The Egyptian Rheumatologist xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

The Egyptian Rheumatologist

journal homepage: www.elsevier.com/locate/ejr

Original Article

Quality of life in Turkish patients with Familial Mediterranean Fever: Association with fatigue, psychological status, disease severity and other clinical parameters

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ARTICLE INFO

Article history:
Received 25 July 2017
Accepted 25 July 2017
Available online xxxx

Keywords:
Familial Mediterranean Fever
Quality of life
Fatigue
Depression
Disease severity

ABSTRACT

Aim of the work: To evaluate the quality of life (QoL) in Familial Mediterranean Fever (FMF) patients, and determine its association with fatigue, depression, disease severity and other clinical parameters. *Patients and methods:* Sixty FMF patients were included. QoL was assessed by Short Form-36 (SF-36), depression by Hamilton Depression Scale (HDS), and fatigue by Fatigue severity scale (FSS). Disease severity score and Mutations of the Mediterranean fever (MEFV) gene were assessed. *Results:* The mean age of patients was 33.73 ± 9.81 years and disease duration 14.6 ± 12.1 years. They were 35 females and 25 males. FMF patients scored significantly higher in FSS (29.9 ± 17.6) and HDS (15.1 ± 8.5) compared to the control (10.6 ± 7.1 and 6.3 ± 9.4; $p < 0.0001$ respectively) while all SF36 sub-items except mental health were significantly lower ($p < 0.05$). MEFV gene mutation was present in 49 (81.7%) patients. The visual analogue scale of pain significantly negatively correlated with the FSS ($p < 0.0001$), HDS ($p < 0.0001$) and all SF36 sub-items except mental health ($p < 0.0001$). Disease duration, age of onset, and duration of attacks showed no significant correlation with FSS, HDS and SF36. Delay in diagnosis significantly correlated with FSS ($p < 0.0001$) and negatively with SF36 sub-items physical role ($p = 0.02$), general health ($p = 0.01$) and social functioning ($p = 0.03$). Age of diagnosis significantly correlated with FSS ($p = 0.03$) and negatively with SF36-vitality ($p = 0.047$). There was a significant effect of disease severity on QoL, fatigue and depression ($p < 0.05$). *Conclusion:* QoL is associated with fatigue, depression and disease severity in FMF patients. It should be used in routine clinical evaluation as an outcome measure in FMF.

1. Introduction

Familial Mediterranean Fever (FMF) is an autoinflammatory disease with autosomal recessive inheritance, characterized by acute episodes of fever, peritonitis, pleuritis, arthritis, or erysipelas-like skin lesions [1]. It affects ethnic populations living at the Mediterranean basin [2]. It is common in Turkish, Armenian, Arabic and Sephardic Jewish populations [3]. It is caused by mutations in the Mediterranean fever (MEFV) gene [4] located on the short (p) arm of chromosome 16. It encodes pyrin. This protein is expressed mainly in myeloid and monocytic cells and modulates interleukin (IL)-1β processing, nuclear factor (NF)-kappa B activation and apoptosis. A mutated pyrin probably results in uncontrolled inflammation [5].

Fatigue is described as 'enduring, subjective sensation of generalized tiredness or exhaustion'. In healthy people, the phenomenon is of natural occurrence, but in the patients, it is considered as a lack of energy [6]. Fatigue is an important symptom in a wide variety of rheumatic disorders including rheumatoid arthritis (RA) [7], ankylosing spondylitis (AS) [8], psoriatic arthritis [9], systemic lupus erythematosus [10], Sjögren's syndrome [11]. Moreover, it is an important outcome for many patients with rheumatic diseases even though the cause of fatigue is not clearly known. However, various contributing factors are likely as disease activity [12], functional loss [13], pain [14], psychological status, poor sleep quality [15] and concomitant fibromyalgia [16]. Common patient complaints often reflect the relationship between pain and fatigue, for example, "The pain wears me down" or "When I am tired, I hurt all over" [14]. Medications which are used in the treatment of

Peer review under responsibility of Egyptian Society of Rheumatic Diseases.
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http://dx.doi.org/10.1016/j.ejr.2017.07.004
1110-1164/

Please cite this article in press as: Guler T et al. Quality of life in Turkish patients with Familial Mediterranean Fever: Association with fatigue, psychological status, disease severity and other clinical parameters. The Egyptian Rheumatologist (2017), http://dx.doi.org/10.1016/j.ejr.2017.07.004

rheumatic diseases are also suspected to cause fatigue [17]. On the other hand, Sternberg et al. [18] suggested that both inflammation and fatigue in rheumatic disorders might derive from dysregulation of hypothalamic-pituitary-adrenal axis.

The World Health Organization has defined quality of life (QoL) as "individuals' perceptions of their conditions in life, with regard to their objectives, expectations, norms and concerns, within the context of their own cultural and value systems" [19]. QoL is an outcome measure that is increasingly being used to evaluate health outcome in clinical studies of the patients with rheumatic diseases [20]. Rheumatic disorders, the most common cause of long term pain, also influence physical and social functioning and diminish QoL [21]. Few studies in the literature assessed the QoL in FMF patients. To the best of our knowledge, there is no study in the literature that evaluated fatigue in FMF patients. The objective of this study was to evaluate the impact of FMF on fatigue, psychological status and various QoL domains in terms of pain, social and emotional functioning as well as to determine the relationship between QoL, fatigue, depression, disease severity and clinical variables.

2. Patients and methods

A total of 60 consecutive patients fulfilling the criteria by Livneh et al. [22] for the diagnosis of FMF, who were admitted to the outpatient physical medicine and rehabilitation and rheumatology clinics were included in the study. Patients which have concomitant rheumatic diseases such as inflammatory bowel disease, Behçet's disease, AS, fibromyalgia and psychiatric diseases were excluded. Patient information regarding age, gender, disease duration, age of onset, age of diagnosis, delay of diagnosis, number of attacks per month, duration of attacks, family history for FMF, and MEFV mutation (retrospective data) was recorded. The symptoms of the patients including abdominal pain, chest pain, fever, arthritis, myalgia and erysipelas-like erythema were noted. Fatigue was assessed by using Fatigue severity scale (FSS) [23]. QoL was evaluated using Short Form-36 (SF-36) [24], and depression by Hamilton Depression Scale (HDS) [25]. Disease Severity Score, developed by Mor [26] was used for measuring disease severity. Severity of pain was measured using 100 mm Visual Analog Scale-Pain (VAS-pain)[27]. Control group consisted of 60 healthy subjects of matched age and sex. The study conforms to the provisions of the World Medical Association's Declaration of Helsinki. Written informed consent was obtained from all of the patients. The study protocol was approved by the Medical Research Ethics Committee.

Statistical Analysis: All analyses were performed using IBM Statistical Package for the Social Sciences (SPSS) for Windows, Version 21.0 (Armonk, New York, USA). Normally distributed variables were compared using independent samples T-test, and abnormally distributed variables were compared using Kruskal Wallis test. The presence of correlation was evaluated by Pearson's correlation coefficient. Statistical significance and the confidence interval was set at $p < 0.05$ and 99%, respectively.

3. Results

Sixty patients with FMF (35 women and 25 men) and 60 healthy controls (35 women and 25 men) were included in the study. Female-male ratio was 1.4. Mean age of the patients 33.73 ± 9.81 years (18–50 years) was comparable to that of the control 34.28 ± 10.36 years (18–50 years)($p = 0.77$). Thirty-two (53.3%) patients experienced <1 attack/6 months, 27 (45%) 2 attacks/ month to1 attack/6 months and 1 patient (1.67%) ≥ 2 attacks/month. 53 patients (88.33%) were receiving regular colchicine treatment. Demographic and clinical features of the patients are presented in Table 1.Mutations of the Mediterranean fever (MEFV) gene are shown in Table 2.

The comparison of QoL, fatigue and depression scores between patients and control are presented in Table 3.

The correlation between SF36, FSS, HDS with some demographic and clinical variables in Familial Mediterranean Fever patients are shown in Table 4. FSS and HDS signifcantly negatively correlated with all SF36 subscales except mental sub-item ($r = -0.12$, $p = 0.18$ and $r = -0.18$, $p = 0.07$ respectively); physical function ($r = -0.51$, $p < 0.0001$ and $r = -0.3$, $p = 0.002$), physical role ($r = -0.63$, $p < 0.0001$and $r = -0.41$, $p = p < 0.0001$), bodily pain ($r = -0.71$, $p < 0.0001$ and $r = -0.49$, $p < 0.0001$), general health ($r = -0.7$, $p < 0.001$ and $r = -0.51$, $p < 0.0001$), vitality ($r = -0.72$, $p < 0.0001$ and -0.54, $p < 0.0001$), social functioning ($r = -0.58$, $p < 0.0001$ and $r = -0.47$, $p < 0.001$) and emotional role ($r = -0.45$, $p < 0.0001$ and $r = -0.42$, $p < 0.0001$). Disease duration, age of onset, and duration of attacks showed no significant correlation with FSS, HDS and SF36 subitems.

Effect of disease severity on QoL, depression and fatigue are presented in Table 5.

4. Discussion

Rheumatic disorders are among the main conditions, in which QoL is decreased. The present study assessed the impact of FMF on QoL among Turkish FMF patients. The first study to demonstrate poor QoL scores in FMF patients was performed by Buskila et al. [28] in 1997. They assessed QoL by using a scale, developed by Flanagan [29], which is inadequate to evaluate the dimensions of QoL. We assessed QoL by using SF36, which assesses eight dimensions of health including limitations in physical functioning, limi-

Table 1
Demographic and clinical features as well as fatigue, depression and functional status scores in the Familial Mediterranean Fever patients.

Parameter mean ± SD (range)/n(%)	FMF patients (n = 60)
Age (years)	33.7 ± 9.8 (18–50)
Disease duration (years)	14.6 ± 12.1 (1 –4 7)
Age of onset (years)	18.6 ± 12.8 (3 –4 4)
Age of diagnosis (years)	28.3 ± 11.5 (3 –4 8)
Delay in diagnosis (years)	9.81 ± 10.3 (0 –4 2)
Clinical features:	
Peritonitis	46 (76.7)
Fever	43 (72.7)
Arthritis	32 (53.3)
Pleuritis	30 (50)
Erysipelas-like eryhtema	1 (1.7)
Duration of attacks (day)	2.6 ± 0.8 (1 –7)
Disease severity score	
Mild	20 (33.3)
Moderate	31 (51.67)
Severe	9 (15)
Visual Analog scale	
VAS-pain (mm)	56.1 ± 26.6 (20–100)
VAS-fatigue (mm)	55.5 ± 28.4 (17–100)
FSS	29.9 ± 17.6 (8 –6 3)
HDS	15.1 ± 8.5 (4 –4 2)
Short form-36 items	
Physical function	68.7 ± 25.0 (0–100)
Physical role	47.9 ± 43.7 (0–100)
Bodily pain	58.1 ± 26.3 (0–100)
General health	49.7 ± 25.7 (0–100)
Vitality	51.5 ± 22.9 (0–100)
Social functioning	64.8 ± 22.9 (0–100)
Emotional role	54.9 ± 40.6 (0–100)
Mental	58.1 ± 14.2 (0–100)

FMF: FMF: Familial Mediterranean Fever, FSS: fatigue severity scale, HDS: HDS: Hamilton Depression Scale.

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