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Clinical and Epidemiological Aspects of Rheumatoid Arthritison Biological Therapy

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Abstract:

Background: Rheumatoid arthritis is a chronic, autoimmune, inflammatory disorder that most commonly affects the joints, causing progressive, symmetric, erosive destruction of cartilage and bone, which is usually associated with autoantibody production.

Objectives: To examines female versus male perspective concerning prevalence, clinical features, complication and functional classes in rheumatoid arthritis patients on biological therapy.

Subjects and Methods: A descriptive; cross sectional study conducted at Baghdad teaching hospital in Baghdad city, (convenient sample) included 210 patients already diagnosed with rheumatoid arthritis. The data collection continued for the period starting on 1th December -2020 ending on 1st April, 2021.

Results: the majority of rheumatoid arthritis cases were females 173 (82. 4%) and 37 of them (17.6%) were males. Female to male ratio was 4.6:1. Mean of age was (50.81 ± 11 years). The majority of studied sample had primary education 38% and unemployed 80%% for both sexes. Males reported to have family history of rheumatic diseases (40%) more than females (24%); smoking also higher in males compared to females 29% vs. 6%. Clinical features were worse in women than men; morning stiffness 64% vs. 62%; fatigue 81% vs. 64%; loss of appetite 33% vs. 10%; weight loss 23% vs. 2%. Similarly complication reported to be more frequent in female patients specifically osteoporosis and sicca symptoms (45% vs. 27%; 50% vs. 32%) respectively.

Conclusion: Females to males ratio was 4.6:1. Clinical features, functional classes and complications worsen in female patients.

Recommendation: Special attention must be given to females rheumatoid arthritis patients particularly in postmenopausal period to prevent complication and deformity of the disease; Health education regarding early diagnosis, early initiation of effective therapy and regular exercise.

Key words: Rheumatoid arthritis, Clinical and epidemiologiclaspects, Gender differences, Biological therapy.

Introduction:

RA is a common chronic systemic autoimmune disorder of unknown etiology, characterized by a synovial hyperplasia, symmetric, and progressive inflammatory

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polyarthritis.Affected patients often experience inflammatory signs in the joints of the hands, wrists, and feet, but many other joints may be involved including the temporo-mandibular joints, elbows, shoulders, hips, knees, and ankles. Its worldwide distribution affects approximately 0.5-1% of the population [1, 2].The arthritis is typically symmetrical, and usually leads, if uncontrolled, to destruction of joints due to erosion of cartilage and bone, causing joint deformities. The disease may also affect other parts of the body. This may result in a low red blood cell count, inflammation around the lungs, and inflammation around the heart. Fever and low energy may also be present [3].Patient's daily activity largely affected by rheumatoid arthritis, therefore physician tend to determine extent of physical disability that patients suffer from, this can be detected by steinbrocker functional classification; it's four level scale range from class I to class IV: 1. Class I – Completely have ability to perform usual daily living activities. 2. Class II – Able to perform usual self-care and vocational activities but limited in avocational activities. 3. Class III – Able to perform usual self-care activities but limited in vocational and avocational activities. 4. Class IV – Limited in ability to perform usual self-care, vocational, and avocational activities [4].

The diagnosis of RA was based on the 1987 American College of Rheumatology (ACR) criteria. These criteria were based on the persistence of arthritic symptoms over time; however, this classification system failed to identify patients with early inflammatory arthritis.It is now recognized that early therapeutic intervention significantly improves clinical outcomes and reduces irreversible joint damage and disability. With this focus, the ACR and the European League Against Rheumatism (EULAR) in 2010 devised new classification criteria for early arthritis, which assess joint involvement, autoantibody status, acute-phase response, and symptom duration, as well as revised criteria for classifying RA in newly presenting patients, those with erosive disease typical of RA, and those with inactive disease with or without treatment[5].
Treatments for rheumatoid arthritis help to prevent or slow down joint damage,decrease inflammation in the joints, relieve pain, improve quality of life and reduce disability [6]. Methotrexate is the cornerstone in the management of RA. Despite the effectiveness of these medications some patients with RA experience failure even with use of combination or triple DMARDs and need for other line of treatment. The use of biologic therapy in treatment of RA has revolutionized the management in the last two decades [7].

Objective of the Study
To examines female versus male perspective concerning prevalence, clinical features, complication and functional classes in rheumatoid arthritis patients on biological therapy.

Subjects and Methods
Study Design
A cross sectional analytical study conducted in Baghdad teaching hospital – Medical City – Baghdad.

Duration of Study
The data collection continued for a period of four months starting on 1thDecember - 2020 ending on 1stApril, 2021.

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Place of Study
The place of study was in Baghdad teaching hospital in Baghdad city.

Inclusion and Exclusion Criteria of Study
Inclusion criteria: Rheumatoid patients fulfilled ACR_EULAR 2010 criteria for the diagnosis of RA; who were aged 18-75 years of either gender accepted to participate in the study.
Exclusion criteria: Patients with active infection and discontinue biological therapy and those having other types of rheumatoic diseases including psoriasis.

Statistical Analysis
Analysis of data was carried out using the available statistical package of SPSS-25 (Statistical Packages for Social Sciences version 25). Qualitative data were presented in simple measures of frequency and percentage whereas quantitative data summarized by mean, standard deviation, and range (minimum, maximum values). The significance of different percentages (qualitative data) was tested using Pearson Chi-square test. Statisticalsignificance was considered whenever the P value was equal or less than 0.05.

Results:

The majority of studied sample were female 173 (82. 4%) and 37 of them (17.6%) were males. Female to male ratio was 4.6:1. Most female patients were in the age group 50-59 years; 89% of female were married vs. 100% of male; highest percentages of both genders found to have primary education 39% female vs. 32% male; 83% of female patients wereunemployed vs. 64% males; family history of rheumatic disease reported in 24%, 40% females and males, respectively. Most cases in both genders found to have higher BMI, overweight more in males 37% whereas obesity higher in females 43%. Significant associations were found among gender and marital status, occupation, family history at (P-value <0.05), highly significant association was found between gender & smoking P- value = 0.0001.

Table (1): Comparison of demographic variables in both genders

Demographic variables		Gender						
		Males (n=37)		Females (n=173)		Total		
		No	%	No	%	No	%	P.V
Age groups	< 40years	6	16.22	30	17.34	36	17.14	0.950
	40-49	10	27.03	47	27.17	57	27.14	
	50-59	13	35.14	53	30.64	66	31.43	
	≥ 60years	8	21.62	43	24.86	51	24.29	
	Mean ± SD	50.56 ±10.73		50.86 ±10.87				
Marital status	Un married	0	.00	19	10.98	19	9.05	0.035*
	Married	37	100.0	154	89.02	191	90.95	
Educational	Illiterate	3	8.11	35	20.23	38	18.10	0.101
	Primary	12	32.43	69	39.88	81	38.57	
	Intermediate	9	24.32	19	10.98	28	13.33	

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level	Secondary	5	13.51	15	8.67	20	9.52	
	College	8	21.62	35	20.23	43	20.48	
Occupation	Employed	13	35.14	29	16.76	42	20.00	0.011*
	Unemployed	24	64.86	144	83.24	168	80.00	
Family history	Absent	22	59.46	131	75.72	153	72.86	0.043*
	Present	15	40.54	42	24.28	57	27.14	
Smoking	Yes	11	29.73	11	6.36	22	10.48	0.0001*
	No	26	70.27	162	93.64	188	89.52	
BMI classification	Under weight	2	5.41	5	2.89	7	3.33	0.066
	Normal weight	12	32.43	29	16.76	41	19.52	
	Over weight	14	37.84	64	36.99	78	37.14	
	Obese	9	24.32	75	43.35	84	40.00	

Statistically significant association was found between gender and clinical features of rheumatoid arthritis i.e. fatigue with highest percentages occur in females patients 81% compared to 64% in males. Gender significantly associated with loss of appetite & weight (P-vale < 0.05) higher percentages of appetite loss found in female 33% compared to 10% male the same things regarding weight loss that higher percentages occur in female compared to male 23% vs. 2%. No statistically significant association detected between genders and other clinical characteristics.

Table (2): Clinical features of rheumatoid patients in both genders

Clinical characteristic		**Gender**						
		Males (n=37)		**Females (n=173)**		**Total**		
		No	**%**	**No**	**%**	**No**	**%**	**P.V**
Morning stiffness	Present	23	62.16	112	64.73	135	64.28	0.766
	Absent	14	37.83	61	35.26	75	35.71	
Fever	Present	19	51.35	98	56.65	117	55.71	0.556
	Absent	18	48.65	75	43.35	93	44.29	
Fatigue	Present	24	64.86	141	81.50	165	78.57	0.025*
	Absent	13	35.14	32	18.50	45	21.43	
Loss of appetite	Present	4	10.81	58	33.53	62	29.52	0.006*
	Absent	33	89.19	115	66.47	148	70.48	
Loss of weight	Present	1	2.70	40	23.12	41	19.52	0.004*
	Absent	36	97.30	133	76.88	169	80.48	
Flare ups**	Present	20	54.05	98	56.65	118	56.19	0.773
	Absent	17	45.95	75	43.35	92	43.81	

* P- value is significant is less than0.05.* Flare up in last 6 months.

Tender joint in patients with rheumatoid arthritis occur more frequently in females compared to males except (fingers, hips and ankles) detected more in males, with no significant association found among them.

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Table (3): Distribution of joints involvement with genders

Most commonly pain in joints	Gender					
	Male		Female		Total	
	No	%	No	%	No	%
Fingers	6	16.22	19	10.98	25	11.90
Wrists	3	8.11	25	14.45	28	13.33
Shoulders	5	13.51	25	14.45	30	14.29
Hips	1	2.70	0	.00	1	.48
Knees	17	45.95	88	50.87	105	50.00
Ankles	2	5.41	0	.00	2	.95
Feet	3	8.11	16	9.25	19	9.05
Total	37	100.00	173	100.00	210	100.00

$\chi 2$ =15.858df= 6 p= 0.015

The women with rheumatoid arthritis have higher percentages than men in class III &IV (23%, 5% in female vs. 13% and 5% in males) respectively while 81% of males categorized in class I& II compared to 71% females.

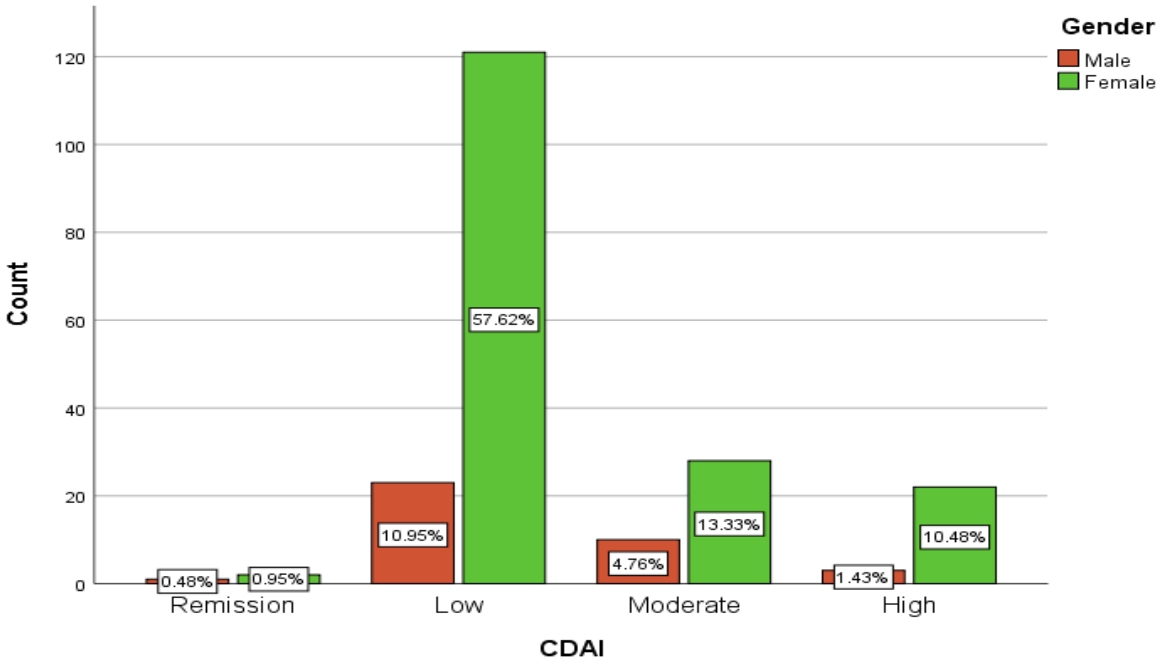

Figure (1): Clinical Disease Activity Index CDAI in rheumatoid arthritis in both genders

Osteoporosis and sicca symptoms were the most important and frequent complications in RA patients, they associated significantly with genders with higher percentage in female compared to male 45% vs. 27%; 50% vs. 32% (P-value= 0.043, 0.042) osteoporosis and sicca symptoms respectively.

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Similarly, other complications as gastrointestinal symptoms & rheumatoid nodules reported more in females than in males but with no significant association.

Table (4): Distribution of Rheumatoid arthritis patients according to complication with gender

Complications		Gender						
		Males (n=37)		Females (n=173)		Total		
		No	%	No	%	No	%	P.V
GIT symptoms	Yes	11	29.73	63	36.42	74	35.24	0.440
	No	26	70.27	110	63.58	136	64.76	
Osteoporosis	Yes	10	27.03	78	45.09	88	41.90	0.043*
	No	27	72.97	95	54.91	122	58.10	
Rheumatoid nodules	Yes	2	5.41	15	8.67	17	8.10	0.509
	No	35	94.59	158	91.33	193	91.90	
SICCA symptoms**	Yes	12	32.43	88	50.87	100	47.62	0.042*
	No	25	67.57	85	49.13	110	52.38	

*p value is significant is less than0.05.**Sicca symptoms: dry mouth and eyes.

Discussion:

Rheumatoid arthritis is a chronic, progressive, inflammatory, autoimmune disorder that involves peripheral joints mostly small and medium size but large joints involvement such as knee joints occur. It's a worldwide disease 0.5- 1% of population. This study was conducted on (210) patients with RA who fulfill ACR/EULAR 2010 criteria with mean age (50.56 ± 10.73 years) for males and (50.86 ±10.87 years) for females. The present study reveals that the prevalence of rheumatoid arthritis was higher in female patients with female to male ratio 4.6:1; this was comparable to that reported in Algeria (5.9:1) [8] but was lower than what reported in the Brazilian population (8:1) (Almeida Mdo et al., 2014) [9] and in in Iraq in 2019 by Faiq et al., (7.6:1)[10] and higher than study performed in Minnesota (3:1) [11]. The differences could be due to genetic, environmental and hormonal factors that have impact on females more than males.

Concerning with smoking, highest percentages of smoking reported among male compared to femaleM. Intriago in Ecuador [12] & Patricia in California [13] agree with these findings whereas (Coffey et al 2019)who reports that smoking was more in female than males [134].

Increasing body weight is public among rheumatoid patients that associated with higher clinical disease activity index CDAI the results from present study showed that females have higher percentages of obesity than males that compatible with another studies performed by (Younis et. al., 2017) in Iraq and (Linauskas et. al., 2017) in Denmark [15, 16].

Morning stiffness detected more in female patients compared to male but statistically non-significant Forslind in 2007 in Sweden found the opposite [17]. Morning stiffness of joints is a very common complaint of patients with RA and is experienced as

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tenderness and restricted movement upon awakening lasting at least 1 hour before maximal improvement for at least 6 weeks (Mackie et al., 2012) [18].

Symptoms like weight lost, appetite lost and fatigue significantly associated with genders, they diagnosed frequently in females, Intriago 2019 [12] found the same results. Most common complication of rheumatoid arthritis is osteoporosis; people with rheumatoid arthritis are at increased risk for osteoporosis for many reasons. To begin with, the glucocorticoid medications often prescribed for the treatment of rheumatoid arthritis can trigger significant bone loss. In addition, pain and loss of joint function caused by the disease can result in inactivity, further increasing osteoporosis risk. Studies also show that bone loss in rheumatoid arthritis may occur as a direct result of the disease. The bone loss is mostly diagnosed in areas immediately surrounding the affected joints [19].

Of concern is the fact that women, a group already at increased risk for osteoporosis particularly postmenopausal women. The present studies show significant association between genders and occurrence of osteoporosis with highest percentages among females; The Aurrecoechea in 2016 agree with these findings [20].

Conclusions:

1- RA more in female than in male with ratio 4.6:1.
2- Clinical features, functional classes and complications worsen in female patients.

Recommendation:

Special attention must be given to females rheumatoid arthritis patients particularly in postmenopausal period to prevent complication and deformity of the disease; Health education regarding early diagnosis, early initiation of effective therapy and regular exercise.

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