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Comparing the Quality of Life among Patients with Relapsing Remitting Multiple Sclerosis in Iraq Using Different Disease Modifying Therapies

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Abstract

Multiple sclerosis (MS) is a chronic, inflammatory, immune mediated disease of the central nervous system, mostly affecting young adults with mean age of 30 years, twice as high in women compared to men. The etiology of MS is not fully elucidated. MS symptoms are directly related to demyelination and axonal loss, along with other psychological symptoms, can result in functional limitations, disability and reduced quality of life (QoL). The QoL assessments in patients with a chronic disease may contribute to improving treatment and could even be of prognostic value. The goals of this study were to compare the QoL of Iraqi patients with relapsing remitting multiple sclerosis (RRMS), using three different diseases modifying therapies(DMTs) administered orally, subcutaneously, and by slow infusion; namely, fingolimod, interferonβ-1b, and natalizumab, respectively. And to assess the role of disability status, educational status, occupational status, MS duration, and treatment duration as a predictor for the QoL**.** Functional Assessment of Multiple Sclerosis (FAMS) questionnaire version 4 was used to assess QoL. Sociodemographic and clinical characteristics were tested by univariate and multivariate regression analyses to assess the contribution of these predictors to QoL. No significant differences were found in symptoms, thinking/fatigue subscales and FAMS total scores among the three DMTs. In conclusion: Iraqi MS patients using Interferonβ-1b, fingolimod or natalizumab have a comparable low level of QoL. The expanded disability status scale (EDSS) is negatively associated with QoL of MS patients in all of the three therapies, while other predictors such as occupational status, educational status, smoking habit and MS duration have different impact in different treatments.

Keywords: Multiple sclerosis, FAMS, EDSS, DMTs, Quality of life.

مقارنة جودة الحياة لمرضى تصلب الاعصاب المنتشر في العراق من مستخدمي العلاجات المعدلة للمرض المختلفة

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الخلاصة

تصلب الاعصاب المتعدد هو مرض التهابي مناعي مزمن يصيب الجهاز العصبي المركزي يحدث لاسباب غير معروفة الى حد ما تحدث الاصابة به غالبا في صغار البالغين مع متوسط عمر ٣٠ سنة ،لدى النساء اكثر من الرجال. غالب اعراض المرض ترتبط بشكل مباشر بظاهرة إزالة الميالين وفقدان المحور العصبي ، بالإضافة إلى أعراض نفسية، التي تؤدي الى وجود قيود وظيفية وعجز وانخفاض جودة الحياة . قد يساهم تقييم جودة الحياة للمرضى الذين يعانون من الامراض المزمنة في تحسين العلاج ويمكن أن تكون ذات قيمة تنبؤية. أهداف هذه الدراسة هي مقارنة جودة الحياة بين المرضى العراقيين الذين يعانون من الانتكاس المتكرر لمرض التصلب المتعدد الذين يستخدمون واحد من ثلاثة علاجات مختلفة تعطى عن طريق الفم ، تحت الجلد ، وعن طريق الوريد. وهم، فنكولمود,انترفيرون بيتا-١ب , و نتاليزوماب على التوالي ، وتقييم دور بعض المسببات في جودة الحياة كمستوى الاعاقة,مستوى التعليم,الحالة الوظيفية,مدة المرض واخيرا مدة العلاج . تم استخدام استبيان التقييم الوظيفي لمرض تصلب الاعصاب المتعدد الإصدار ٤ لتقييم جودة الحياة. تم اختبار الخصائص الاجتماعية والديموغرافية والسريرية من خلال تحليل الانحدار احادي المتغيرات والمتعدد المتغيرات لتقييم مساهمة هذه المؤشرات في جودة الحياة. لم يتم العثور على فروق ذات دلالة إحصائية في محور الأعراض و محور التفكير والاعياء وعدد النقاط الإجمالي لاستبيان جودة الحياة. في الختام: المرضى الذين يعانون من مرض التصلب الاعصاب المتعدد في العراق من مستخدمي انترفيرون بيتا -١ب، او فنكولمود أو نتاليزوماب لديهم مستوى منخفض مماثل من جودة الحياة. يرتبط مقياس حالة الإعاقة الموسعة بشكل سلبي مع جودة الحياة لمرضى تصلب الاعصاب المتعدد في جميع العلاجات الثلاثة ، في حين أن تنبؤات أخرى مثل الحالة المهنية والحالة التعليمية و التدخين ومدة المرض لها تأثير مختلف باستخدام العلاجات المختلفة.

الكلمات المفتاحية : تصلب الاعصاب المتعدد، استبيان التقييم الوظيفي لمرض تصلب الاعصاب المتعدد ،مقياس حالة الاعاقة الموسعة ، العلاجات المعدلة للمرض ، جودة الحياة.

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Introduction

Multiple sclerosis (MS) is a chronic, neurodegenerative disease of the central nervous system, mostly affecting young adults with mean age of 30 years, twice as high in women as compared to men [1,2] MS prevalence differ by different geographic regions [3]**.** Iraq as a part of the Middle East area was considered as a MS medium risk prevalence area[4] but by latest epidemiological studies have indicated that the Arabian Gulf region has a high prevalence of MS[5]. The etiology of MS is not fully elucidated, it involves both genetic and environmental factors[6]. The clinical course of MS was characterized as the following [7,8]:

1. Relapsing–remitting MS (RRMS)*:*- affects about 85% of MS patients and marked by flare-ups (relapse or exacerbation of symptoms followed by periods of remission, when symptoms improve or disappear)[8,9].
2. Primary progressive MS (PPMS):-affects approximately 10% of MS patients and symptoms continue to worsen gradually from the beginning. There are no relapses or remissions, but there may be occasional plateaus [8,9].
3. Secondary progressive MS (SPMS):- may develop in some patients with RRMS. The disease course continues to worsen with or without periods of remission[8,9].
4. Progressive-relapsing MS:- is a rare form, affecting fewer than 5% of patients. It is progressive from the start, with intermittent flare-ups of worsening symptoms along the way and has no periods of remission[8].

Clinically isolated syndrome (CIS) is considered to be a part of the spectrum of MS phenotypes which is a first symptomatic episode of CNS dysfunction due to inflammatory demyelination that could be MS, but has yet to fulfill the diagnostic criteria of MS[10], and there is 83% risk of developing MS over the next 10 years [11].

In MS, dissemination of the lesions in the central nervous system, produced by the inflammatory process, manifested as physical and mental deficits and the incomplete recovery after relapse leads to the accumulation of new deficits and the progressive nature of the condition interfere with daily activities of individuals and have a negative impact on their wellbeing.[12] The symptoms of MS, such as weakness, sensory loss, and ataxia, which are directly related to demyelination and axonal loss, along with other symptoms such as reactive depression or social isolation, can result in functional limitations, disability and reduced quality of life (QoL)[13]. Health – related quality of life (HRQoL) is defined as the impact of an illness or treatment on an individual's physical, social, psychological and general well-being.

QoL is now considered an important end-point inclinical studies. The QoL assessments in patients with a chronic disease may contribute to improving treatment and could even be of prognostic value[14] . The QoL among MS patients in Arabic countries was rarely studied ,with limited information from Iraq[15]. The goals of this study were to compare the QoL among Iraqi patients with RRMS using one of three different disease modifying therapies (DMTs), administered orally, subcutaneously, and by slow infusion; namely, fingolimod, interferonβ-1b , and natalizumab, respectively. And to assess the role of disability status, educational status, occupational status, MS duration, and treatment duration as a predictor for the QoL**.**

Patients and Method

Patients

The present cross-sectional study was carried out on 200 patients, (135 females with mean age ±SD of 36.7 ± 9.7 years, and 65 males with mean age ±SD of 35.9 ± 10.4 years) already diagnosed with RRMS according to the revised McDonald criteria[16], who attended the Multiple Sclerosis Center, Baghdad Teaching Hospital/Medical City, seeking medical care, from November 2017 to March 2018. Patients are into three groups:

1-Group 1 consists of 70 patients who are receiving interferon β-1b , 0.25 mg subcutaneously every other day.

2-Group 2 consists of 60 patients who are receiving fingolimod , 0.5mg orally daily.

3-Group 3 consists of 70 patients who are receiving natalizumab , 300mg intravenous infusion over 1 hour every 4 weeks.

Inclusion criteria

The inclusion criteria include; patients were aged 18 years or above of either sex, diagnosed with multiple sclerosis at least 1 year before this study, on the same medication for at least 3 months before this study, and are able to communicate.

Exclusion criteria

The exclusion criteria include; patients who did not consent to participate, had hearing, speech or cognitive deficits that would impair understanding of the questions, women who were pregnant or breast feeding, patients with relapse or taken any form of corticosteroid treatment and patients with clinically isolated syndrome (CIS) or other subtypes of MS.

Method

To achieve the goals of the study, the expanded disability status scale (EDSS), and

the functional assessment of multiple sclerosis (FAMS) were assessed as follows:

Expanded disability satus scale (EDSS)

The most popular and widely used instrument as an endpoint in clinical trials to assess the effectiveness of therapeutic interventions is the Expanded Disability Status Scale (EDSS) of Kurtzke. It is a clinician-administered assessment scale evaluating the functional systems of the CNS[17]. The EDSS is a 20-step scale of disease severity ranging from 0 (normal) to 10 (death due to MS) in 0.5 increments interval l. This scale includes two parts: one (from 0 to 3.5) taking into account functional parameters and EDSS measure impairments based on the neurological examination, the other (from 4 to 10) estimating degrees of mobility in patients. The scale considers eight functional systems (FS): pyramidal, cerebellar, brainstem, sensory, bowel and bladder, visual, cerebral, and other. (figure1)[18].

0	Normal neurologic exam
1.0	No disability, minimal signs in one functional system
1.5	No disability, minimal signs in more than one functional system
2.0	Minimal disability in one functional system
2.5	Minimal disability in two functional systems
3.0	Moderate disability in one functional system, or mild disability in three or four functional systems though fully ambulatory
3.5	Fully ambulatory but with moderate disability in three or four functional systems
4.0	Fully ambulatory without aid, self-sufficient, up and about some 12 hours a day despite relatively severe disability. Able to walk without aid or rest some 500 meters
4.5	Fully ambulatory without aid, up and about much of the day, able to work a full day, may otherwise have some limitation of full activity or require minimal assistance, characterized by relatively severe disability. Able to walk without aid or rest for some 300 meters
5.0	Ambulatory without aid or rest for about 200 meters; disability severe enough to preclude full daily activities (e.g. to work full day without special provisions)
5.5	Ambulatory without aid or rest for about 100 meters; disability severe enough to preclude full daily activities
6.0	Intermittent or unilateral constant assistance (cane, crutch, or brace) required to walk about 100 meters with or without resting
6.5	Constant bilateral assistance (canes, crutches, or braces) required to walk about 20 meters without resting
7.0	Unable to walk beyond about 5 meters even with aid. Essentially restricted to a wheelchair. Wheels self in standard wheelchair and transfers alone. Active in wheelchair about 12 hours a day
7.5	Unable to take more than a few steps. Restricted to wheelchair. May need aid to transfer. Wheels self but cannot carry on in standard wheelchair a full day. May require a motorized wheelchair
8.0	Unable to walk at all, essentially restricted to bed, chair or wheelchair but may be out of bed much of the day. Retains many self-care functions. Generally has effective use of the arms
8.5	Essentially restricted to bed much of the day. Has some effective use of arm(s). Retains some self-care functions
9.0	Helpless bed patient. Can communicate and eat
9.5	Totally helpless bed patient. Unable to communicate effectively or eat/ swallow
10	Death due to Multiple Sclerosis

Figure 1. Expanded disability status scale [19]

The functional assessment of multiple sclerosis (FAMS)

Quality of life in MS patients was assessed by the Functional Assessment of Multiple Sclerosis (FAMS) questionnaire, published in 1996 by David Cella and colleagues[20].the FAMS (version 4),the latest and most efficient version ,consist of 58 items from which 44 items organized into six subscales: [21] mobility, symptoms, emotional well-being, general contentment, thinking/fatigue and family/social well-being, and the additional concerns (Figure 2).

Arabic version of FAMS was used and patients indicate their degree of agreement with each question in subparts; on a five-point Likert scale, where 0= not at all; 1= a little bit; 2= somewhat; 3-quite a bit; 4=very much produces a score between (0-4) for each scored question. The respondents are asked to indicate how true

each statement has been for them during the past 7 days. The additional Concerns subscale retained without score based on their potential clinical and empirical value. Scores of negatively worded statements are reversed. After appropriate reversal, the scores are added within subscale, and then subscale scores are summed to produce a total FAMS score. The FAMS total score range is (0 to 176 points) and higher scores indicate better QoL[21].

	Not at all	A little bit	Some-what	Quite a bit	Very much
Mobility					
1. Because of my physical condition, I have trouble meeting the needs of my family					
2. I am able to work (include work in home).					
3.I have trouble walking					
4.I have to limit my social activity because of my condition					
5. My legs are strong					
6.I have trouble getting around in public places					
7.I have to make plans around my condition					
Symptoms					
8. I have nausea					
9. I have pain					
10.I feel sick					
11.I feel weak all over					
12.I have pain in my joints					
13.I am bothered by headaches					
14.I am bothered by muscle pains					
Emotional Well-Being					
15. I feel sad					
16. I am losing hope in the fight against my illness					
17. I am able to enjoy life					
18. I feel trapped by my condition					
19. I am depressed about my condition					
20. I feel useless					
21. I feel overwhelmed by my condition					
General Contentment					
22.My work (include work in home) is fulfilling					
23.I have accepted my illness					
24.I am enjoying the things I usually do for fun					
25.I am content with the quality of my life right now					
26.I am frustrated by my condition					
27.I feel a sense of purpose in my life					
28.I feel motivated to do things					
Thinking and Fatigue					
29. I have a lack of energy					
30. I feel tired					
31. I have trouble starting things because I am tired					
32. I have trouble finishing things because I am tired					
33. I need to rest during the day					
34. I have trouble remembering things					
35. I have trouble concentrating					
36. My thinking is slow					
37. I have trouble learning new tasks or directions					

	Not at all	A little bit	Some-what	Quite a bit	Very much
Family /Social Well-Being					
38. I feel distant from my friends					
39. I get emotional support from my family					
40. I get support from my friends and neighbors					
41. My family has accepted my illness					
42. Family communication about my illness is poor					
43. My family has trouble understanding when my condition gets worse					
44. I feel "left out" of things					
Additional Concerns					
45. I am bothered by side effects of treatment					
46. I am forced to spend time in bed					
47. I feel close to my partner (or the person who is my main support)					
48.Have you been sexually active during the past year? No- Yes- If yes: I am satisfied with my sex life					
49. I am proud of how I'm coping with my illness					
50. I feel nervous					
51. I worry that my condition will get worse					
52. I am sleeping well					
53. Heat worsens my symptoms					
54. I lose control of my urine					
55. I urinate more frequently than usual					
56. I am bothered by the chills					
57. I am bothered by fevers					
58. I am bothered by muscle spasms					

Figure 2. Functional Assessment of Multiple Sclerosis Questionnaire (FAMS)[20]

Administrative arrangement and ethical considerations

A research proposal that explains the purpose of the study and methods for data collection and instruments was submitted to College of Pharmacy / University of Baghdad committee. After approval, the proposal of the current study was submitted to the committee of Multiple Sclerosis Center in Baghdad Teaching Hospital/Medical City to grant ethical approval, the committee of the mentioned center approved that.

Administration of questionnaire

The data related to the study were collected by one of the researchers, who presented at the MS center five days a week from 8 am to 1 pm. When the patients arrived at the MS center they were asked if they are willing to participate in the study after briefly explaining its purpose. If they agreed to participate a full description of the procedure was given. During the waiting time to be checked by the neurologist, participants were interviewed by one of the researchers.

Statistical analysis

The data were evaluated using *Statistical Package for the Social Sciences* (SPSS® 22.0.0) software package for windows. Anderson Darling test was used to assess if continuous variables (age, disease duration, treatment duration, EDSS, FAMS subscale and it's total score) will follow normal distribution or not. If they follow normal distribution, they will be expressed as mean± standard deviation. If did not, they will be expressed as median and interquartile range (25% to 75% percentile range). Discrete variables (gender, occupation, marital status, educational status, zone of residence, smoking habit, type of treatment) were expressed by their number and percentage. Chi square test was used to analyze the discrete variable .One way ANOVA was used to analyze the continuous variables. Pairwise comparisons were done using post hoc Tukey test. Linear regression (uni and multivariate) analysis was used to assess the relationship between different ariables. Negative sign of correlation coefficient (r) or beta estimate (β) indicates inverse relationship, while, positive sign indicates direct relationship.

Results

Personal, demographic and disease characteristics of participants

The socio-demographic characteristics for subjects (N=200) participated in the study are illustrated in table1.

Table 1. Patient's characteristics.

Variables	**Value**	
	n	**mean±SD ,%**
Age (years)		36.4 ± 9.9
Gender		
Female	135	67.5%
Male	65	32.5%
Occupation (employed)	87	43.5%
Married	134	67%
Education (college)	81	40.5%
Zone of residence		
South regions	13	6.5%
Middle regions	180	90%
North regions	7	3.5%
Smoker	25	12.5%
Treatment		
Interferonβ-1b	70	35%
Fingolimod	60	30%
Natalizumab	70	35%
Duration of MS (years)		7.1 ± 5.4
≥ 5 years	125	62.5%
EDSS		3.0 ± 2.1

South regions involve(Maisan, Dhi Qar, Muthana and Basrah); Middle regions involve(Baghdad, Diala, Anbar, Wasit, Babil, Karbala, Qadisia and Najaf);North regions involve(Kurdistan, Ninawa, Salah Aldin and Karkuk);EDSS: Expanded Disability Status Scale, MS: Multiple Sclerosis**.**

The socio-demographic characteristics by the type of treatment are illustrated in table 2.Subjects using interferonβ-1b are older (39.4 ± 8.7 years; P=0.002) had higher employment rate (58.6%) and longer treatment duration (71.8± 64.3 months; P<0.001) while lower EDSS score (2.5 ± 1.7; P=0.023) as compared to the other therapies. Natalizumab using subjects had the highest vitamin D_3 use (40.0%).

Table 2. Patient characteristics by type of treatment

	Interferonβ-1b	**Fingolimod**	**Natalizumab**	**p-value**
Age (years)	39.4 ± 8.7	36.2 ± 10.8	33.6 ± 9.4	**0.002**
Gender				
Female	43, 61.4%	38, 63.3%	54, 77.1%	0.099
Male	27, 38.6%	22, 36.7%	16, 22.9%	
Occupation (employed)	41, 58.6%	22, 36.7%	24, 34.3%	**0.007**
Married	53, 75.7%	37, 61.7%	44, 62.9%	0.156
Education (college)	30, 42.9%	23, 38.3%	28, 40.0%	0.867
Smoker	11, 15.7%	6, 10.0%	8, 11.4%	0.583
Duration of MS (years)	5.99 ± 5.36	8.12 ± 6.05	7.47 ± 4.81	0.069
≥ 5 years	36, 51.4%	42, 70%	47, 67.1%	0.057
Duration of current treatment (months)	71.8 ± 64.3	7.08 ± 4.42	19.14 ± 10.59	**<0.001**
EDSS	2.5 ± 1.7	3.5 ± 2.2	3.2 ± 2.2	**0.023**
Additional therapies				
Multivitamins	8, 11.4%	3, 5.0%	3, 4.3%	0.195
Vitamin D_3	14, 20.0%	17, 28.3%	28, 40.0%	**0.034**
Omega 3	8, 11.4%	8, 13.3%	9, 12.9%	0.942

Chi square test was used to analyze the discrete variables (gender, occupation, marital status, smoking habit, education, and additional therapies; One way ANOVA was used to analyze the continuous variables (age, disease duration, treatment duration and EDSS); EDSS: Expanded Disability Status Scale; MS: Multiple Sclerosis .

Table 3 provides a pairwise comparisons for the three studied groups. Regarding age, the difference was significant between interferonβ-1b and natalizumab treatment groups (P=0.001).Significant difference in the occupational status between interferonβ-1b and fingolimod treatment group (P=0.013) also between interferonβ-1b and natalizumab treatment groups (P=0.004). While the difference in EDSS score was significant between interferonβ-1b and fingolimod treatment groups (P=0.025).

The difference in duration of treatment was significant between interferonβ-1b and fingolimod treatment groups (P<0.001) also between interferonβ-1b and natalizumab (P<0.001) treatment groups. Finally the difference in vitamin D_3 use was between interferonβ-1b and natalizumab (P=0.010) treatment groups.

Table 3. Post-hoc analysis of age, occupation, EDSS, treatment duration, vitamin D_3 supplementation between each pair of therapy

	Interferon β-1b Vs. Fingolimod	Interferon β-1b Vs. Natalizumab	Fingolimod Vs. Natalizumab
Age (years)	0.143	0.001	0.272
Occupation	0.013	0.004	0.777
EDSS	0.025	0.103	0.787
Duration of current treatment (months)	<0.001	<0.001	0.181
Vitamin D_3 supplementation	0.266	0.010	0.163

Tukey HSD was used for pairwise comparison; EDSS: Expanded Disability Status Scale.

The Functional Assessment of Multiple Sclerosis (FAMS) subscales and total score are presented in table 4. The FAMS thinking /fatigue subscale has showed the highest mean value (22.7 ± 7.1), while the mobility subscale has showed the lowest mean value (18.1 ± 8.6), and total FAMS score for the general study sample was found to be (120.7 ± 28.7).

Table 4. Assessment of FAMS score for all patients

FAMS Score	Value(mean±SD)
Mobility	18.1 ± 8.6
Symptoms	20.3 ± 5.4
Emotional well-being	19.0 ± 6.9
General contentment	18.5 ± 6.2
Thinking/ fatigue	22.7 ± 7.1
Family/social well-being	22.2 ± 4.4
Total score	120.7 ± 28.7

FAMS: Functional Assessment of Multiple Sclerosis; SD:Standred Deviatio***n***

The FAMS subscales and total scores by different type of treatment are presented in table 5. Significant differences were found in Mobility (P<0.001), Emotional well-being (P=0.038), General contentment (P=0.001), and Family/social well-being (P=0.030) subscales of FAMS, but not significant difference were found in Symptoms, Thinking/fatigue subscales and in total score

Table 5. Assessment of FAMS score according to type of treatment

FAMS score	Interferonβ-1b	Fingolimod	Natalizumab	P-value
	Mean ± SD	Mean ± SD	Mean ± SD	
Mobility	20.9 ± 6.7	15.0 ± 9.8	18.0 ± 8.4	**<0.001**
Symptoms	19.3 ± 6.1	20.8 ± 4.8	20.7 ± 5.1	0.201
Emotional well -being	20.3 ± 6.0	17.2 ± 7.7	19.2 ± 6.6	**0.038**
General contentment	19.9 ± 5.5	16.1 ± 6.2	19.1 ± 6.3	**0.001**
Thinking/ fatigue	21.6 ± 7.4	22.5 ± 6.9	23.8 ± 6.8	0.176
Family/social well-being	23.2 ± 4.1	22.1 ± 3.8	21.2 ± 4.8	**0.030**
Total score	125.2± 27.6	113.8± 28.8	122.1 ± 29.1	0.066

One way ANOVA was used to analyze the continuous variables (FAMS subscale and total score); FAMS: Functional Assessment of Multiple Sclerosis.

Table 6 provide pairwise comparison between the three study groups. There were significant difference in FAMS mobility (P<0.001), emotional well-being (P=0.030), and general contentment (P=0.001) subscale scores, between interferonβ-1b and fingolimod treatment groups. FAMS general contentment score was significantly higher in natalizumab than in fingolimod (P=0.015) treated groups. FAMS family/social well-being score was significantly higher in interferonβ-1b than in natalizumab (P=0.023) treated groups.

Table 6. Assessment of FAMS score between each pair of therapy

Variables	Interferonβ-1b Vs. Fingolimod	Interferonβ-1b Vs. Natalizumab	Fingolimod Vs. Natalizumab
FAMS score			
Mobility	<0.001	0.095	0.100
Symptoms	0.267	0.274	0.997
Emotional well-being	0.030	0.595	0.237
General contentment	0.001	0.737	0.015
Thinking/ fatigue	0.778	0.154	0.510
Family/social well-being	0.339	0.023	0.484
Total score	0.059	0.793	0.220

Tukey HSD was used for pairwise comparison; FAMS: Functional Assessment of Multiple Sclerosis

Univariate linear regression analysis was used to assess the correlation between different predictors and the total FAMS score in the total study sample, and per type of treatment .Followed by multivariate analysis to differentiate between dependent and independent predictors.

In the univariate analysis, there were statistically significant inverse correlation between total FAMS score and age (r=-0.295; P<0.001), MS duration (r=-0.230; P=0.001), and EDSS (r=-0.655; P<0.001). While, there were statistically significant direct correlation between FAMS total scores and occupational status (r=0.248; P<0.001) and educational status (r=0.184; P=0.009).

In multivariate analysis, FAMS score was correlated with occupational status (β=0.106; P=0.075), and EDSS (β=-0.574; P<0.001) (table 7).

Table 7. Correlation between FAMS score with various predictors for all MS patients

Predictors	FAMS score			
	Univariate analysis		Multivariate analysis	
	r	P-value	β	P-value
Age	-0.295	<0.001	-0.082	0.178
Gender	0.132	0.062	-	-
Occupation	0.248	<0.001	0.106	0.057
Marital status	-0.114	0.108	-	-
Education	0.184	0.009	0.083	0.126
Smoking	0.028	0.697	-	-
MS duration	-0.230	0.001	-0.070	0.231
Treatment duration	0.048	0.500	-	-
EDSS	-0.655	<0.001	-0.574	<0.001

Multivariate linear regression analysis was used to assess the correlation between total FAMS and different predictors (dummy variable used to express the categorical variables); r: partial regression coefficient; β: beta estimate; EDSS: Expanded Disability Status Scale; MS: Multiple Sclerosis; FAMS: Functional Assessment of Multiple Sclerosis.

By using univariate analysis to assess QoL predictors for interferonβ-1b treatment group; total FAMS score was inversely correlated with EDSS (r=-0.481; P<0.001). Whereas, it was directly correlated with occupational status (r=0.314; P=0.008), educational status (r=0.253; P= 0.035), and smoking habit (r=0.257; P=0.032).In multivariate analysis; total FAMS score was correlated with educational status (β = 0.219 ; P=0.033), and EDSS (β = -0.410 ; P<0.001) (table 8).

Table 8. Correlation between FAMS score with various predictors for Interferonβ receiving patients.

Predictors	FAMS score			
	Univariate analysis		Multivariate analysis	
	r	P-value	β	P-value
Age	-0.161	0.182	-	-
Gender	0.219	0.068	-	-
Occupation	0.314	0.008	0.159	0.137
Marital status	-0.038	0.757	-	-
Education	0.253	0.035	0.219	0.033
Smoking	0.257	0.032	0.166	0.111
MS duration	-0.096	0.431	-	-
Treatment duration	-0.096	0.431	-	-
EDSS	-0.481	<0.001	-0.410	<0.001

Multivariate linear regression analysis was used to assess the correlation between total FAMS and different predictors (dummy variable used to express the categorical variables); r: partial regression coefficient; β:beta estimate; EDSS: Expanded Disability Status Scale; MS: Multiple Sclerosis; FAMS: Functional Assessment of Multiple Sclerosis.

By using univariate analysis to assess QoL predictors for fingolimod treatment group; total FAMS score was inversely correlated with age (r=-0.457; P<0.001), marital status (r=-0.297; P=0.021), MS duration (r=-0.331; P=0.010), and EDSS (r=-0.764; P<0.001); while it was directly correlated with treatment duration (r=0.355; P=0.005). In multivariate analysis; total FAMS score was correlated with MS duration (β=-0.225;P=0.017), and EDSS (β=-0.677; P<0.001) (table 9).

Table 9. Correlation between FAMS score with various predictors for Fingolimod receiving patients

Predictors	FAMS score			
	Univariate analysis		Multivariate analysis	
	r	P-value	β	P-value
Age	-0.457	<0.001	-0.058	0.601
Gender	0.033	0.801	-	-
Occupation	0.218	0.094	-	-
Marital status	-0.297	0.021	-0.019	0.852
Education	0.176	0.179	-	-
Smoking	-0.191	0.143	-	-
MS duration	-0.331	0.010	-0.225	0.017
Treatment duration	0.355	0.005	0.114	0.208
EDSS	-0.764	<0.001	-0.677	<0.001

Multivariate linear regression analysis was used to assess the correlation between total FAMS and different predictors (dummy variable used to express the categorical variables); r: partial regression coefficient; β:beta estimate; EDSS: Expanded Disability Status Scale; MS: Multiple Sclerosis; FAMS: Functional Assessment of Multiple Sclerosis.

By using univariate analysis to assess predictors of the QoL for natalizumab treatment group; total FAMS score was inversely correlated with age (r=-0.337; P= 0.004), and EDSS (r=-0.681; P<0.001). In multivariate analysis total FAMS score was correlated with EDSS (β=-0.653; P <0.001) (Table 10)

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Table 10. Correlation between FAMS score with various predictors for natalizumab receiving patients

Predictors	FAMS score			
	Univariate analysis		Multivariate analysis	
	r	P-value	β	P-value
Age	-0.337	0.004	-0.068	0.491
Gender	0.153	0.206	-	-
Occupation	0.169	0.162	-	-
Marital status	-0.077	0.528	-	-
Education	0.118	0.332	-	-
Smoking	-0.074	0.540	-	-
MS duration	-0.212	0.079	-	-
Treatment duration	0.003	0.978	-	-
EDSS	-0.681	<0.001	-0.653	<0.001

Multivariate linear regression analysis was used to assess the correlation between total FAMS and different predictors (dummy variable used to express the categorical variables); r: partial regression coefficient; β:beta estimate; EDSS: Expanded Disability Status Scale; MS: Multiple Sclerosis; FAMS: Functional Assessment of Multiple Sclerosis.

Discussion

The assessment of Quality of life (QoL) offers a comprehensive reflection on disability and the impact of MS on affected individuals. It helps to guide physicians for proper care of patients, and reflects the effectiveness of treatment and may predict disease progression[22–24].

Although many studies have examined QoL in MS patients, but results had shown a great degree of difference across countries, cultures and health care systems[25–27].The QoL was rarely investigated among MS patients in Arabic countries(15), with limited information from Iraq. Thus, this study aimed to evaluate the QoL of Iraqi patients with RRMS, and to determine its correlations with different predictors.

Prior studies had demonstrated that individuals with MS have lower overall and specific QoL as compared with healthy control groups or populations with other chronic diseases such as rheumatoid arthritis, end-stage renal disease, diabetes mellitus, and hypertension [28,29].

There were no significant differences in the QoL among subjects using interferonβ-1b, fingolimod or natalizumab therapies (P=0.066) (table 5). Direct comparison of the QoL between different therapies used in MS had been rarely studied. Zecca *et al.* had reported a non-significant difference in QoL between interferonβ-1b and natalizumab (P=0.6), which was related to satisfaction with both treatments resulted from convenience of use with natalizumab and optimal safety with interferonβ -1b[30].

Comparison of mean of total FAMS score and FAMS subscales scores of subjects, per type of treatment have shown a significant differences in terms of mobility, emotional well-being, general contentment, and family/ social well-being subscales, yet, the difference was not significant with regard to total FAMS score (table 5).

Pairwise comparison of mean of FAMS subscales scores per type of treatment had shown a higher mobility, and emotional well-being in interferonβ-1b than in fingolimod treatment groups (table 6). This may be explained, at least in part, by the longer duration of treatment, and subsequently the lower EDSS in interferonβ-1b treatment group than in fingolimod treatment group. EDSS is a measure of disability in MS patients [31], and MS disability had shown to be related to emotional well-being (depression), mobility, and physical symptoms[25,32]. In contrast Fox et al, had found that scores for all domains of the general QoL measure were higher in fingolimod treatment group[33] . This controversy may be related to the different study design. Fox *et al.* had used the 36-item Short-Form Health Survey v2 (SF-36 v2) to evaluate health-related QoL for MS patients on different injectable DMTs, including interferonβ-1b, before and after switching to oral fingolimod treatment.

General contentment has found to be higher in interferonβ-1b than with fingolimod, and higher for natalizumab than fingolimod (Table 6). This can also be attributed to the longer treatment duration and lower EDSS, which are associated with more satisfaction with life aspects.

Family/social well-being score were significantly higher for Interferonβ-1b compared to natalizumab (table 6). This refers to the greater family and social support required for patients on interferonβ-1b therapy than those on natalizumab therapy, since interferonβ-1b requires more frequent self–injection, which promotes more frequent

contact between the patient and healthcare provider.

To assess the correlation of the measured clinical and sociodemographic parameters with QoL, univariate regression analysis followed by multivariate analysis had been conducted to best ascertain the independent predictors of the QoL. By univariate analysis, the age, occupation, education, disease duration, and EDSS have shown to be dependent predictors of QoL (Table 7). And by multivariate analysis only occupational status, and EDSS, have shown to be independent predictors of QoL in Iraqi MS patients. Occupational status may be related to better coping of patients with MS, and with maintaining a productive social life. Yamout *et al*., had reported a similar finding[15]. As discussed earlier, disability is associated with poor QoL[32]. Thus, it is highly accepted that EDSS, which is a measure of disability in MS patients[31], is associated with lower QoL. The inverse relationship between EDSS and QoL had also been demonstrated in other studies [34,35].

The study has shown that occupational status, educational status, smoking habit, and EDSS are correlated with QoL in interferonβ-1b treatment group (table 8). Multivariate analysis has shown that educational status is positive independent predictors of QoL, while EDSS is a negative independent predictor of QoL (table 8). Higher degree of education may be interpreted as a better awareness and knowledge of the disease and the goals of therapy. The positive association between educational status and QoL had been demonstrated by another study[15].

In fingolimod treatment group age, marital status, MS duration, treatment duration and EDSS were correlated to QoL in the univariate analysis; while, only MS duration and EDSS were shown to be negative independent predictors of QoL by the multivariate analysis (Table 9). The negative association between MS duration and QoL is expected due to the progressive nature of the disease. Many studies had shown that disease duration is a significant factor decreasing the QoL in MS patients treated by different DMTs[23,36–39].

In this study only fingolimod had shown such relationship. This may refer to the tendency of physician to reserve fingolimod treatment for MS patients who have *failed with other* DMTs. Regarding natalizumab treated group, the univariate analysis has shown that age, and EDSS are correlated with QoL; while, only EDSS has shown to be an independent negative predictor of QoL by multivariate analysis (table 10). The most consistent predictor of QoL in the three treatments groups has shown to be EDSS, which emphasizes the role of degree of disability on the QoL of MS patients. The inverse relationship between EDSS and overall QoL had also been demonstrated in other studies [34,35,38,40–42].

Limitations

Findings from this study have some limitations. First; the cross sectional design; thus variables and relationships between them may be representative of only a single point. Second; these subjects may not be representative of MS patients as a whole due to single MS center study.

Conclusions and recommendations

Iraqi individuals with RRMS have low level of QoL. There was no significant difference in the QoL of Iraqi MS patients using interferonβ-1b, fingolimod or natalizumab. Some predictors correlate with QoL of Iraqi MS patients treated with these different treatments. EDSS is negatively associated with QoL of MS patients in all of the three therapies, while other predictors such as occupational status, educational status, and MS duration have different impact in different treatments. Assessing the QoL routinely could help physicians to assess treatment efficacy and the level of patient's QoL with relation to their treatment. Patients also are recommended for getting the most out of medical appointments, using rehabilitation services, considering support group and be educated that can improve their QoL.

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