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Research Paper

New and emerging therapies: review the latest advancements in rheumatology treatments, including biologic therapies, targeted therapies, regenerative medicine, and novel drug development, assessing their potential benefits and limitations

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ABSTRACT

Background: Rheumatic diseases are chronic inflammatory conditions associated with joint damage, functional disability, and reduced quality of life. Recent advances in biologic therapies, targeted treatments, and disease-modifying antirheumatic drugs (DMARDs) have improved disease management.
Objective: To evaluate clinical outcomes, treatment patterns, disease activity, and quality of life among patients with rheumatic diseases receiving contemporary therapeutic approaches.
Methods: A cross-sectional study was conducted involving 80 patients with rheumatic diseases from hospitals in Iraq between February 2022 and September 2023. Demographic characteristics, clinical manifestations, comorbidities, treatment regimens, and disease activity were assessed. Disease activity was classified using the DAS28 scale, while quality of life was evaluated across physical, psychological, emotional, social, and daily activity domains.
Results: Females accounted for 80% of patients, and obesity was reported in 50%. Joint pain and stiffness (85%), joint swelling and tenderness (80%), and fatigue (60%) were the most common symptoms. Conventional DMARDs were administered to 70% of patients, while 15% received combined conventional and biologic DMARDs. Remission was achieved in 45%, low disease activity in 25%, moderate disease activity in 20%, and high disease activity in 10%. Quality-of-life scores ranged from 69.85 to 74.40.
Conclusion: Modern rheumatological treatments were associated with favorable disease activity outcomes and improved quality-of-life measures among patients with rheumatic diseases.

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1. INTRODUCTION

Rheumatoid arthritis (RA) is a complex autoimmune disease in which chronic inflammation in the joints leads to progressive small joint erosion and functional disability with significant morbidity [1]. It is estimated to affect 0.5-1% of the world's population and is more common in women than in men [2].

In the United States alone, approximately 1.3 million people have RA, making it a significant health problem. However, advances in medical research have led to the development of many treatment options that can effectively manage symptoms and even slow the progression of the disease [3], [4], [5], [6]. Currently, the main strategy for treating RA is the use of drugs known as DMARDs, which stand for disease-modifying anti-rheumatic drugs such as methotrexate and other biologic therapies - TNF inhibitors as well as the use of glucocorticoids. These drugs reduce the pain of inflammation, reduce tissue damage, and slow the progression of joint infection [7], [8]. The management plan includes monitoring progress with a screening programme and monitoring side effects. However, there is a significant proportion of the population who are not cured or whose symptoms become uncontrollable [9].

The usual way to treat RA is to take DMARDs [10]. These work by calming down the immune system so that it fights inflammation less and does not damage your joints. If you have RA, it is better to take methotrexate because it is the most commonly prescribed DMARD for this condition. It should be noted that this drug controls swelling in the joints while protecting them from destruction [11], [12], [13]. It can be taken by mouth or by injection and has been shown to be effective in controlling symptoms and improving patients' long-term outlook. However, many patients do not respond to methotrexate or cannot tolerate it because of its side effects, so other treatments are needed [14], [15]. Other DMARDs used instead of methotrexate include sulfasalazine, leflunomide, and hydroxychloroquine. Doctors often combine these drugs to get the most benefit. However, they can sometimes be harmful, and patients need to be monitored regularly to detect any adverse effects [16].

There are situations where DMARDs are ineffective in treating symptoms and using biological response modifiers may be the best option [17]. These are also called biologics. These biological therapies have changed the way RA is treated by focusing on specific molecules involved in the inflammatory cascade [18]. Drugs such as TNF inhibitors (including the three different types mentioned above) have been found to be beneficial. The action of TNF inhibitors such as infliximab may involve reducing the activity of TNF also known as adalimumab, etanercept among others [19], [20], [21].

Tofacitinib and baricitinib work by inhibiting JAKs, which play a role in the inflammatory signalling cascade associated with RA. While biologics are highly effective for many people with RA, they tend to cost more than conventional DMARDs. In addition, increased susceptibility to infection, hepatoxicity, and skin reactions are potential consequences of their use [22].

It is, therefore, important to monitor the use of these drugs carefully and to have regular blood tests [23], [24]. In recent years, there has been a growing interest in the use of holistic and other forms of therapy to manage the symptoms of RA [25]. These include exercise programmes, physiotherapy, occupational therapy, and counselling to help people understand and cope with the psychological aspects of having arthritis [26]. In addition, changes in diet and the use of supplements such as fish oil and turmeric have some benefits in reducing inflammation and improving overall health [27].

2. RELATED WORK

Rheumatoid arthritis (RA) is a chronic inflammatory disease of the joints and tendon sheaths that can destroy the joints. It is the most common inflammatory rheumatic disease. Although at present, unfortunately, the disease is still incurable, in recent years innovative drug therapies have been developed that allow to significantly improve the quality of life of patients. Research confirms that the earlier you take action on the disease, the more likely you are to continue to lead a normal life. With a few tricks and medications, many people with RA are able to lead an almost normal daily life. Therefore, it is very important to seek medical attention (rheumatologist) if symptoms such as morning stiffness and joint pain persist. The review discusses the latest advancements in rheumatology treatments, including biologics, targeted therapies, regenerative medicine, and novel drug development, evaluating their potential benefits and limitations. In RA, there is an overreaction of the immune system, which does not recognize the synovial membrane and considers it a foreign body, triggering an immune reaction, that is, inflammation. Unlike normal inflammation, this inflammation cannot heal because the "crazy" immune system continues to produce T and B cells that cause joint inflammation. The review discusses the latest advancements in rheumatology treatments, including biologics, targeted therapies, regenerative medicine, and novel drug development, evaluating their potential benefits and limitations. Review the latest advancements in rheumatology treatments Early treatment of rheumatoid disease, especially with methotrexate, in addition to other medications to help control the disease. Multivariate analysis of risk factors affecting patients with rheumatic diseases.

3. METHODOLOGY

We conducted a cross-sectional study of rheumatology patients, which included 80 cases who underwent all modern treatments and methods within the disease management programme conducted in different hospitals in Iraq. The study period was from 7 February 2022 to 24 September 2023. This study collected demographic and clinical data including age, sex, body mass index classified into (underweight, normal weight, overweight, and obese), smoking status, family history of the disease, previous surgeries, duration of the disease, and comorbidities including (obesity, hypertension, diabetes, chronic renal failure, cerebrovascular disease, heart disease, lung disease, and asthma), and level of education and income of the patients. The study also recorded the most common symptoms in rheumatism patients, including joint pain and stiffness, swelling and pain in the joints, decreased range of motion, fatigue, muscle weakness, fever, numbness or tingling in the hands or feet, skin rash, weight loss, and difficulty with daily activities.

Eighty patients were receiving rheumatology care, with disease management provided by specialist clinics that recorded the number of annual visits to each service area, including rheumatology, physical medicine and rehabilitation, nutrition, psychology, physiotherapy, occupational therapy, and education. Accordingly, this study identified treatment data including corticoids, cDMARD, bDMARD, cDMARD combined bDMARD, and determined the disease management of patients treated for more than seven months according to the Disease Activity Scale DAS28, which was classified into remission (DAS28 <2.6), low (DAS28 ≥2.6 and <3.2), moderate (DAS28 ≥3.2 and <5.1), high (DAS28 ≥5.1). In addition, the prevalence of complications was distributed across all rheumatology patients. Patient's quality of life after rheumatology treatment was also assessed and ranged between (0 - 100), with 0 representing the poor quality of life and 100 representing the optimal quality of life, determined within criteria that included all (physical function, psychological function, emotional, social aspects, and daily activity). We performed a multivariate analysis of risk factors affecting patients with rheumatic diseases.

4. RESULTS AND DISCUSSION

Table 1. Demographic and Clinical Features of Rheumatoid Arthritis (RA) Patients

Features	Number of Patients (n = 80)	Percentage [%]
Age		
40 – 50	12	15%

51 – 60	20	25%
61 – 70	48	60%
Sex		
Male	16	20%
Female	64	80%
BMI, kg/m3		
Underweight	12	15%
Normal weight	4	5%
Overweight	24	30%
Obesity	40	50%
Smoking status		
Yes	24	30%
No	56	70%
Family history of the disease		
Yes	20	25%
No	60	75%
Previous surgery		
Yes	28	35%
Mo	52	65%
Disease duration (years)	3.6 ± 1.02	
Morbidities		
Obesity	40	50%
Hypertension	64	80%
Diabetes	44	55%
Chronic Kidney disease	20	25%
Cerebrovascular disease	24	30%
Heart diseases	16	20%
Pulmonary disease	12	15%
Asthma	8	10%
Education status		
Not in the school	8	10%
Primary	12	15%
Secondary	16	20%
College/university	44	55%
Monthly income, $		
< 800	40	50%
800 – 1000	24	30%
> 1000	16	20%

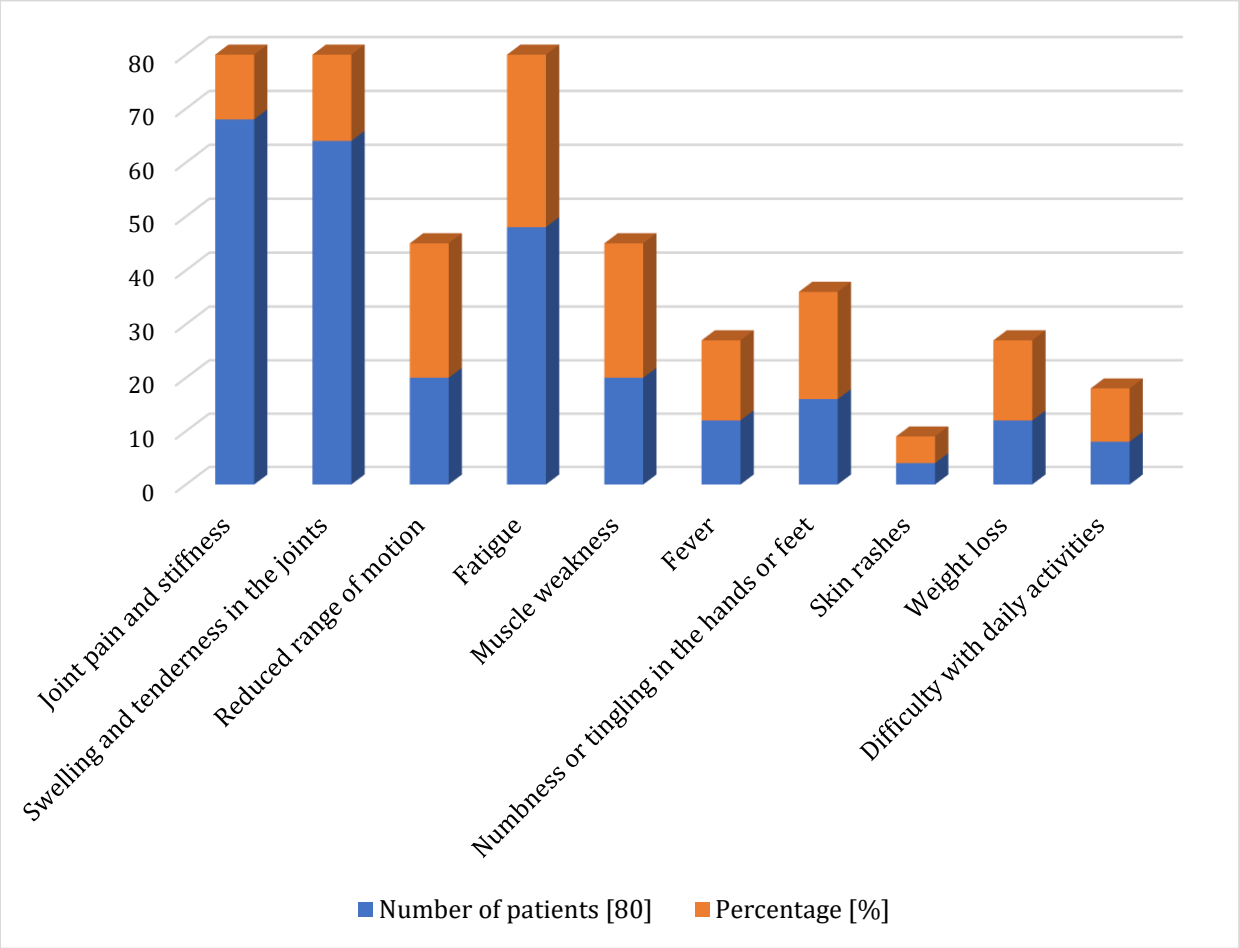


Figure 1. Identification of Main Symptoms Prevalence in Patients with Rheumatology

Table 2. Disease Management in Specialized Hospitals in Terms of the Number of Visits per Year

Items	**Disease Activity**		
	High	Moderate	Low
Rheumatology	10	5	3
Physical Medicine and Rehabilitation	5	4	2
Nutrition	3	2	1
Psychology	5	4	1
Physical therapy	7	3	1
Occupational therapy	6	3	2
Educational sessions	7	4	2
Total	43	25	12

Table 3. Determination of Types of Treatments Used in Patients with Rheumatology

Treatments	**Number of Patients (n = 80)**	**Percentage [%]**
Corticoids	8	10%
cDMARD	56	70%
bDMARD	4	5%
cDMARD combined bDMARD	12	15%

Table 4. Diseases Management of Patients who Underwent Treatment for More than Seven Months by Disease Activity DAS28 Scale

DAS28 scale	**Number of Patients (n = 80)**	**Percentage [%]**

Remission (DAS28 <2.6)	36	45%
Low (DAS28 ≥2.6 and <3.2)	20	25%
Moderate (DAS28 ≥3.2 and <5.1)	16	20%
High (DAS28 ≥5.1)	8	10%

Table 5. Distribution of Complications Related to Patients after Treatments Received

Complications	**Number of Patients (n = 80)**	**Percentage [%]**
Infection	6	7.5%
Gastritis	5	6.25%
Cardiovascular issues	2	2.5%
Osteoporosis	2	2.5%
Liver and kidney damage	1	1.25%
Total	**16**	**20%**

Table 6. Assessment of Quality of Life in Patients who underwent to Program Treatment of Rheumatology

Items	**QoL Scores**
Physical function	72.51 ± 4.81
Psychological function	69.85 ± 5.05
Emotional and social aspects	73.87 ± 3.38
Daily activity	74.40 ± 4.20

Table 7. Multivariate Analysis of Risk Factors Affecting Patients with Rheumatic Disease

Risk Factors	**OR**	**CI 95%**
Age [60 - 70]	3.61	0.60 ± 5.91
Sex [females]	2.65	2.1 ± 4.48
Rheumatoid arthritis	4.70	3.37 ± 6.88
Smoking	8.80	4.35 ± 9.78
Infection	6.50	2.75 ± 9.86
Obesity	5.30	3.21 ± 7.54
Autoimmune diseases		

4.1 Discussion

Our study showed the clinical and demographic results of patients with rheumatic disease, which found patients with age (61 -70) years had the highest rate with 60%, followed by patients with age (51 - 60) years had rate with 25%, and patients with age (40 - 50) years were 15%, Males were 16 cases, and females were 64 cases, BMI classifications consisted of underweight with 12 cases, normal weight with 4 cases, overweight with 24 cases and obesity with 40 cases, smokers rate was 30%, and non-smokers was 70%, family history of the disease included 20 cases, disease duration was 3. 6 ± 1.02 years, morbidities included the most common diseases affected on patients, which are obesity was 50%, hypertension was 80%, diabetes was 55%, and cerebrovascular disease was 30%. In

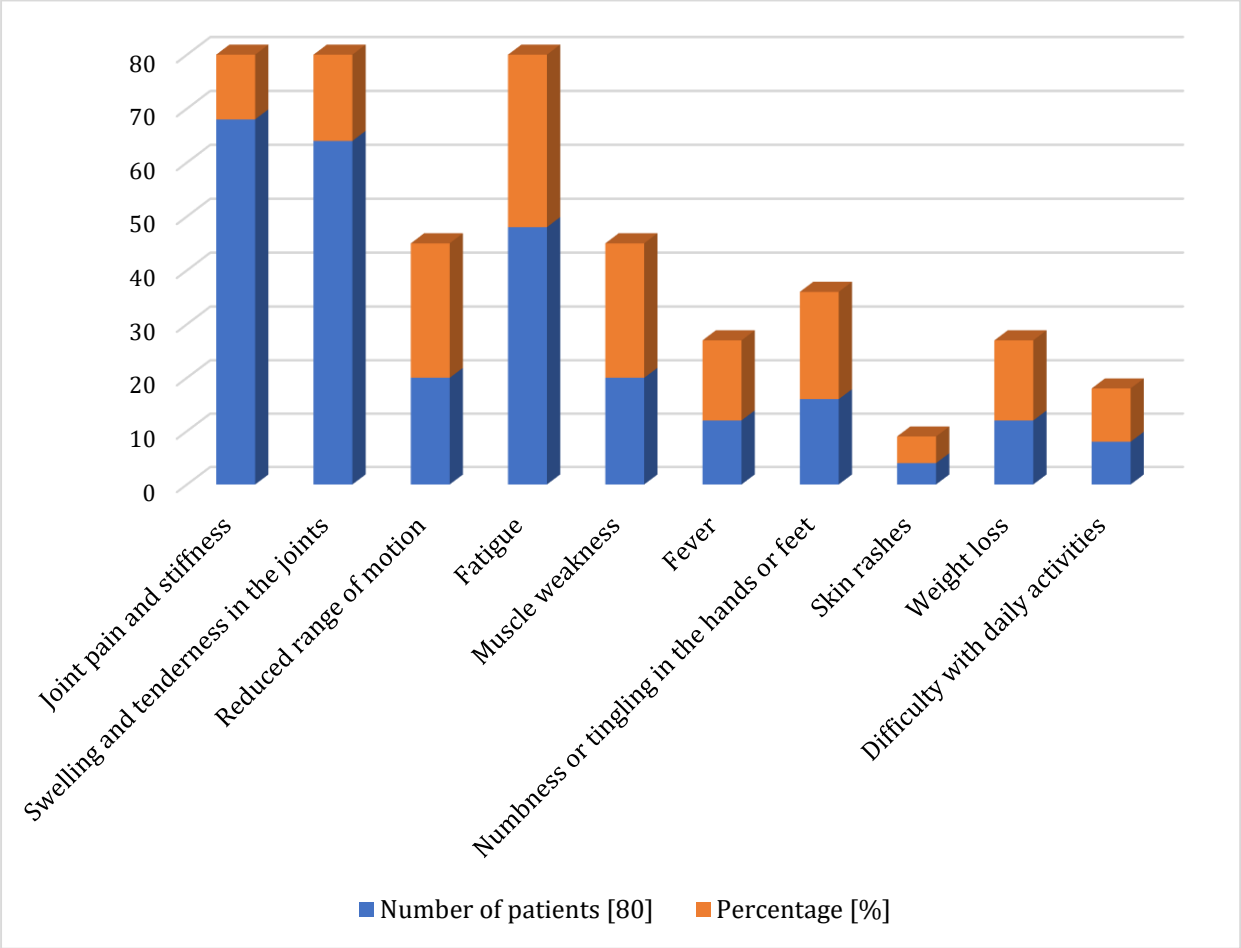


Figure *1*, our study was determined to be the most common symptoms of rheumatic disease, which were distributed in patients: swelling and tenderness in the joints was 80%, joint pain, and stiffness was 85%, and fatigue was 60%. According to disease management in specialist hospitals, we determined the number of visits to hospitals where the number of visits for patients with high disease activity was 43 visits, the number of visits for patients with moderate disease activity was 25 visits, and the number of visits for patients with low disease activity was 12 visits. In addition, we determined the types of treatments used in patients with rheumatology containing corticoids included 8 cases, cDMARD included 56 cases, bDMARD included 4 cases, and cDMARD combined bDMARD included 12 cases. Based on DAS28 scores, we identify rheumatic disease activity classified into remission got 36 cases, low got 20 cases, moderate got 16 cases, and high got 8 cases. In addition, we identify QoL assessment of general life, which showed physical function was 72.51 ± 4.81, psychological function was 69.85 ± 5.05, emotional and social aspects were 73.87 ± 3.38, and daily activity was 74.40 ± 4.20. We also identified common risk factors affecting patients, which were age [60 - 70], gender [female], rheumatoid arthritis, smoking, infections, obesity, and autoimmune diseases.

Biologic treatments are made from living organisms and target certain elements of the immune system to reduce inflammation and halt disease progression [28]. Their effectiveness has greatly increased survival rates for these patients by helping to relieve symptoms, minimise suffering or halt joint destruction. On the other hand, targeted therapies have been developed to specifically target abnormal cells or pathways involved in causing rheumatic diseases [29]. Essentially, such treatments have the ability to be individualised and precise because they focus on the main causes of these disorders, thereby reducing the severity of side effects while increasing their overall effectiveness [30], [31].

The use of tissue engineering, stem cell therapy, and other restorative methods represents a potentially effective way of treating rheumatic diseases by harnessing the body's own repair mechanisms to repair damaged tissues and joints. In this way, these strategies may help to restore function and improve the quality of life of people suffering from debilitating rheumatic diseases [32], [33].

In addition, recent advances in drug development have led to the discovery of new medicines that target specific pathways and mechanisms in connective tissue diseases (rheumatological diseases). These cutting-edge medicines offer patients more options for managing their disease and achieving positive outcomes [34], [35].

5. CONCLUSION

In conclusion, the significance of other drug therapies, targeted therapies, cell-based treatments, or the development of new drugs in managing patients with rheumatology cannot be overemphasized. This has changed how people with these difficult disorders receive health care through fresh expectations and better standards of living.

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Author Contributions Statement

Name of Author	C	M	So	Va	Fo	I	R	D	O	E	Vi	Su	P	Fu
Dr. Murooj Luai Majeed Altimimi	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓

C : **C**onceptualization
M : **M**ethodology
So : **So**ftware
Va : **Va**lidation
Fo : **Fo**rmal analysis
I : **I**nvestigation
R : **R**esources
D : **D**ata Curation
O : Writing - **O**riginal Draft
E : Writing - Review & **E**diting
Vi : **Vi**sualization
Su : **Su**pervision
P : **P**roject administration
Fu : **Fu**nding acquisition

Conflict of Interest Statement

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Informed Consent

All participants were informed about the purpose of the study, and their voluntary consent was obtained prior to data collection.

Ethical Approval

Not Applicable.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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