Haniya Noun[1], Rami Atat[2], Georges Hatem[1, 3], Roula Ajrouche[1], Sara Nahas[4], Maya El-Hajj[1], Salam Zein[1], Sanaa Awada[1]

[1]Clinical and Epidemiological Research Laboratory, Faculty of Pharmacy, Lebanese University, Hadat, Lebanon
[2]Zahraa Hospital, University Medical Center, Beirut, Lebanon
[3]Faculty of Medicine, University of Porto, Portugal
[4]Nutrition-Wellness Center, Beirut, Lebanon

Health-related quality of life of relapsing or remitting multiple sclerosis patients: a case-control study

Abstract

Background: Patients with multiple sclerosis (MS) report lower health-related quality of life (HRQoL) than other chronic disease populations. This study aims to identify risk factors of relapsing or remitting multiple sclerosis (RRMS) and assess its impact on HRQoL in Lebanese MS patients.

Patients and methods: A three-month case-control study was performed among 75 RRMS case patients recruited from two clinics in Beirut and 225 controls from the general population.

Results: Heavy cigarette smoking, moderate and heavy water pipe smoking, vitamin D deficiency, cardiovascular disease, and psychological disorders were significantly associated with RRMS. Linear regression showed that the multiple sclerosis international quality of life global index significantly decreased with the number of relapses, the incomplete recovery between relapses, and the psychological disorder. Higher-income and physical activity had a positive effect on quality of life (QoL).

Conclusions: Findings of this study highlighted the risk factors of RRMS, which can be used for informed decision-making and targeted awareness campaigns. Other factors affecting the HRQoL of MS patients should be considered to improve their experience throughout and after treatment.

Palliat Med Pract 2023; 17, 2: 73–83

Key words: multiple sclerosis, quality of life, relapsing/remitting, Lebanon, predictors

Introduction

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system characterized by various symptoms [1]. It is the most common neuro-immunological disorder and among the leading causes of disability in young adults [2]. Relapsing-remitting MS (RRMS) is the most common subtype characterized by relapses followed by partial or complete recovery [3]. There is an estimated

Address for correspondence:
Georges Hatem
Clinical and Epidemiological Research Laboratory, Faculty of Pharmacy, Lebanese University, Hadat, Lebanon
e-mail: georges.r.hatem@gmail.com; phone: +9615463375, fax: +9615463312

Palliative Medicine in Practice 2023; 17, 2, 73–83

DOI: 10.5603/PMPI.a2023.0008

Received: 5.12.2022 Accepted: 23.01.2023 Early publication date: 25.01.2023

global prevalence of 36 MS cases per 100 000 persons, affecting approximately 2.8 million people worldwide [4]. The disease can occur at any age, but it primarily affects young adults with a peak age at onset between 20–40 years of age [1]. Women are more likely to develop MS than men, with at least twice a higher prevalence that can reach 3 or 4 females to 1 male in some countries [4].

The exact aetiology of MS is unknown. Pathogenic mechanisms underlying its development have yet to be identified. It involves complex interactions between individual genetic susceptibility and environmental factors. The genetic contribution could explain only 20% to 30% of MS heritability [5]. The remainder is likely due to environmental risk factors or genetic--environment interactions [6]. The risk factors include vitamin D deficiency [7], low sunlight exposure [8], Epstein-Barr virus seropositivity [9], infectious mononucleosis [10], smoking [11], and obesity [12].

Living with MS impacts patients' quality of life (QoL) by interfering with the ability to work, pursue leisure activities, and undertake daily life tasks [13]. Health-related quality of life (HRQoL) is a narrower concept. It is defined by the Centre for Disease Control and Prevention (CDC) as "an individual's or group's perceived physical and mental health over time" [14]. The construct of HRQoL is subjective and includes physical and occupational functions, and psychological and social domains [15]. In recent decades, HRQoL measurements are becoming increasingly important to evaluate disease progression, treatment response, and level of assistance required by MS patients [16]. It can help clinicians improve knowledge about the determinants of QoL changes and their potential predictive role on disability. Clinicians can assess QoL to check whether interventions have been as effective from the patient's point of view as from the clinician's and to determine whether further action is needed. In practice, MS--specific questionnaires are more appropriate due to a better ability to discern QoL differences in patients than the 36-item short form which is a generic instrument [17]. Several disease-specific QoL measures have been validated for MS patients, including the MS International QoL (MusiQoL) questionnaire [18]. It is a well-validated MS-specific, self-administered, multidimensional, patient-based HRQoL instrument, which assesses different MS-related domains: activities of daily living, psychological well-being, symptoms, relationships, sentimental and sexual life, coping, and rejection [19].

In Lebanon, the prevalence of MS was found to be 62.91 people per 100 000 people classifying it as a moderate to the high-risk area for MS [20]. Few studies examined predictors of RRMS and MS patients' HRQoL. Identification of predictors that reduce QoL can help determine which action has more impact, particularly due to the recent prioritization of treatments recently [21]. Therefore, this study aims primarily to identify the risk factors of RRMS and to assess its impact on patients' HRQoL.

Patients and methods

Study design

This observational case-control study was performed over three months (August to October 2021). Cases were selected from patients visiting two neurology clinics in Beirut, Lebanon, and controls were randomly selected from the general population with a case: control ratio of 1:3. The scheme of this study maintained the total anonymity and confidentiality of the participants. Written informed consent was obtained from both physicians and participants before starting the data collection.

Study population

Lebanese MS patients of both genders were included in this study if they (1) were above 18 years; (2) had a confirmed RRMS diagnosis according to the 2010 McDonald diagnostic Criteria [22], and (3) were maintained on a disease-modifying treatment for at least 3 months. Matched controls were randomly selected from patients visiting different community pharmacies in Beirut during the same study period. Patients who were previously diagnosed with any other neurological disease or cancer, those with any cognitive impairment, or were pregnant were excluded from the study.

Data collection

Data were collected using a structured questionnaire in face-to-face interviews. The medical information was retrieved from the patients 'medical charts. The questionnaire was administered in Arabic, the official language in Lebanon, and included four parts: (1) socio-demographic characteristics including sex, age, body mass index, marital status, educational level and monthly income; (2) lifestyle data such as smoking status, caffeinated drinks and alcohol consumption, involvement in sports activities and work status; (3) past medical history and MS clinical data related to the onset of MS [duration of disease, number of relapses, incomplete recovery between relapses, expanded disability status scale (EDSS) and medications]; (4) MS-related complications and other co-morbidities (cardiovascular diseases, diabetes mellitus, psychological disorders, family history of

MS, vitamin D deficiency, infectious mononucleosis, childhood and adolescent obesity).

Quality of life assessment

Quality of life of MS patients was assessed using an Arabic version of the MusiQoL questionnaire (version 5.4) [19] after obtaining approval from the publisher. This questionnaire is shorter than other similar tools and its psychometric properties have been assessed in the Lebanese population [23]. It consists of 31 items describing nine dimensions of HRQoL that are specific to MS patients: Activities of daily living (ADL), Psychological well-being (PWB), Symptoms (SPT), Relationships with friends (RFriends), Relationships with family (RFamily), Sentimental and sexual life (SSL), Coping (COP), Rejection (Reject) and relationship with the healthcare system (RHealth). The global index "MusiQol index" is calculated from these nine-dimension scores. The nine dimensions scores and the global index are linearly transformed and standardized on a 0–100 scale. A higher score indicates a better HRQoL. The English version of the MusiQoL is known to have good reliability, with Cronbach's alpha coefficients (a) ranging from 0.68 to 0.92 [19].

Statistical analysis

The sample size was calculated using Epi Info 7, assuming a type I error of 5%, a study power of 80%, and a confidence interval of 95%. Previous literature provided a frequency of exposure of about 0.25 in the control group [24]. The minimal sample necessary to show a 2.5-fold increase in the risk of MS consisted of 55 cases and 163 controls with a case/control ratio of 1:3. Data were entered and analysed using Statistical Package for Social Sciences version 28 (SPSS Inc., Chicago, IL, USA). Data were normally distributed and converged to their expected values based on skewness and kurtosis [25]. Descriptive analyses were performed to present the distribution of the sociodemographic characteristics of the patients, their lifestyle behaviours, and their medical history. Categorical variables were presented in frequencies and percentages, while continuous variables were presented using means and standard deviations. Bivariate and multivariate analyses were conducted to identify the risk factors of MS using MS as the dependent variable. Bivariate analysis of qualitative variables was done using the chi-square test or Fisher exact test. However, the effect of quantitative variables was determined using the student T-test. In addition, a forward logistic regression was performed and included all the independent variables with p-values < 0.2 in the bivariate model. The Hosmer-Lemeshow test and omnibus test checked the model adequacy.

Similarly, a bivariate analysis was conducted for the global index score and each of the MusiQoL dimension scores. For continuous variables, Pearson's correlation test was used. For categorical variables, the student T-test or ANOVA in case of a normal distribution and equality of variances were used; however, in case one of these two conditions is not satisfied, the Mann-Whitney U test or Kruskal-Wallis H test was used. Multivariate analysis using linear regression was carried out for the MusiQol index and its nine dimensions to determine predictive factors affecting the HRQoL. Conditions of normality, linearity and homoscedasticity were checked. A p-value < 0.05 was considered significant in all tests.

Results

Socio-demographic characteristics of the study population

Three hundred patients were recruited, of whom 75 were diagnosed with RRMS and 225 were controls. The characteristics of the study population are described in Table 1. Most participants were females in both MS and control groups (74.7% and 57.3% respectively, $p = 0.009$). The ratio of males/females in the MS group was approximately 1:3. Significant differences were observed in terms of age ($p = 0.039$) and BMI classes ($p = 0.033$). The percentages of participants aged between 31–40 and overweight individuals were significantly higher in the MS group (33.3% and 44.0% respectively) than in the control group (18.7% and 31.6% respectively). No significant differences were found between cases and controls regarding marital status, education, and monthly income ($p > 0.05$).

Lifestyle characteristics

Table 2 shows that MS patients were more likely to be passive smokers ($p = 0.001$), waterpipe smokers ($p = 0.004$), moderate or heavy waterpipe smokers ($p = 0.015$), and moderate or heavy cigarette smokers ($p = 0.003$) with significantly higher percentages. A significant difference was seen in those control participants practising sport ($p = 0.005$), the frequency and the duration of sport/week ($p = 0.005$ and $p = 0.011$ respectively). Alcohol consumption, intake of caffeinated drinks, and shift work showed no significant differences.

Medical history

Compared with controls, MS patients were significantly more likely to have cardiovascular problems

Table 1. Multiple sclerosis and related sociodemographic characteristics

Characteristics	Cases [n (%)] n = 75	Controls [n (%)] n = 225	p-value*
Gender			
Male	19 (25.3%)	96 (42.7%)	**0.009**
Female	56 (74.7%)	129 (57.3%)	
Age class [years]			
18–30	25 (33.3%)	100 (44.4%)	
31–40	25 (33.3%)	42 (18.7%)	**0.039**
41–50	9 (12.0%)	40 (17.8%)	
> 50	16 (21.3%)	43 (19.1%)	
BMI class			
Underweight	0 (0.0%)	6 (2.7%)	
Normal	30 (40.0%)	125 (55.6%)	**0.033***
Overweight	33 (44.0%)	71 (31.6%)	
Obese	12 (16.0%)	23 (10.2%)	
Marital status			
Single	20 (26.7%)	73 (32.4%)	0.213
Married	50 (66.7%)	146 (64.9%)	
Divorced/widowed	5 (6.7%)	6 (2.7%)	
Educational level			
Illiterate	12 (16.0%)	22 (9.8%)	
Primary/Elementary	3 (4.0%)	27 (12.0%)	0.073
Secondary	39 (52.0%)	99 (44.0%)	
University	21 (28.0%)	77 (34.2%)	
Monthly income			
< 675 000 LP	0 (0.0%)	8 (3.6%)	
675 000–1 million LP	4 (5.3%)	28 (12.4%)	0.102
1 million–2 million LP	42 (56.0%)	107 (47.6%)	
> 2 million LP	29 (38.7%)	82 (36.4%)	

*p-values in bold are significant; BMI — body mass index; LP — Lebanese pound

(p = 0.002), psychological disorders (p < 0.001), vitamin D deficiency (p < 0.001), and adolescent obesity (p = 0.002). However, family history of MS, childhood obesity and past medical history of infectious mononucleosis were not statistically significant between the two groups (Table 3).

Clinical characteristics of multiple sclerosis patients

At the time of the study, MS patients had a mean disease duration of 59.52 ± 48.2 months and a mean EDSS of 1.65 ± 1.3. The mean age at the onset of MS was 32.68 ± 10.42 years with a peak at 22–40 years old. Around half of the patients experienced 2–5 relapses (50.7%) and reported incomplete recovery between relapses (56%). As for MS therapies, all patients maintained Disease Modifying Therapies (DMTs) with 62.7% on interferon beta (INF-β), 20% on Rituximab, and 16% on Fingolimod (Table 4).

Health-related quality of life score

Figure 1 represents the mean ± SD for the MusiQoL index and the nine dimensions of this score. The overall index was 72.95 ± 14.35 out of a possible 100. Patients' HRQoL was most impaired in the RFriends dimension followed by PWB and ADL dimensions, and the least impaired in the RHealth dimension.

Variables associated with health-related quality of life

The MusiQoL score was highly significantly associated with several sociodemographic, lifestyle, and clinical variables (Supplementary Table A1 and A2). Younger age (p = 0.001), employment (p < 0.001), sports activity (p < 0.001), a higher monthly income (> 2 million LBP) or higher education (p < 0.001), and a decreasing number of relapses (p < 0.001) were significantly associated with higher HRQoL. Reduced HRQoL was significantly associated with incomplete recovery between relapses (p < 0.001), concomitant physical comorbidity (p < 0.001), psychological disorder (p = 0.001), higher EDSS (p < 0.001), and higher disease duration (p < 0.001).

As for gender, women scored higher on the RFriends dimension (p = 0.014) than men, while men scored higher on the PWB (p < 0.001) and COP (p = 0.046)

Table 2. Multiple sclerosis and related lifestyle characteristics

Characteristics	Cases [n (%)] n = 75	Controls [n (%)] n = 225	p-value*
Active smoking			
No	33 (44.0%)	133 (59.1%)	**0.023**
Yes	42 (56.0%)	92 (40.9%)	
Cigarette smokers			
Light smokers	0 (0.0%)	20 (33.3%)	**0.003**
Moderate smokers	5 (25.0%)	13 (21.7%)	
Heavy smokers	15 (75.0%)	27 (45.0%)	
Waterpipe smokers			
Light smokers	0 (0.0%)	8 (21.1%)	**0.015**
Moderate smokers	13 (56.5%)	18 (47.4%)	
Heavy smokers	10 (43.5%)	12 (31.5%)	
Passive smoking			
No	18 (24.0%)	105 (46.7%)	**0.001**
Yes	57 (76.0%)	120 (53.3%)	
Alcohol drinking			
No	71 (94.7%)	203 (90.2%)	0.444
Yes	3 (4.0%)	19 (8.4%)	
Ex-alcoholic	1 (1.3%)	3 (1.3%)	
Intake of caffeinated drinks			
No	9 (12.0%)	18 (8.0%)	0.295
Yes	66 (88.0%)	207 (92.0%)	
Sport activity			
No	59 (78.7%)	136 (60.4%)	**0.005**
Yes	16 (21.3%)	89 (39.6%)	
Sport [times/week]			
0	59 (78.7%)	136 (60.4%)	**0.005**
< 5	15 (20%)	65 (28.9%)	
≥ 5	1 (1.3%)	24 (10.7%)	
Duration of sport/week [min]			
0	59 (78.7%)	136 (60.4%)	**0.011**
< 150	6 (8.0%)	47 (20.9%)	
≥ 150	10 (13.3%)	42 (18.7%)	
Shift work			
No	68 (90.7%)	210 (93.3%)	0.443
Yes	7 (9.3%)	15 (6.7%)	

*p-values in bold are significant

dimensions. Marital status was significantly associated with ADL ($p = 0.021$) and PWB ($p = 0.020$) dimensions. Smoking cigarettes and waterpipe use were significantly associated with reduced scores in RFriends and ADL respectively ($p = 0.010$). However, alcohol consumption was not statistically significant when associated with the MusiQoL score. Contrarily, the intake of caffeinated drinks showed significantly higher scores in the ADL dimension ($p = 0.033$). Sports activity was associated with increased considerably ADL ($p < 0.001$), PWB ($p = 0.005$) and other dimensions except for COP and SPT.

Furthermore, EDSS, disease duration and the number of relapses were negatively correlated with approximately all dimensions ($p < 0.005$). Patients with psychological disorders or physical comorbidity reported lower scores in some dimensions such as ADL ($p = 0.004$, $p < 0.001$ respectively), SSL ($p = 0.006$, $p = 0.001$ respectively) and reject ($p = 0.042$, $p = 0.040$ respectively). Significant differences in the ADL ($p = 0.038$) and RFriends ($p = 0.039$) dimensions were noted between different prescribed DMTs.

Predictors of multiple sclerosis

Table 5 displays the predictors of RRMS performed on all cases and controls. Vitamin D deficiency (ORa = 8.09; $p< 0.001$), heavy cigarette smoking (in comparison with non-smokers; ORa = 5.24, $p = 0.001$), moderate (ORa = 3.58; $p = 0.013$) and heavy (ORa = 4.06; $p = 0.013$) waterpipe smoking (in comparison with non-smokers), passive smoking (ORa = 2.56; $p = 0.010$), psychological

Table 3. Multiple sclerosis and health-related variables

Variables	Cases [n (%)] n = 75	Controls [n (%)] n = 225	p-value*
Cardiovascular problems			**0.002**
No	62 (82.7%)	211 (94.2%)	
Yes	13 (17.3%)	13 (5.8%)	
Psychological disorders			**< 0.001**
No	54 (72.0%)	219 (97.8%)	
Yes	21 (28.0%)	5 (2.2%)	
Family history of MS			0.190
No	69 (92.0%)	216 (96.0%)	
Yes	6 (8.0%)	9 (4.0%)	
Vitamin D deficiency			**< 0.001**
No	18 (24.0%)	138 (61.3%)	
Yes	57 (76.0%)	87 (38.7%)	
Infectious mononucleosis			0.438
No	75 (100%)	224 (99.6%)	
Yes	0 (0%)	1 (0.4%)	
Childhood obesity			0.623
No	68 (90.7%)	208 (92.4%)	
Yes	7 (9.3%)	17 (7.6%)	
Adolescent obesity			**0.002**
No	58 (77.3%)	205 (91.1%)	
Yes	17 (22.7%)	20 (8.9%)	

MS — multiple sclerosis; Additional non-significant variables (p-value > 0.05): hypertension (p-value = 0.079); dyslipidaemia (p-value = 0.321); diabetes (p-value = 0.100); arthritis (p-value =1.0); respiratory disease (p-value = 0.306); p-values in bold are significant

Table 4. Clinical characteristics of multiple sclerosis patients (n = 75)

Characteristics		N (%)
Age at onset [years]	19–30	37 (49.3%)
	31–40	22 (29.3%)
	41–50	12 (16.0%)
	> 50	4 (5.3%)
Number of relapses	1	23 (30.7%)
	2–5	38 (50.7%)
	> 5	13 (17.3%)
Incomplete recovery between relapses	No	33 (44%)
	Yes	42 (56%)
Current DMTs	Interferon β	47 (62.7%)
	Fingolimod	12 (16.0%)
	Rituximab	15 (20.0%)
	Cladribine	1 (1.3%)
Characteristics		**Mean ± SD**
Disease duration in months		59.52 ± 48.2
EDSS		1.65 ± 1.3

DMTs — disease-modifying therapies, EDSS — expanded disability status scale

disorders (ORa = 5.47; p = 0.001), and cardiovascular disease (ORa = 4.47; p = 0.006) were the variables significantly associated with RRMS.

Predictors of the MusiQoL score

In the multivariable linear regression (Table 6) estimating the overall MusiQoL Index, results showed that "incomplete recovery between relapses" was the most significant predictor of the MusiQoL index (β = –8.93, p = 0.001). The higher number of relapses (β = –1.65, p = 0.004) or psychological disorders (β = = –7.73, p = 0.002) were also inversely correlated to the MusiQoL index. Moreover, higher monthly income (> 2 million LBP, compared with lower income of < 2 million LBP) (β = 7.29, p = 0.002), and sports activity (β = 6.59, p = 0.015) were associated with a higher overall HRQoL score.

While estimating the dimensions of MusiQoL, sports activity (β = 8.02, p = 0.023) was positively associated with the ADL dimension. However, higher EDSS (β = –8.57, p < 0.001), a higher number of relapses (β = –2.78, p = 0.002), incomplete recovery between relapses (β = –13.47, p < 0.001), having psychological disorder (β = –7.36, p = 0.022) and taking Fingolimod (compared to INF-β) (β = –14.23, p < 0.001) were inversely related to ADL. However, the PWB dimension was inversely associated with a psychological disorder and incomplete recovery between relapses (β = –18.17, p < 0.001; β = –8.79, p = 0.019 respectively), and positively associated

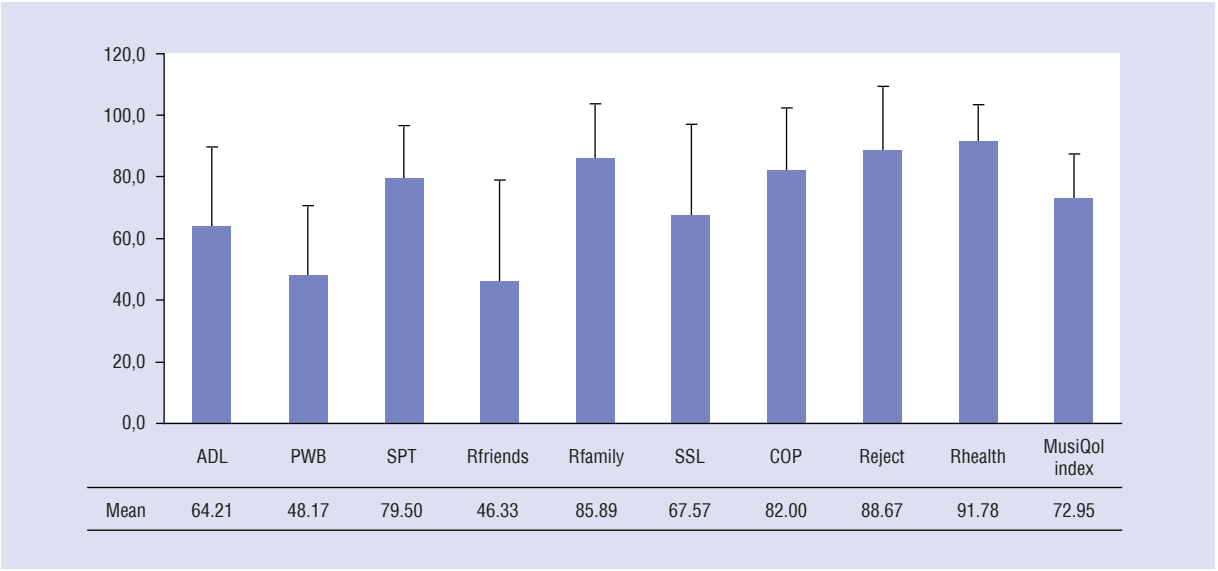

Figure 1. Mean with a standard deviation of the nine dimensions and the overall score of the MusiQoL
ADL — activities of daily living; PWB — psychological wellbeing; SPT — symptoms; RFriends — relationships with friends; RFamily — relationships with family; SSL — sentimental and sexual life; COP — coping; reject — rejection; RHealth — relationship with healthcare system; SD — standard deviation

Table 5. Multiple sclerosis risk factors in the study Lebanese population

Predictors	ORa	CI (95%)	p-value
Vitamin D deficiency	8.09	3.71; 17.62	< 0.001
Heavy cigarette smokers	5.24	1.90; 14.40	0.002
Moderate waterpipe smokers	3.58	1.33; 9.83	0.013
Heavy waterpipe smokers	4.06	1.43; 12.18	0.013
Passive smoking	2.56	1.25; 5.25	0.010
Cardiovascular disease	4.47	1.52; 13.16	0.006
Psychological disorder	5.47	2.10; 14.27	0.001

ORa — adjusted odds ratio, CI — confidence interval

with sport activity ($\beta = 9.37$, $p = 0.038$) and gender ($\beta = 22.55$, $p < 0.001$).

As for the SPT dimension, factors such as high monthly income (> 2 million LBP) increased the dimension ($\beta = 11.21$, $p = 0.004$), while being overweight or obese decreased it ($\beta = -7.51$, $p = 0.017$). When examining the RFriends and RFamily dimensions, higher education level was positively associated with these two dimensions. Thus, incomplete recovery between relapses ($\beta = -10.49$, $p = 0.005$) and overweight or obesity ($\beta = -10.26$, $p = 0.005$) affected RFamily negatively. However, RFriends are inversely proportional to the number of relapses ($\beta = -5.59$, $p < 0.001$).

A strong inverse association is noted between EDSS ($\beta = -12.74$, $p < 0.001$) and the SSL dimension. This dimension is also decreased with psychological disorders ($\beta = -14.18$, $p = 0.004$), incomplete recovery between relapses ($\beta = -14.34$, $p = 0.001$) and smoking cigarettes ($\beta = -12.26$, $p = 0.038$). When exploring the COP dimension, only incomplete recovery between relapses ($\beta = -11.85$, $p = 0.011$) was found to be a predictor; those who have complete recovery have higher coping scores. For the Reject dimension, predictors were: the number of relapses, having a partner, sports activity and incomplete recovery between relapses. Finally, the higher EDSS ($\beta = -2.64$, $p = 0.009$) and incomplete recovery between relapses ($\beta = -6.36$, $p = 0.018$) negatively affect the RHealth dimension.

Discussion

The objectives of this study were to identify the risk factors of RRMS and to assess predictive factors of HRQoL in RRMS Lebanese patients. This study showed that vitamin D deficiency, cardiovascular disease, psychological disorder, active smoking, and

Table 6. Predictors of the MusiQoL score and its dimensions in the study Lebanese population

	Predictors	Unstandardized β	Standardized β	CI (95%)	p-value
MUSIQOL	Number of relapses	–1.65	–0.27	–2.75; –0.55	0.004
	Incomplete recovery between relapses	–8.93	–0.31	–13.89; –3.97	0.001
	Psychological disorders	–7.73	–0.25	–12.58; –2.88	0.002
	Monthly income (> 2 million LP)	7.29	0.25	2.80; 11.78	0.002
	Sport activity	6.59	0.19	1.31; 11.88	0.015
ADL	EDSS	–8.57	–0.45	–11.10; –6.04	< 0.001
	Incomplete recovery between relapses	–13.47	–0.26	–20.24; –6.89	< 0.001
	Number of relapses	–2.78	–0.25	–4.47; –1.08	0.002
	Taking fingolimod/INF-β	–10.23	–0.16	–18.77; –3.69	< 0.001
	Psychological disorder	–7.36	–0.13	–13.61; –1.12	0.022
	Sport activity	8.02	0.13	1.14; 14.90	0.023
PWB	Gender	22.55	0.44	14.21; 30.88	< 0.001
	Psychological disorders	–18.17	–0.37	–26.39; –9.95	< 0.001
	Incomplete recovery between relapses	–8.79	–0.19	–16.07; –1.51	0.019
	Sport activity	9.37	0.17	0.53; 18.22	0.038
SPT	Monthly income	11.21	0.32	3.80; 18.62	0.004
	Overweight or obese	–7.51	–0.22	–14.84; –0.188	0.045
RFriends	Education (university)	30.64	0.42	16.98; 44.31	<0.001
	Number of relapses	–5.59	–0.39	–8.23; –2.95	< 0.001
RFamily	Incomplete recovery between relapses	–10.49	–0.29	–17.08; –3.35	0.005
	Overweight or obese	–10.26	–0.28	–17.39; –3.13	0.005
	Education (university)	9.36	0.24	1.17; 17.55	0.026
SSL	EDSS	–12.74	–0.53	–17.82; –7.67	< 0.001
	Incomplete recovery between relapses	–14.34	–0.24	–25.36; –3.32	0.001
	Psychological disorder	–14.18	–0.18	–26.62; –2.74	0.004
	Smoking cigarette	–12.26	–0.18	–23.78; –0.73	0.038
COP	Incomplete recovery between relapses	–11.85	–0.29	–20.85; –2.95	0.011
Reject	Number of relapses	–2.94	–0.33	–4.76; –1.11	0.007
	Having a partner	18.86	0.44	11.90; 26.93	< 0.001
	Sport activity	12.15	0.24	2.87; 21.28	0.011
	Incomplete recovery between relapses	–9.24	–0.22	–17.57; –0.91	0.030
RHealth	EDSS	–2.64	–0.35	–4.59; –0.69	0.009
	Incomplete recovery between relapses	–6.36	–0.27	– 11.61; –1.11	0.018

ADL — activities of daily living; PWB — psychological wellbeing; SPT — symptoms; RFriends — relationships with friends; RFamily — relationships with family; SSL — sentimental and sexual life; COP — coping; reject — rejection; RHealth — relationship with healthcare system; EDSS — expanded disability status scale; LP — Lebanese pound; INF-β — interferon beta; CI — confidence interval

exposure to passive smoking were associated with an increased risk of RRMS. In addition, the association between smoking and MS seems to be dose-dependent because heavy waterpipe smokers have a higher risk than moderate waterpipe smokers. The present results are concordant with those of other studies that identified smoking [11] and vitamin D deficiency [7] as risk factors for MS. There was no clear indication of cardiovascular and psychological diseases being risk factors for RRMS, but as these comorbidities are common in MS patients, further investigation is needed. The present results confirm in part the findings of the

pilot study conducted in Lebanon [26] showing that MS patients had higher Epstein-Barr virus seropositivity, lower vitamin D levels, and were more likely to be overweight and heavy smokers.

This study showed that there is a female predominance versus male in the MS group which is consistent with the literature [4]. However, the female sex was not significantly associated with MS in multivariate analysis, possibly because the percentage of females was also high in the control group.

In contrast with other studies that have suggested a higher risk of MS associated with a family history of MS [27], shift work [28], infectious mononucleosis [10], childhood and adolescent obesity [29, 30], no role of these variables in predicting the risk of MS was observed. The present results may not truly indicate the effect of infectious mononucleosis on the risk of MS because the authors relied on the memory of patients in this question without performing the confirmation test. Moreover, this study showed that several socio-demographic, lifestyle and clinical characteristics were significant predictors of HRQoL. In the present study, the MusiQoL survey was used which is a valid tool for the assessment of the HRQoL of MS patients in Lebanon [23]. Results of the linear regression reported that more relapses and incomplete recovery between them, linked to disease severity, and psychological disorders affect HRQoL negatively, while high income and sports activity have a positive impact on HRQoL. These findings are in agreement with previous studies concerning disease severity [31], income, sports activity [32], and psychological comorbidity. In addition, depression has frequently emerged as one of the most important predictors of QoL [33].

Furthermore, EDSS score and gender were significantly associated with a worse MusiQoL index in some dimensions, which is in line with previous studies [23, 34]. Thus, MS had less impact on males' PWB. Research showed higher morbidity among women due to acute and chronic physical and mental health conditions [35], which could explain this finding. A similar study conducted among primary care patients with multimorbidity also reported a higher HRQoL among men than women [36].

The present results also showed that a BMI of > 25 kg/m^2 (overweight or obese) was associated with a worse QoL in the SPT and RFamily dimensions. Obesity can make symptoms of MS more severe and harder to deal with, trigger more frequent relapses and also accelerate the progression of MS towards increasing disability [30]. As for DMTs, the use of fingolimod (in comparison with INF-β) was significantly associated with the worsening of ADL. However, in the PERFORMS study [37], fingolimod showed a greater positive effect than the other DMTs on the ADL dimension. Therefore, further investigation is needed. No role of age or disease duration in the prediction of QoL was found. Previous studies have reported contradictory results with regard to their influence. D'Alisa et al. [38] reported that age and disease duration were not found to be significant determinants of HRQoL. However, older age was significantly correlated with a worse HRQoL in previous studies [34, 39], and the duration of illness was impacting most of the dimensions in a longitudinal study [39].

This study has several strengths. First, to the authors' knowledge, this is the first study that assesses the impact of lifestyle characteristics in addition to other sociodemographic and clinical characteristics on the QoL of MS patients in Lebanon. A second strong point of the study is the use of the MusiQoL questionnaire, which is specific for MS and is much shorter than many other MS-specific instruments. Thirdly, the use of a control group in the assessment of risk factors of MS added value to the present results. Some limitations can be pointed out in this study. Data was collected from an outpatient clinic and did not consider inpatients. Furthermore, MS patients were identified from two clinics located in Beirut, and thus, the study may represent mainly the RRMS patients living in Beirut. There could also be a possibility of recall bias by participants during data collection. Social desirability bias might have influenced responses. Respondents may provide socially acceptable responses.

Conclusions

Multiple sclerosis is a multifactorial disease with both environmentally acquired and genetic-related risk factors. In addition to its clinical and economic consequences, MS can affect patients' HRQoL.

The present study confirmed that moderate waterpipe smoking or heavy smoking (cigarette and waterpipe), passive smoking, vitamin D deficiency, and the presence of cardiovascular diseases or psychological disorders are risk factors for MS. Identifying MS risk factors is crucial to initiate awareness about this disabling disease among the Lebanese population especially that MS is associated with a considerable effect on the patients' HRQoL. Moreover, this study showed that incomplete recovery between relapses, a higher number of relapses, and psychological disorders, hurt MS patients' HRQoL, whereas, high income and sports activity were associated with increased HRQoL, concluding that HRQoL should be assessed regularly and frequently in RRMS patients and predictor factor should be taken into consideration in further studies.

Acknowledgements

A special thanks to Dr MZ for the language assistance and her valuable support to obtain MusiQoL approval from the publisher.

Authors' contributions

HN and SA contributed to the conception and design of the work and prepared the first draft. RAT, SN, and HN acquired the data. HN, RAJ, and GH contributed to the interpretation of the data and statistical analysis. ME and SZ provided critical revision for methodology. HN, GH and SA finalized and approved the final version of the manuscript. All authors reviewed the manuscript and approved the final version of the article.

Declaration of conflict of interests

The authors declare that there is no conflict of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Huang WJ, Chen WW, Zhang X. Multiple sclerosis: pathology, diagnosis and treatments. Exp Ther Med. 2017; 13(6): 3163–3166, doi: 10.3892/etm.2017.4410, indexed in Pubmed: 28588671.
2. Wallin MT, Culpepper WJ, Nichols E. GBD 2016 Neurology Collaborators. Global, regional, and national burden of multiple sclerosis 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019; 18(3): 269–285, doi: 10.1016/S1474-4422(18)30443-5, indexed in Pubmed: 30679040.
3. Dendrou CA, Fugger L, Friese MA. Immunopathology of multiple sclerosis. Nat Rev Immunol. 2015; 15(9): 545–558, doi: 10.1038/nri3871, indexed in Pubmed: 26250739.
4. Walton C, King R, Rechtman L, et al. Rising prevalence of multiple sclerosis worldwide: Insights from the Atlas of MS, third edition. Mult Scler. 2020; 26(14): 1816–1821, doi: 10.1177/1352458520970841, indexed in Pubmed: 33174475.
5. Zuvich RL, McCauley JL, Pericak-Vance MA, et al. Genetics and pathogenesis of multiple sclerosis. Semin Immunol. 2009; 21(6): 328–333, doi: 10.1016/j.smim.2009.08.003, indexed in Pubmed: 19775910.
6. Nourbakhsh B, Mowry EM. Multiple sclerosis risk factors and pathogenesis. Continuum (Minneap Minn). 2019; 25(3): 596–610, doi: 10.1212/CON.0000000000000725, indexed in Pubmed: 31162307.
7. Mokry LE, Ross S, Ahmad OS, et al. Vitamin d and risk of multiple sclerosis: a mendelian randomization study. PLoS Med. 2015; 12(8): e1001866, doi: 10.1371/journal.pmed.1001866, indexed in Pubmed: 26305103.
8. Hedström AK, Olsson T, Kockum I, et al. Low sun exposure increases multiple sclerosis risk both directly and indirectly. J Neurol. 2020; 267(4): 1045–1052, doi: 10.1007/s00415-019-09677-3, indexed in Pubmed: 31844981.
9. Salvetti M, Giovannoni G, Aloisi F. Epstein-Barr virus and multiple sclerosis. Curr Opin Neurol. 2009; 22(3): 201–206, doi: 10.1097/WCO.0b013e32832b4c8d, indexed in Pubmed: 19359987.
10. Nielsen TR, Rostgaard K, Nielsen NM, et al. Multiple sclerosis after infectious mononucleosis. Arch Neurol. 2007; 64(1): 72–75, doi: 10.1001/archneur.64.1.72, indexed in Pubmed: 17210811.
11. Handel AE, Williamson AJ, Disanto G, et al. An updated meta-analysis of risk of multiple sclerosis following infectious mononucleosis. PLoS One. 2010; 5(9): e16149, doi: 10.1371/journal.pone.0012496, indexed in Pubmed: 20824132.
12. Mokry LE, Ross S, Timpson NJ, et al. Obesity and multiple sclerosis: a mendelian randomization study. PLoS Med. 2016; 13(6): e1002053, doi: 10.1371/journal.pmed.1002053, indexed in Pubmed: 27351487.
13. Zwibel HL, Smrtka J. Improving quality of life in multiple sclerosis: an unmet need. Am J Manag Care. 2011; 17 Suppl 5 Improving: S139–S145, indexed in Pubmed: 21761952.
14. Control CfD, Prevention. Measuring healthy days: Population assessment of health-related quality of life 2001.
15. Testa MA, Simonson DC. Assessment of quality-of-life outcomes. N Engl J Med. 1996; 334(13): 835–840, doi: 10.1056/NEJM199603283341306, indexed in Pubmed: 8596551.
16. Lysandropoulos AP, Havrdova E. ParadigMS Group. 'Hidden' factors influencing quality of life in patients with multiple sclerosis. Eur J Neurol. 2015; 22 Suppl 2: 28–33, doi: 10.1111/ene.12801, indexed in Pubmed: 26374511.
17. Freeman JA, Hobart JC, Thompson AJ. Does adding MS-specific items to a generic measure (the SF-36) improve measurement? Neurology. 2001; 57(1): 68–74, doi: 10.1212/wnl.57.1.68, indexed in Pubmed: 11445630.
18. Baumstarck K, Boyer L, Boucekine M, et al. Measuring the quality of life in patients with multiple sclerosis in clinical practice: a necessary challenge. Mult Scler Int. 2013; 2013: 524894, doi: 10.1155/2013/524894, indexed in Pubmed: 23533758.
19. Simeoni Mc, Auquier P, Fernandez O, et al. Validation of the multiple sclerosis international quality of life questionnaire. Mult Scler. 2008; 14(2): 219–230, doi: 10.1177/1352458507080733, indexed in Pubmed: 17942521.
20. Zeineddine M, Hajje A, Ayoubi N, et al. Prevalence and incidence rates of multiple sclerosis in lebanon. Mult Sclerosis Rel Disord. 2020; 37: 101608, doi: 10.1016/j.msard.2019.11.083.
21. Hatem G, Goossens MM. Health care system in Lebanon: a review addressing health inequalities and ethical dilemmas of frontline workers during COVID-19 pandemic. BAU J — Health Well-Being. 2022; 5(1), doi: 10.54729/yvaa4887.
22. Polman CH, Reingold SC, Banwell B, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. Ann Neurol. 2011; 69(2): 292–302, doi: 10.1002/ana.22366, indexed in Pubmed: 21387374.
23. Farran N, Safieddine BR, Bayram M, et al. Factors affecting MS patients' health-related quality of life and measurement challenges in Lebanon and the MENA region. Mult Scler J Exp Transl Clin. 2020; 6(1): 2055217319848467, doi: 10.1177/2055217319848467, indexed in Pubmed: 31976081.
24. El-Muzaini H, Akhtar S, Alroughani R, et al. A matched case-control study of risk factors associated with multiple sclerosis in Kuwait. BMC Neurol. 2020; 20(1): 64, doi: 10.1186/s12883-020-01635-1, indexed in Pubmed: 32085743.
25. Hatem G, Zeidan J, Goossens M, et al. Normality testing methods and the importance of skewness and kurtosis in

statistical analysis. BAU J - Sci Technology. 2022; 3(2), doi: 10.54729/ktpe9512.
26. Mouhieddine TH, Darwish H, Fawaz L, et al. Risk factors for multiple sclerosis and associations with anti-EBV antibody titers. Clin Immunol. 2015; 158(1): 59–66, doi: 10.1016/j.clim.2015.03.011, indexed in Pubmed: 25805657.
27. Al-Afasy HH, Al-Obaidan MA, Al-Ansari YA, et al. Risk factors for multiple sclerosis in Kuwait: a population-based case-control study. Neuroepidemiology. 2013; 40(1): 30–35, doi: 10.1159/000341240, indexed in Pubmed: 23075770.
28. Hedström AK, Åkerstedt T, Olsson T, et al. Shift work influences multiple sclerosis risk. Mult Scler. 2015; 21(9): 1195–1199, doi: 10.1177/1352458514563592, indexed in Pubmed: 25698167.
29. Hedström AK, Lima Bomfim I, Barcellos L, et al. Interaction between adolescent obesity and HLA risk genes in the etiology of multiple sclerosis. Neurology. 2014; 82(10): 865–872, doi: 10.1212/WNL.0000000000000203, indexed in Pubmed: 24500647.
30. Oliveira SR, Simão AN, Kallaur AP, et al. Disability in patients with multiple sclerosis: influence of insulin resistance, adiposity, and oxidative stress. Nutrition. 2014; 30(3): 268–273, doi: 10.1016/j.nut.2013.08.001, indexed in Pubmed: 24484677.
31. Stojanov A, Malobabic M, Milosevic V, et al. Psychological status of patients with relapsing-remitting multiple sclerosis during coronavirus disease-2019 outbreak. Mult Scler Relat Disord. 2020; 45: 102407, doi: 10.1016/j.msard.2020.102407, indexed in Pubmed: 32702641.
32. Jelinek GA, De Livera AM, Marck CH, et al. Lifestyle, medication and socio-demographic determinants of mental and physical health-related quality of life in people with multiple sclerosis. BMC Neurol. 2016; 16(1): 235, doi: 10.1186/s12883-016-0763-4, indexed in Pubmed: 27876009.
33. Berrigan LI, Fisk JD, Patten SB, et al. Health-related quality of life in multiple sclerosis: Direct and indirect effects of comorbidity. Neurology. 2016; 86(15): 1417–1424, doi: 10.1212/WNL.0000000000002564, indexed in Pubmed: 26962068.
34. Fernández O, Baumstarck-Barrau K, Simeoni MC, et al. MusiQoL study group. Patient characteristics and determinants of quality of life in an international population with multiple sclerosis: assessment using the MusiQoL and SF-36 questionnaires. Mult Scler. 2011; 17(10): 1238–1249, doi: 10.1177/1352458511407951, indexed in Pubmed: 21669936.
35. Carmel S. Health and well-being in late life: gender differences worldwide. Front Med (Lausanne). 2019; 6: 218, doi: 10.3389/fmed.2019.00218, indexed in Pubmed: 31649931.
36. Peters M, Potter CM, Kelly L, et al. Self-efficacy and health-related quality of life: a cross-sectional study of primary care patients with multi-morbidity. Health Qual Life Outcomes. 2019; 17(1): 37, doi: 10.1186/s12955-019-1103-3, indexed in Pubmed: 30764833.
37. Achiron A, Aref H, Inshasi J, et al. Effectiveness, safety and health-related quality of life of multiple sclerosis patients treated with fingolimod: results from a 12-month, real-world, observational PERFORMS study in the Middle East. BMC Neurol. 2017; 17(1): 150, doi: 10.1186/s12883-017-0913-3, indexed in Pubmed: 28784108.
38. D'Alisa S, Miscio G, Baudo S, et al. Depression is the main determinant of quality of life in multiple sclerosis: a classification-regression (CART) study. Disabil Rehabil. 2006; 28(5): 307–314, doi: 10.1080/09638280500191753, indexed in Pubmed: 16492625.
39. Baumstarck K, Pelletier J, Boucekine M, et al. MusiQoL study group. Predictors of quality of life in patients with relapsing-remitting multiple sclerosis: a 2-year longitudinal study. Rev Neurol (Paris). 2015; 171(2): 173–180, doi: 10.1016/j.neurol.2014.09.005, indexed in Pubmed: 25558798.