Short communication

Fatigue, anxiety and depression in Tunisian sarcoidosis patients

ABSTRACT

Aims: In sarcoidosis patients, fatigue in one of the most frequent symptoms. It represents an integral part of the clinical picture. The aim of this study was to assess the degree of fatigue within sarcoidosis patients along with their psychiatric state and to identify the influencing factors.

Study design: We conducted an observational, descriptive, transversal and analytic study

Place and Duration of Study: Patients were included from the internal medicine department and the pneumo-allergology department in Sahloul and Farhat Hached hospitals (between October 2018 and March 2019).

Methodology: We included 34 patients from two internal medicine department. Two scores were used: the « Fatigue Assessment Scale » (FAS) and the « Hospital Anxiety and Depression Scale » (HAD).

Results: The population was predominantly female (70.6%) with an average age of 49.77 years ± 12.32. Fatigue was noted in 52.9% of the patients. Ten patients had a score ≥ 35 (29.4%). Bone and joint involvement had a significant impact on the FAS. The disease duration and general signs were found as independent factors. The HAD score was ≥ 8 in 58.9% of the cases for anxiety and in 50% of the cases for depression. Anxiety was found to be an independent factor associated with fatigue.

Conclusion: Our results are quite worrying. The impact of sarcoidosis must be assessed regularly to ensure a better quality of life.

Keywords: Sarcoidosis – Fatigue – Anxiety – Depression

1. INTRODUCTION

Fatigue is a heterogeneous entity which can be described in different terms. It has yet no exact definition. Researchers distinguished physical and mental fatigue [1], and passive and active fatigue [2].

In sarcoidosis, fatigue in one of the most frequent symptoms that must be objectively measured. Using validated questionnaires, fatigue incidence was evaluated between 33% and 100% [3].

The aim of this study was to assess the degree of fatigue within Tunisian sarcoidosis patients along with their psychiatric state and to identify the influencing factors.

2. MATERIAL AND METHODS

We conducted an observational, descriptive, transversal and analytic study to evaluate fatigue and psychiatric status among 34 sarcoidosis patients from the internal medicine department and the pneumo-allergology department in Sahloul and Farhat Hached hospitals (between October 2018 and March 2019).

Two scores were used: the « Fatigue Assessment Scale » (FAS) and the « Hospital Anxiety and Depression Scale » (HAD).

We used the **SPSS®** (Statistical Package for the Social Science 20.0) for statistical analysis.

2.1 The FAS is a recent validated tool [4]. It is widely used for sarcoidosis patients. A score ≥ 22 points implies the existence of fatigue while a score ≥ 35 points implies severe fatigue [5]. A drop of at least four points is considered clinically significant [6].

2.2 The HAD was developed by Drs Phillip Snaith and Anthony Zigmond in 1983 [7]. An overall score of 15 to 42 points indicates the existence of an anxiety-depressive disorder. A score of eight to ten is suggestive of a suspected mood disorder, and a score of 11 or more indicates a proven disorder.

3. RESULTS AND DISCUSSION

3.1 RESULTS

Socio-demographic, clinical and biological characteristics of the patients are summarized in table 1.

Table 1 Socio-demographic, clinical, biological and therapeutic characteristics of the studied population

	Number (%)
Women	24 (70.6%)
Age (years)	49.77 years ± 12.32
Life habits	
Married	27 (79.4%)
University studies	12 (35.3%)
Professional activity	16 (47.1%)
Tabacco exposure	19 (55.9%)
Comorbiditis	
Diabetes	12 (35.3%)
High blood pressure	6 (17.6%)
Overweight or obesity	21 (61.8%)
Sleep apnea syndrome	2 (5.9%)
Hypothyroidism	2 (5.9%)
Heart disease	4 (11.8%)
Pulmonary hypertension	1 (2.9%)
Sjögren syndrome	1 (2.9%)
Vogt-Kayanagi-Harada disease	1 (2.9%)

Clinico-biological characteristics	
Age at the onset	44.68 ± 11.32 years
Duration (average) [extremes]	5.8 years [1 month - 14 years]
Relapses	32 (94.1%)
General signs	9 (26.5%)
Pulmonary involvement	34 (100%)
Rheumatologic involvement	13 (38.2%)
Extra-thoracic lymphadenopathy	10 (29.4%)
Hepatomegaly	7 (20.6%)
Otorhinolaryngological and glandular involvement	7 (20.6%)
Skin localisation	6 (17.6%)
Splenomegaly	5 (14.7%)
Ocular localisation	5 (14.7%)
Neurologic localisation	3 (8.8%)
Cardiac localisation	1 (2.9%)
Hypercalcemia	10 (29.4%)
High converting enzyme	10 (29.4%)
Lymphopenia	9 (26.5%)
Anemia	6 (17.6%)
Hypercalciuria	2 (5.9%)
Severe disease	9 (26.5%)
Active disease	4 (11.8%)
Treatments	
Corticosteroids	29 (85.3%)
Methotrexate	3 (8.8%)

Azathioprine	4 (11.8%)
Etanercept	1 (2.9%)

3.1.1 Fatigue and psychiatric status evaluation

The average duration of completing the FAS and the HAD was 2.41 and 5 minutes respectively. Table 2 summarizes the different results of the two scores.

Table 2 « Fatigue Assessment Scale » and « Hospital Anxiety and Depression Scale » results

Scores		Value
FAS	Average score (points)	25 ± 12
	Average physical score (points)	14.2
	Average mental score (points)	11.2
	Fatigue (N ; %)	**18 ; 52.9%**
	Severe fatigue (N ; %)	**10 ; 29.4%**
HAD	HAD-A ≥ 8 (N ; %)	9 ; 26.5%
	HAD-A ≥ 11 (N ; %)	**11 ; 32.4%**
	HAD-D ≥ 8 (N ; %)	5 ; 14.7%
	HAD-D ≥ 11 (N ; %)	**12 ; 35.3%**

FAS: Fatigue Assessment Scale, HAD: Hospital Anxiety and Depression Scale, HAD-A: Anxiety score, HAD-D: Depression Score.

3.1.2 Correlations

Women had more fatigue than men even if this was not significant (58.3% vs 40% ; *p=0.45*). No socio-demographic characteristic or comorbidity had a significant impact on the fatigue score. Regarding the disease features, only the existence of general signs (*p = 0.01* ; OR = 12 and $CI_{95\%}$

[1.294 – 111.323]) and rheumatologic manifestations (*p = 0.028*; OR = 5.417 and $CI_{95\%}$ [1.136 – 25.832]) had a significant influence on the FAS.

Concerning the HAD, a HAD-A ≥ 8 and a HAD-D ≥ 8 had a significant influence on fatigue with *p = 0.01*, OR = 5.833 and $CI_{95\%}$ [1.298 – 26.223], and *p = 0.001*, OR = 15.167 and $CI_{95\%}$ [2.837 – 81.095] respectively.

Finally, three independent factors were associated with fatigue: general signs, anxiety (HAD-A ≥ 8) and sarcoidosis duration (Table 3).

Table 3 Independent factors associated with fatigue

Variables	Adjusted OR	[$CI_{95\%}$]	*p*
General signs	27.417	[1.681-447.108]	***0.02***
Anxiety (HAD-A ≥ 8)	10.027	[1.221-82.351]	***0.03***
Sarcoidosis duration	1.031	[1.002-1.060]	***0.03***

3.2 Discussion

Fatigue can be caused by many diseases such as cancer, multiple sclerosis, rheumatoid arthritis and depression [8]. Fatigue associated with sarcoidosis is one of the most frequent disease manifestations [9]. This symptom must be objectively measured using validated tools. Various questionnaires and scores have been tested [1,10-12] but the FAS is the one recommended for sarcoidosis patients and exists in several languages [13].

Fatigue pathogenesis is still mysterious even if some factors have been incriminated such as sleep disorders, depression, neuropathy [14] and exercise intolerance with reduced physical activity [15]. Korenromp and al. had concluded that the low level of IL-4, IL-5 and IL-10 was contributory in the genesis of chronic fatigue [16].

In our population, the FAS mean score was 25±12 points. The percentage of patients with confirmed fatigue was 52.9% (n=18/34). Among them, ten had severe fatigue. More than half of the patients complaining of fatigue had a physical score higher than the mental score (12/18 or 66.7%). All studies

revealed a high prevalence of fatigue in sarcoidosis populations. The review of 20 studies by De Kleijn and al. had found a variable prevalence of 33% to 100%, exceeding the prevalence in cancer patients (48%) [3]. The German study conducted by Michielsen and al. concluded that fatigue was the most reported symptom among patients with sarcoidosis [17]. Nevertheless, severe fatigue remains lesser, rarely exceeding 20% [18,19].

Regarding influencing factors, studies concerning the level of predilection of gender, age and race for fatigue occurence were controversial. Some studies, unlike ours, found an important impact of comorbidities (sleep apnea syndrome, diabetes mellitus, dysthyroidism and pulmonary hypertension) on fatigue [20]. Also, systemic and extra-pulmonary manifestations were more correlated to fatigue [11]. However, fatigue does not seem to be always associated with symptoms since even patients who were initially asymptomatic were still fatigued [10].

The objective parameters of continuous evaluation and follow-up of the disease (respiratory functions, chest X-ray and biological tests) have only a minimal correlation with the subjective feeling of well-being [21] and fatigue response to conventional treatments is unclear.

In our population, the psychiatric status was altered in more than half of the patients. Anxiety (HAD-A $\geq$ 8 points) was an independent factor associated with fatigue.

There is an overlap between depression, anxiety and fatigue in sarcoidosis. Indeed, high levels of stress were linked to greater fatigue even after excluding depressive symptoms [22]. Fatigue was also linked to depression [23].

Faced with the complexity of identifying the exact etiology of fatigue and the real factors involved in its genesis, a specific treatment cannot be advanced. Nevertheless, the action of few molecules was studied (Dexmethylphenidate [24], Modafinil [25], Armodafinil [26]), in addition to sarcoidosis conventional treatments. Gradual physical exercises should also be considered in the therapeutic strategy as they have proven their effectiveness [27,28].

4. CONCLUSION

To our knowledge, our study, evaluating fatigue and psychiatric status in sarcoidosis patients, is the first in Tunisia. Our results are quite worrying. The study of such repercussions becomes imperative to better preserve the quality of life of patients with chronic diseases such as sarcoidosis.

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