improved patient outcomes.[10] While the direct effects of RA on joint health are well documented, an often-underestimated aspect of this condition is its interaction with comorbidities. These comorbidities can significantly affect the course of the disease, influencing its progression, treatment strategies, and overall patient outcomes.[11] Comorbidities such as cardiovascular diseases, metabolic syndrome, osteoporosis, psychological diseases have all been reported to occur at a higher prevalence in RA patients compared to the general population. These additional health burdens not only complicate disease management but also impact the overall prognosis of RA.[11-13] According to the findings of the COMORA trial, CVD is the third most common diagnosed comorbidity in RA.[11] In these studies, the higher death rate of RA appears to be due to an increased frequency of cardiovascular disease, an increased incidence of infections, and the development of specific cancers in RA patients. Some of these comorbidities are more common in RA patients because of the medications they are taking, particularly glucocorticoids.[14] There are studies demonstrating that RA is frequently worsened by accelerated atherosclerosis and an elevated risk of CVD.[15, 16] Furthermore, RA has been linked to several autoimmune disorders, including thyroid dysfunction. It was observed that people with RA who also had hypothyroidism had greater disease activity.[17] Obesity is also linked to increased inflammatory activity, as evidenced by a higher number of tender and swollen joints in RA patients, which indicate increased disease activity.[18] Understanding the multifaceted impact of comorbidities on RA is essential for devising effective therapeutic strategies that address the entirety of a patient's health status. The object of the present study is to delve into the various comorbidities associated with RA and the implications they pose for clinical management. It is mainly aimed at investigating alterations in the activity of RA in patients with and without

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comorbidities and influence of chronic illnesses on the course of RA using DAS28 score.

Patient and methods

Data for this cross-sectional study was collected at rheumatology outpatient of Rizgary teaching hospital in Erbil city of Kurdistan-Iraq from August 2022-August 2023 for 120 patients of RA with (n=60) and without (n=60) comorbidities such as cardiovascular diseases, hypertension, diabetes, thyroid disorders, and obesity. The diagnosis of Rheumatoid Arthritis` was confirmed both clinically and using laboratory parameters according to ACR/EULAR criteria for RA which is published in 2010. The study abided all the regulations related to the Declaration of Helsinki. Demographic data, disease activity variables, laboratory data including ESR, CRP, RF, and ACPA were collected and recorded in a standard study form while interviewing patients. All study participants signed an informed consent before participation in the study. Rheumatoid Arthritis disease activity was categorized according to DAS28 score in this study. The inclusion criteria included patients who were 16 years and above regardless of gender who fulfilled the 2010 ACR/ EULAR criteria for diagnosis of RA. In addition, comorbidities were confirmed based on investigations and medical reports provided by treating physicians. Ethical approval for the scientific evaluation was granted by the Ethics and Scientific Committees of the Kurdistan Higher Council of Medical Specialties under approval number 852 on July 4th, 2022. The study also ensured the confidentiality of the collected data. The data is analyzed by SPSS program-26. The chi square and fishers' exact tests were performed for statistical relationships. *P* value of ≤0.05 was considered as significant.

Results

This study included sixty RA patients with clinical comorbidities (Group 1) and 60 RA patients without comorbidities (Group 2). The comorbidity in group 1 is commonly hypertension (45%), followed by hypertension & diabetes mellitus (15%), hypothyroidism (13.3%), hypertension & heart disease (6.7%), hypertension & hypothyroidism (6.7%) and diabetes mellitus (5%) Figure (1).

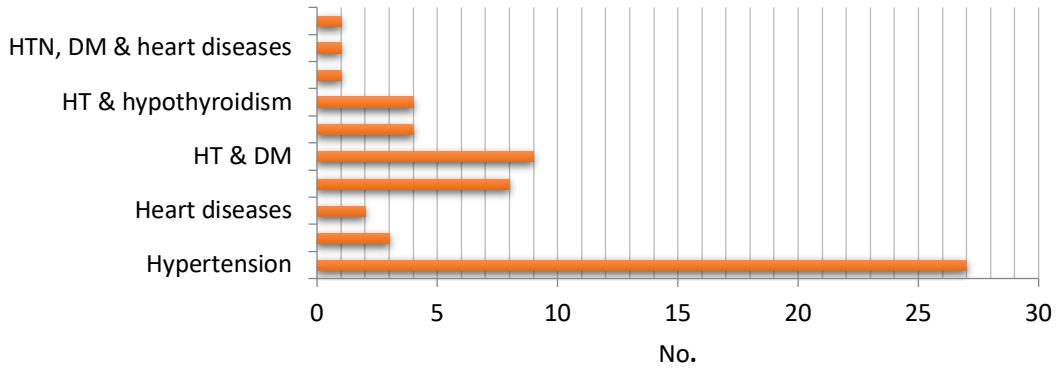

Figure (1): Incidence of comorbidities in patients diagnosed with RA.

There was a highly significant association between increase in the age of RA patients and comorbidities (p<0.001). No significant differences were observed between group 1 and group 2 in terms of gender (p=1.0). A significant association was observed between obesity of RA patients and comorbidities (p=0.03), Table (1).

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Table (1): General characteristics of RA patients in study groups

Variables	Study groups				p value
	Group 1		Group 2		
	No.	%	No.	%	
Age (years)					<0.001 S
<40	3	5.0	20	33.3	
40-49	11	18.3	15	25.0	
50-59	28	46.7	15	25.0	
≥60	18	30.0	10	16.7	
Gender					1.0 NS
Male	9	15.0	9	15.0	
Female	51	85.0	51	85.0	
Body mass index					0.03 S
Normal	7	11.7	18	30.0	
Overweight	25	41.7	23	38.3	
Obese	28	46.7	19	31.7	

S=Significant, NS=Not significant

No significant differences were observed between group 1 and group 2 patients regarding conventional DMARDs (p=0.4), biological DMARDs (p=0.2) and steroids (p=0.358), Table (2).

Table (2): Treatments received by RA patients in the study groups

Variables	Study groups				p value
	Group 1		Group 2		
	No.	%	No.	%	
Conventional DMARDs					0.4 NS
No	11	18.3	7	11.7	
Methotrexate	18	30.0	22	36.7	
Hydroxychloroquine	6	10.0	3	5.0	
Leflunomide	0	.0	5	8.3	
Sulfasalazine	2	3.3	1	1.7	
Azathioprine	1	1.7	1	1.7	
MTX & HCQ	9	15.0	11	18.3	
MTX & LEF	5	8.3	4	6.7	

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Other combinations	8	13.3	6	10.0	
Biological DMARDs					0.2 NS
No	23	38.3	31	51.7	
TNF blocker	26	43.3	17	28.3	
Rituximab	11	18.3	12	20.0	
Steroids					0.58 NS
No	33	55.0	31	51.7	
Prednisolone 5mg	21	35.0	23	38.3	
Prednisolone 10mg	2	3.3	2	3.3	
Prednisolone 20 mg	2	3.3	0	-	
Medrol 4mg	2	3.3	4	6.7	

NS=Not significant

There was a highly significant association between high activity of RA disease and comorbidities (p=0.03). Mean DAS28 score was significantly higher among RA patients with comorbidities when compared to RA patients without comorbidities (p=0.02), Table (3).

Table (3): Rheumatoid arthritis disease activity according to study groups

Variables	Study groups				p value
	Group 1		Group 2		
	No.	%	No.	%	
DAS28 score					0.03 S
Remission	4	6.7	5	8.3	
Low activity	0	.0	5	8.3	
Moderate activity	19	31.7	26	43.3	
High activity	37	61.7	24	40.0	
Mean±SD	5.4±1.6		4.7±1.5		0.02 S

S=Significant

Discussion

Assessing comorbidities in patients with RA is essential in planning for management. From a clinical perspective, it is crucial to strike a balance between addressing the treatment requirements of RA concurrent comorbidities. Additionally, it is necessary to take these co-morbidities in consideration in assessment of RA activity and severity.[19] Present study showed that comorbidities in RA patients is commonly hypertension (45%), followed by; hypertension & diabetes mellitus (15%), hypothyroidism (13.3%). The study findings are in line with results of Noori et al which is a cross sectional study in Iraq demonstrated hypertension was the

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commonest co-morbidity among RA patients followed by diabetes mellitus and thyroid diseases.[20] Furthermore, our study findings are also in line with results of Al-Bishri et al where they displayed that hypertension was the commonest co-morbidity in RA patients, followed by diabetes mellitus, osteoporosis and dyslipidemia.[21] Jeong et al stated that RA patients had more comorbidities than non-RA patients including hypertension, dyslipidemia and heart diseases.[22] Our study demonstrated a highly significant association between elderly patients with RA patients and comorbidities ($p<0.001$). This finding goes in parallel with results of van Onna and Bonnen study which reported that co-morbidities are more prevalent among elderly RA patients.[23] Mousavi et al study showed higher incidence of RA among elderlies that is accompanying comorbidities.[24] Findings in the current study indicated a considerable association between obesity in RA patients and comorbidities ($p=0.03$). This finding is consistent with results of Balsa et al national sub-analysis of the COMORA study which revealed a significant link between obesity and prevalence of co-morbidities in RA patients. This finding is consistent with results of Balsa et al national sub-analysis of the COMORA study which revealed a significant link between obesity and prevalence of co-morbidities in RA patients.[25] On the other hand, our study revealed no significant differences between group 1 and group 2 patients regarding conventional DMARDs, biological DMARDs and steroids ($p>0.05$). These findings are similar to results of Tidblad et al nationwide clinical study which reported that most comorbid conditions do not limit the commencement or continuation of treatment like methotrexate or other DMARDs in early rheumatoid arthritis.[26] In present study, there was a highly noteworthy association between high activity of RA disease and comorbidities ($p=0.03$). This finding is in parallel to results of many previous studies such as Innala et al nationwide study and Garip et al cross-sectional study which all documented high disease activity or high DAS28 score among RA with comorbidities as compared to RA patients without co-morbidities.[27, 28] In our study, mean DAS28 score was significantly higher among RA patients with co-morbidities as compared to RA patients without co-morbidities ($p=0.02$). This finding is consistent with results of Kłodziński and Wisłowska study which found that mean DAS28 score was significantly higher among RA patients with hypertension as compared to RA patients without hypertension.[29] In Iraq, a cross sectional study conducted by Jwad et al on 250 RA patients found that RA patients with chronic diseases had higher medication-related burden and high RA disease activity.[30] Different authors found that comorbidities have obvious effect on RA disease activity which in turn leads to increased pain and death rate in addition to their effect by increasing risk of RA development and progression.[31-33]

Conclusion

Comorbidities have a profound effect on disease activity in RA. Advanced age and obesity are risk factors associated with comorbidities in individuals with RA. The management approaches in RA are not affected by presence or absence of comorbidities. Our study recommends that physicians to take the comorbidities accompanying RA into consideration when planning for management especially in elderly and obese patients. Further national multi-center studies on role of comorbidities in development and severity of RA are warranted.

Conflict of interest

The authors declare that there is no conflict of interest related to this study.

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