Functional Health Status among Patients Receiving Biological Treatment for Rheumatoid Arthritis in Selected Hospital, UAE

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Abstract

Background of the Study: Rheumatoid arthritis (RA), is an autoimmune and inflammatory disease affecting joints of the hands, wrists, and knees. Rheumatoid arthritis has many physical and social consequences that can lower the quality of life. Moreover, RA affects many aspects of daily living. In this study, we aim to determine the functional health status and its association with selected demographic variablesof patients receiving biological therapy for rheumatoid arthritis at Ibrahim Bin Hamad Obaidallah hospital (IBHOH), Ras AlKhaimah, UAE.

Materials and Methods: A quantitative research approach with a descriptive observational survey design was used. Data were obtained from adult clients who fulfilled the inclusion criteria using the Health Assessment Questionnaire-Disability Index (HAQ-DI), Pain visual analog scale (P-VAS), and Global visual analog scale (G-VAS) tools to elicit demographic profile and functional disability index. Sample participation was voluntary, complying with the consent procedure in force, ensuring confidentiality and anonymity. A total of 100 valid responses were obtained. Descriptive statistics were utilized to analyze the frequency and percentage distribution of sociodemographic variables of the patients. Chi-square and Fischer's exact tests were used to assess any association between demographic variables and functional health status.

Major findings of the Study: Among 100 patients were studied, of which (89%) were females, and (11%) were males, (10%) of them were aged between 20 – 30 years, (17%) between 31–40 years, (25%) between 41 – 50 years, (19%) between 51 – 60 years, and (29%) between 60 – 65 years. Most of the patients were on biological therapy from 1 – 12 months (29%), [median 36 months and range 2- 180 months]. The most frequently prescribed biological therapy was Adalimumab (21% of patients) and Etanercept was the second most frequently prescribed (13% of patients), followed by Tofacitinib (12% of patients) and Tocilizumab (10% of patients). The results showed a mean (SD) of 0.8775 (0.7797104) and a median (0.75) of the functional disability index. The data showed that most

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of the patients had mild to moderate functional disability (46%); (25%) had moderate to severe disability, (18%) of patients had No functional disability, and (11%) had severe to very severe functional disability. The majority of patients (45%) had mild pain, (33%) and (13%) had moderate and severe pain correspondingly (median P-VAS 30, mean 32, and range 0 - 100). Furthermore, most of the patients (54%) reported mild disease effects on their global health, (33%) reported moderate effects, and (13%) severe effects (median G-VAS 30, mean

35.8, and range 0 – 100). A strong association (P 0.0415) between age and functional health status scores was identified.

Conclusion: HAQ-DI assesses the patient's level of functional ability and includes questions about fine movements of the upper extremities, locomotor activities of the lower extremities, and activities that involve both upper and lower extremities. Standard processes for quantitative monitoring of RA for therapeutic purposes should be implemented as part of routine clinical practice in rheumatology clinics. Therefore, this study supports the use of functional health assessment (HAQ-DI tool) in routine clinical practice at the IBHOH Rheumatoid Clinic. This helps physicians monitor the disease and its treatment outcomes in relation to the quality of life of RA patients.

Keywords: Rheumatoid arthritis; UAE, Biological therapy; Functional Health Status; Disease Activity.

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INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune and inflammatory disease affecting joints of the hands, wrists, and knees. It can affect other tissues in the body and causes problems in other organs such as the lung, heart, and eyes. Rheumatoid arthritis has many physical and social consequences that can lower the quality of life. Moreover, RA affects many aspects of daily living including work, leisure, and social activities. Treatment of RA usually includes the use of medications that slow the progression of the disease and prevent deformity. Biological response modifiers are medications that are used in the treatment of RA as recommended by the American Association of Rheumatology clinical practice guidelines.[1]

Out of every 100,000 people, 71 are diagnosed with RA every year. About 1.5 million Americans have RA. Women are about two to three times more likely to get RA than men.[2]

Rheumatoid arthritis causes joint pain and swelling, reduced mobility, and physical weakness. General tiredness, trouble sleeping, and exhaustion are other common symptoms. All of these symptoms can greatly affect your everyday life and overall wellbeing. Living with rheumatoid arthritis isn't always easy. One reason is that it's often difficult to predict the symptoms: They may get better or worse the next day it's hard to know in advance.[3] Worldwide, more than 50 million people are diagnosed with some form of arthritis, as well as 1 in 5 people in the UAE.[4]

The Middle East Arthritis Foundation (formerly Emirates Arthritis Foundation) announced that "Rheumatoid arthritis is chronic, inflammatory arthritis with a higher likelihood of permanent disability. After 10 years of disease onset, 50% of young, working adults will be disabled." Also, they added that "There are no UAE specific statistics but numbers from the Gulf region suggest that the prevalence is around 20% of the population." They concluded that Arthritis is an immune system problem and there is no prevention or cure. However, with early diagnosis and treatment deformity and disability can be lessened.[5]

The disease, which eventually leads to deformities and disability, has become a public health concern principally in the Gulf countries, where RA is becoming more recognized.[9]

Meanwhile, an average of 138 patients visit the outpatient rheumatology clinic at Ibrahim Bin Hamad Obaidallah Hospital (IBHOH), United Arab Emirates each month. About 45 patients are receiving biological treatment. However, quality of life has not been assessed, including the functional health status of patients undergoing biological treatment at Ibrahim Bin Hamad Obaidallah Hospital (IBHOH) in RAK, United Arab Emirates.

Therefore, we aim to incorporate the functional health status assessment of patients undergoing biological treatment for rheumatoid arthritis into the routine daily clinical activities at the clinic. This helps doctors make clinical decisions regarding rehabilitation therapy.

METHODOLOGY

A quantitative approach with a descriptive observational survey design was used to determine the functional health status of patients with rheumatoid arthritis receiving biological treatment at Ibrahim Bin Hamad Obaidallah Hospital, Ras

AlKhaimah, UAE. Inclusion criteria included adult patients aged between 20 and 65 years diagnosed with RA and receiving biological therapy. A convenience sampling technique was adopted for the study. Consecutive patients who are coming to their regularly scheduled rheumatology clinic visit were asked to participate voluntarily in the study provided they fitted the inclusion criteria and signed the informed consent. The study was conducted over a period of four months and a sample of 100 patients was recruited. With extensive literature review and discussions with faculties and experts, the self-reported Health Assessment Questionnaire Disability Index (HAQ-DI) tool,[6-14] which is frequently used and recommended by the American College of Rheumatology (RCA) for the evaluation of RA disease activity and outcome, evaluates patient's ability to perform activities of daily living through their answers to 20 questions designed to assess upper and lower extremity use, was adopted to assess the functional health status. These questions are organized into 8 categories: dressing, arising, eating, walking, hygiene, reach, grip, and usual activities.

Each question is answered on a 4 level scale of impairment ranging from 0 to 3:

0 = No difficulty

1 = Some difficulty

2 = Much difficulty

3 = Inability to do

Furthermore, Visual Analog Scales (VASs) were used, on which patients had to indicate on a scale from 0 (none) to 100 (worst) mm their rating of:

A.   (P-VAS). It is a unidimensional scale in which pain intensity receives scores ranging from 0 to 100 mm.[10-11]

Mild pain: 0 – 34

Moderate pain: 35 – 67

Severe pain: Greater than 67

B.   Global Visual Analogue Scale (G-VAS) to evaluate the perception of the patient of his/her general status in the previous week.

Mild: 0 - 34

Moderate: 35 - 70

Severe: 71 - 100

Data collection started after approval by the GMU IRB and relevant hospital authorities, including the MOHAP - Ras AlKhaimah Research Ethical Committee. After receiving administrative approval from the hospital director, informed consentwas obtained from the participants. The data were collected by researchers using a self-reporting (HAQ-DI) tool for patients who are receiving biological treatment and met the inclusion criteria at the IBHOH outpatient department. The collected data were summarized in a table, entered into an Excel spreadsheet, and further analyzed in the R software. The data were analyzed as follows

- Descriptive analysis was done in the form of mean, median, and standard deviation for quantitative variables.

- Chi-Square and Fischer's exact tests for association of demographic variables and HAQ-DI score.

Data analysis and interpretation

The study findings are organized and presented in the following sections:

OBJECTIVES

1. To determine the functional health status of patients receiving biologics for rheumatoid arthritis.

2. Find the association between functional health status and selected demographic variables.

Section A: Demographic characteristics of patients who attended the rheumatology clinic.

Section B: Assessment of the functional disability among the participants

Section C: Association of functional health status with selected demographic variables.

Section A: Demographic characteristics of patients who attended therheumatology clinic.

Table 4.1: Frequency and Percentage distribution of demographic variables of patients

n=100

Demographic Variables	Frequency (f)	Percentage (%)
Age in years		
20-30	10	10
31-40	17	17

Table Cont.......

41-50	25	25
51 -60	19	19
61- 65	29	29
Gender		
Male	11	11
Female	89	89
Educational Status		
Primary School	44	44
High school	25	25
Diploma	13	13
Undergraduate	18	18
Post-Graduate	0	0
Occupation		
Private/Company	5	05
Governmental Job	16	16
Self-employed	5	05
Homemaker	62	62
Unemployed	12	12
Marital Status		
Married	75	75
Divorced	5	05
Separated	1	01
Unmarried	19	19
History of Chronic Illness		
Yes	59	59
No	41	41
Do you have a habit of smoking?		
Yes	3	03
No	97	97
Height(m)		
Less than 1.40	0	0
1.40- 1.60	66	66
1.61 – 1.80	34	34
1.8 and more	0	0
Weight (kg)		
Less than 40	0	0
40 – 60.9	10	10
61 – 80.9	37	37
81 – 100.9	34	34
101 and more	19	19
BMI		
Less than18.5	0	0
18.5 – 24.9	14	14
25.0 – 29.9	24	24
30.0 - 35	19	19
More than 35	43	43
Duration of Biological Therapy in months		
1 - 12	29	29

13 - 24	18	18
25 - 36	15	15
37 - 48	12	12
49 - 60	11	11
More than 60	15	15
Type of Biological Therapy		
Abatacept	2	02
adalimumab	21	21
baricitinib	8	08
Belimumab	3	03
Etanercept	13	13
Golimumab	4	04
Guselkumab	4	04
Infliximab	2	02
Rituximab	6	06
Secukinumab	5	05
Tocilizumab	10	10
Tofacitinib	12	12
Upadacitinib	10	10

Table 4.1 results reveal that 29% were in the age group of 61-65, 89% were female, about educational status majority 44% had primary education, 62% were homemakers, Marital status data shows that 75% were married, 59% had the history of chronic illness, 97% reported no history of smoking. Most of the patients (43%) were having morbid obesity (BMI more than 35), (19%) were obese (BMI between 30 – 35), (24%) were overweight (BMI between 25 – 29.9), and only (14%) were having healthy weight (BMI 18.5 – 24.9).
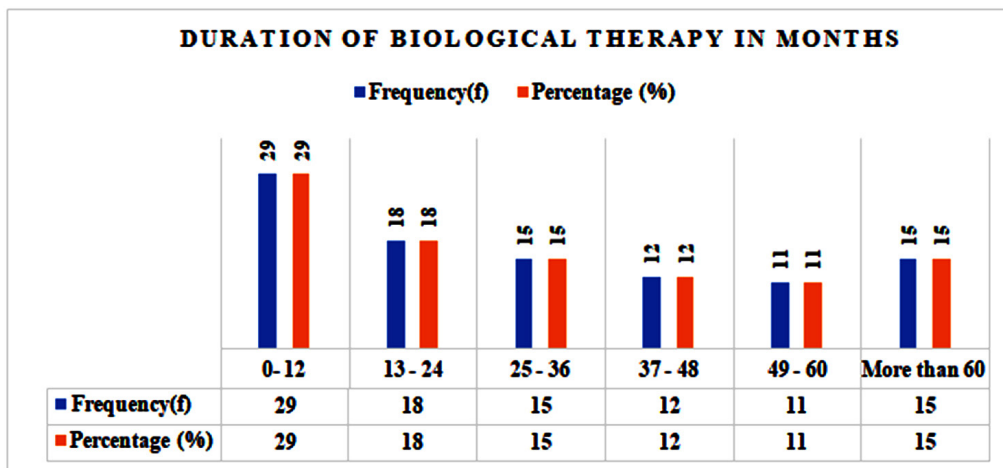

Fig. 4.6: Distribution of Duration of Biological Therapy in months by Frequency and Percentage

Most of the patients (62%) were on biological treatment for 3 years and less, out of which (29%, 18%, and 15%) were receiving biological for 1 year, 2 years, and 3 years respectively, however, (38%) of patients were on biological therapy for more than 3 years, out of which (12%, 11%, and 15%) were on biological therapy for 4 years, 5 years and more than 5 years respectively.

The most frequently prescribed biological therapy was Adalimumab (21%) and Etanercept was the second most frequently prescribed (13%), followed by Tofacitinib (12%) and Tocilizumab (10%). However, the least prescribed medications were Abatacept (2%) and Infliximab (2%).

Section B: Assessment of the functional disability among the participants

Table 4.2: Frequency and Percentage distribution of disability per category

n=100

Disability Indicators	Category							
	No Disability		Mild		Moderate		Severe	
	f	%	f	%	F	%	f	%
Dressing & Grooming	64	64%	28	28%	07	7%	01	1%
Activities	33	33%	18	18%	09	9%	40	40%
Arising	46	46%	38	38%	13	13%	03	3%
Eating	53	53%	30	30%	08	8%	09	9%
Walking	44	44%	34	34%	15	15%	07	7%
Hygiene	40	40%	42	42%	07	7%	11	11%
Reach	36	36%	35	35%	17	17%	12	12%
Grip	58	58%	21	21%	08	8%	13	13%

Most of the patients 40 (40%) reported severe disability in the category of activities followed by grip category 13 (13%) and reach 12 (12%), however, for moderate disability, 17 (17%) reported disability in Reach category, followed by walking 15 (15%) and arising 13 (13%) respectively. A Marked number of patients 42 (42%) reported mild disability in the Hygiene category followed by arising 38 (38%) and reach 35 (35%). A Significant number of patients 64 (64%) had no disability in dressing and grooming, followed by Grip 58 (58%) and eating 53 (53%).
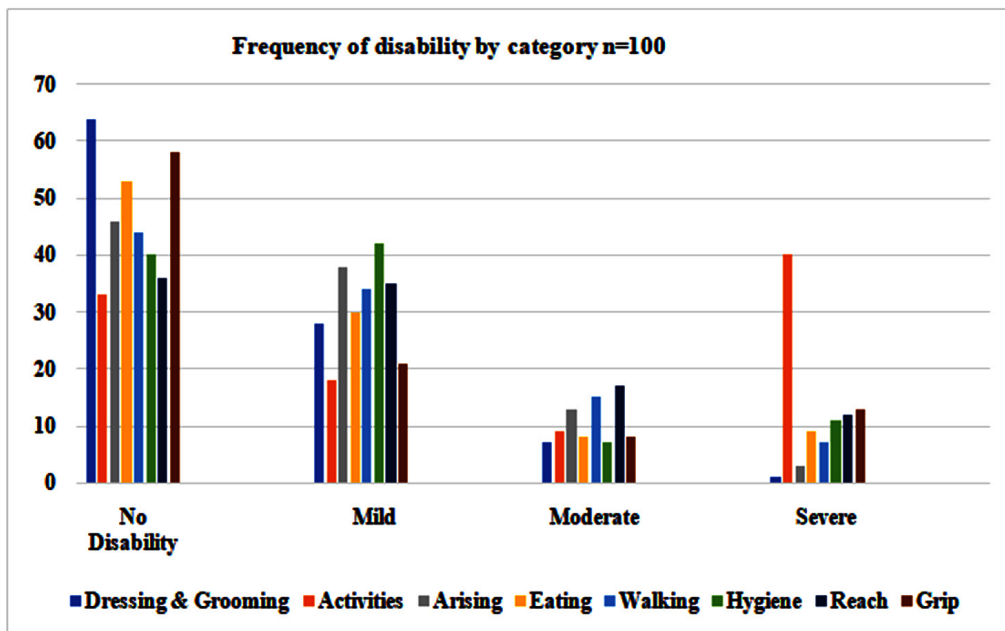

Fig. 4.7: Frequency distribution of Disability by Category

Most of the patients (40%) reported severe **disability** in the category of activities followed by the grip (13%) and reach (12%). However, for **moderate disability, (17%) reported disability in the Reach category**, and among the samples (15%) had difficulty in walking and (13%) had in the arising category respectively. A marked number of **patients (42%) reported mild disability in the Hygiene** category followed by arising (38%) and the reach (35%). A significant number of patients **(64%) had no disability** in dressing and grooming, Grip (58%), and eating (53%).

Table 4.3: Frequency and Percentage distribution of Disability by Severity,

n=100

Level of Disability	Frequency	Percentage	Mean & SD
No Disability (0)	18	18%	Mean 0.8775
Mild to Moderate Disability (0.125 – 1)	46	46%	SD
Moderate to Severe Disability (1.125 – 2)	25	25%	0.7797104
Severe to very Severe Disability (2.125 – 3)	11	11%	Median 0.75

The data showed that most of the patients had mild to moderate functional disability (46%), (18%) of patients had No functional disability, (25%) had moderate to severe disability, and (11%) had severe to very severe functional disability, out of which only one patient (1%) reported complete functional disability.

Most of the patients (45%) had mild pain over the past week of appointment, (38%) and (17%) had moderate and severe pain respectively.

Finally, most of the patients (54%) reported the mild effects of the disease on their general health over the past week of appointment, however, (33% and 13%) reported moderate to severe effects respectively.

Section C: Association of functional health status with selected demographic variables.

Chi-Square test and Fischer's exact test showed no association between a selected demographic variable and functional health status scores except for age (p <0.05).

Variable	p-Value	Variable	p-Value
Age	0.0415	Smoking Habit	0.30
Gender	1	Height	0.53
Educational Status	0.3106	Weight	0.6
Occupation	0.55	BMI	0.18
Marital Status	0.24	Duration of Biological Therapy	0.55
History of Chronic Illness	0.33	-	-

DISCUSSION

Objective 1: To determine the functional health status of patients receiving biologics for rheumatoid arthritis.

The results indicated that no functional disability was obtained in 18 (18%) of patients, mild to moderate disability in 46 (46%), moderate to severe disability in 25 (25%), and severe to very severe disability in 11 (11%) out of which complete disability was in one patient only. The mean (standard deviation), and median of the Functional Disability Index among the participants were 0.8775 (0.7797104), and 0.75. Most of the patients were on biological therapy from 1 – 12 months 29 (29%) with a median of 36 months and range of 2- 180 months. The most frequently prescribed biological therapy was Adalimumab 21 (21% of patients) and Etanercept was the second most frequently prescribed 13 (13% of patients), However, the least prescribed medications were Abatacept 2 (2% of patients) and Infliximab 2 (2% of patients). However, the least prescribed medications were

Abatacept 2 (2% of patients) and Infliximab 2 (2% of patients).

Most of the patients 40 (40%) reported severe disability in the category of activities such as getting in and out of a car, doing vacuuming or yard work, gripping, and opening things; followed by grip category 13 (13%) and reach 12 (12%) such as bending down and picking up clothes from the floor or raising a 2kg bag above the head level. However, for moderate disability, 17 (17%) reported disability in the Reach category, followed by walking 15(15%) including walking outdoors on flat ground or climbing up 5 steps and arising 13 (13%) respectively. A marked number of patients 42 (42%) reported mild disability in the Hygiene category followed by arising 38 (38%) and the reach 35 (35%). A significant number of patients 64 (64%) had no disability in dressing and grooming, followed by Grip 58 (58%) and eating 53 (53%).

The majority of patients 45 (45%) had mild pain, 33 (33%), and 13 (13%) had moderate and severe pain correspondingly [median P-VAS 30, mean 32, and range 0 - 100]. Furthermore, most of the patients 54 (54%) reported mild disease effects on

their global health, 33 (33%) moderate effects, and 13 (13%) severe effects [median G-VAS 30, mean 35.8, and range 0 – 100].

The study results were consistent with our literature review that concluded biological therapy improves the quality of life of patients with RA as reflected by a decrease in HAQ scores from 1.97 to 1.23 (P< 0.01) after 6 months of biological therapy in a study conducted in Brazil by De Araújo Mariano MHQ, et al, 2014.

Moreover, the results were consistent with a study conducted in Portugal by Fernandes M, *et al* between 2017 and 2018. Rheumatoid patients who received biological therapy (n=77) were recalled. Clinal and demographic data, compliance, disease activity, functional status, joint deformities, and general health related quality of life were documented. At Recall, DAS28-ESR and HAQ were significantly lower when compared to the pre-biological therapy values, both with P-value < 0.001 (Wilcoxon Signed Rank Test). The study concluded that biological therapy provided therapeutic benefits as reflected by significant improvement in functional status.

For HAQ-DI scores, the average score reported for RA patients is 1.2.[15] In the current study, the median HAQ-DI score for RA patients was 0.75, while the scores for studies using HAQ-DI in Egyptian patients were 1.08[16], and 1.45.[17] In Moroccan patients, the median HAQ-DI values for RA patients were 1.40[18] and 1.63[19], while for Tunisian patients the value was 1.7[20]

Objective 2: To find the association between functional health status and selected demographic variables.

Chi-Square test and Fischer's exact test showed no association between selected demographic variable and functional health status scores except for age which had a significant association with functional disability score (p 0.0415).

SUMMARY OF THE STUDY

A quantitative research approach with a descriptive observational survey design was used to determine the functional health status of patients with rheumatoid arthritis receiving biological treatment. After getting ethical clearance from IRB at GMU (Ref. no. IRB/CON/STD/23/Feb-2022) and the Ministry of Health and Prevention research ethical Board (MOHAP/REC/2002/9-2022-UG-N), the project work was initiated Informed consent was obtained from the study sample prior to the

study. Then data was obtained from the clients who fulfilled the inclusion criteria using the Health Assessment Questionnaire-Disability Index (HAQ-DI) tool, Pain visual analog scale (P-VAS), and Global visual analog scale (G-VAS) to elicit demographic profile and functional disability index. Participation of the selected sample was voluntary. Confidentiality and anonymity were maintained and had the right to withdraw from the study at any given point. A total of 100 valid responses through face-to-face interviews were obtained. Descriptive statistics were utilized to analyze the frequency and percentage distribution of socio-demographic variables of the patients. Chi-square and Fischer's exact tests were used to assess any association between demographic variables and functional health status.

The aim of the study was to determine the functional health status among patients receiving biological treatment for rheumatoid arthritis in a selected hospital, in UAE. A standard health assessment questionnaire was used to assess functional health status and determine the association between functional health status and demographic variables among the sample of 100 participants. A nonprobability convenience sampling technique was used to select the sample. The data was collected after the ethical approval of the study and the informed consent of the participants.

A hundred patients were studied of which 89 (89%) were females and 11 (11%) males. Most of the patients were on biological therapy from 1 – 12 months (29%), followed by 13 – 24 months (18%) [median 36 months and range 2- 180 months]. The most frequently prescribed biological therapy was Adalimumab (21% of patients) and Etanercept was the second most frequently prescribed (13% of patients), followed by Tofacitinib (12% of patients) and Tocilizumab (10% of patients). However, the least prescribed medications were Abatacept (2% of patients) and Infliximab (2% of patients).

The results showed a mean (SD), and median functional disability index of 0.8775 (0.7797104) and 0.75. Most of the patients (49%) reported moderate and severe disabilities in performing activities, (29%) of patients had a moderate and severe functional disability of reach, (22% and 21%) of patients reported moderate and severe functional disability in walking and gripping respectively. The majority of patients (45%) had mild pain, (33%) and (13%) had moderate and severe pain correspondingly [median P-VAS 30, mean 32, and range 0 - 100].

Furthermore, most of the patients (54%) reported mild disease effects on their global health, (33%) moderate effects, and 13% severe effects [median G-VAS 30, mean 35.8, and range 0 – 100].

Out of the 100 patients, 10 (10%) of them were aged between 20 – 30 years, 17 (17%) between 31 – 40 years, 25 (25%) between 41 – 50 years, 19 (19%) between 51 – 60 years, and 29 (29%) between 60 – 65 years; of which (89%) were females and (11%) males. Most of the patients (44%) had completed their primary education only. Also, a significant percentage (97%) of patients were nonsmokers. Finally, most of the patients (43%) were having morbid obesity (BMI more than 35), (19%) were obese (BMI between 30 – 35), (24%) were overweight (BMI between 25 – 29.9), and only (14%) were having healthy weight (BMI 18.5 – 24.9). The study showed an association between age and HAQ-DI scores (p 0.0415).

To conclude, standard processes for quantitative monitoring of RA for therapeutic purposes should be implemented as part of routine clinical practice in rheumatology clinics. Therefore, this study supports the use of functional health assessment (HAQ-DI tool) in routine clinical practice at the IBHOH Rheumatology Clinic. This helps physicians monitor the disease and its treatment outcomes in relation to the quality of life of RA patients.

REFERENCES

1. Moufarrej MN, Mahfoud Z, Badsha H. Barriers to achieving controlled rheumatoid arthritis in the United Arab Emirates: a cross-sectional study. Rheumatol Int. 2015 Apr;35(4):759-63. DOI: 10.1007/s00296-014-3151-7. Epub 2014 Oct 15. PMID: 25315703.

2. Abdullah A, Amin R, Feras Emaddin K, Osman AS, Isaa AS, Rizwana Burhanuddin S. Arthritis among patients attending GMC hospital, Ajman, UAE: a cross sectional survey. 2014;3:52–9.

3. Informed Health.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-. Everyday life with rheumatoid arthritis. [Updated 2020 May 20]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK384458/.

4. Namas R, Joshi A, Ali Z, Al Saleh J, Abuzakouk M. Demographic and Clinical Patterns of Rheumatoid Arthritis in an Emirati Cohort from United Arab Emirates. Malemud CJ, editor. Int J Rheumatol [Internet]. 2019;2019:3057578. Available from: https://doi.org/10.1155/2019/3057578.

5. Dr Humeira Badsha Consultant Rheumatologist and Board Member of the Middle East Arthritis Foundation, Life in the UAE: What does Arthritis really feel like? How this chronic disease can affect people of all ages and severely impact quality of life, Published: February 17, 2019 11:55 Yousra Zaki, available from:https://gulfnews.com/lifestyle/health-fitness/life-in-the-uae-what-does-arthritis-really-feel-like-1.1550390374763.

6. Maska L, Anderson J, Michaud K. Measures of functional status and quality of life in rheumatoid arthritis: Health Assessment Questionnaire Disability Index (HAQ), Modified Health Assessment Questionnaire (MHAQ), Multidimensional Health Assessment Questionnaire (MDHAQ), Health Assessment Questionnaire II (HAQ-II), Improved Health Assessment Questionnaire (Improved HAQ), and Rheumatoid Arthritis Quality of Life (RAQoL). Arthritis Care Res. 2011;63(SUPPL. 11).

7. Fries JF, Spitz P, Kraines G, Holman H. Measurement of Patient Outcome in Arthritis. Arthritis Rheum 1980; 23:137-45.

8. The Health Assessment Questionnaire Manual. Stanford University School of Medicine. Division of Immunology & Rheumatology. Disponible en [http://www.chcr.brown.edu/pcoc/ EHAQDESCRSCORINGHAQ372.PDF] (Acessoem 12 de maio de 2008).

9. Ramey DR, Fries JF, Singh G. The Health Assessment Questionnaire. 1995 Status and Review. In B. Spilker Quality of Life and Pharmacoeconomics in Clinical Trials, 2nd ed. Philadelphia, Lippincott-Raven Publishers, 1996.

10. Bird SB, Dickson EW. Clinically significant changes in pain along the visual analog scale. Annals of emergency medicine. 2001 Dec 1;38(6):639-43.

11. Pincus T, Sokka T. Quantitative measures for assessing rheumatoid arthritis in clinical trials and clinical care. Best Pract Res Clin Rheumatol 2003; 17(5):753-81.

12. Wilson IB, Cleary PD. Linking clinical variables with health-related quality of life. *A conceptual model of patient outcomes. JAMA.* 1995;273(1):59–65. [PubMed] [Google Scholar].

13. Norton S, Fu B, Scott DL, Deighton C, Symmons DPM, Wailoo AJ, et al. Health Assessment Questionnaire disability progression in early rheumatoid arthritis: systematic review and analysis of two inception cohorts. Semin Arthritis Rheum. 2014;44:131–44.

14. Informed Health.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-. Everyday life with rheumatoid arthritis. [Updated 2020 May 20]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK384458/

15. Bruce B, Fries JF. The Stanford Health Assessment Questionnaire: dimensions and practical applications. Health Qual Life Outcomes.

2003;1:20.

16. Hassan WA, Baraka EA, Fouad NA. Clinical significance of soluble programmed death-1 (sPD-1) in rheumatoid arthritis patients: Relation to disease activity and functional status. Egypt Rheumatol. 2015;37(4):165–9.

17. Mostafa H, Radwan A. The relationship between disease activity and depression in Egyptian patients with rheumatoid arthritis. Egypt Rheumatol. 2013; 35(4):193–9.

18. Ibn Yacoub Y, Amine B, Laatiris A, Wafki F, Znat F, Hajjaj-Hassouni N. Fatigue and severity of rheumatoid arthritis in Moroccan patients. Rheumatol Int. 2012;32(7):1901–7.

19. Ibn Yacoub Y, Amine B, Laatiris A, Wafki F, Znat F, Hajjaj-Hassouni N. Prevalence of overweight in Moroccan patients with rheumatoid arthritis and its relationships with disease features. Clin Rheumatol. 2012;31(3):479–82.

20. Asma K, Hèla Z, Hosni B, Najla A, Habib A, Imène B, Boutheina K, Elyes B. Quality of life in tunisian patients with rheumatoid arthritis: a cross-sectional study about 200 patients. Ann Rheum Dis. 2013;71(Suppl 3):654.

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