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Prevalence of Depression and Anxiety in Patients with Autoimmune Disease: A Comparative Study with a Diabetic Population

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Abstract

Introduction: Systemic diseases are a variety of heterogeneous autoimmune and/or autoinflammatory diseases and syndromes usually affecting multiple systems and resulting from immune system dysregulation. We evaluated risk factors for depression and anxiety in an autoimmune disease cohort compared with diabetic patients. **Patients and Methods:** We conducted an observational, cross-sectional, case-control survey comparing two groups: individuals with connective tissue disease (CTD) and diabetic controls who were followed within three Dakar University hospitals during the period from April to June 2023. **Results:** The sample comprised 106 participants, of whom 51 (48%) had CTD and 55 (52%) served as diabetic controls. In the CTD group, the majority had lupus (19) and rheumatoid arthritis (23). The CTD patients had a mean age of 41.0 years (SD 16.9), while the diabetic patients had a mean age of 55.9 years (SD 11.7), with a significant difference observed ($p < 0.001$). The prevalence of anxiety was higher in patients with CTD (37%) than in those with diabetes (5%) ($p < 0.001$). Of all anxious patients in both groups, 86% had CTD and 14% had diabetes. In the case of depression, CTD patients had a higher prevalence, but the associated difference was not significant. Indeed, it was seven times higher in patients with CTD than in those with diabetes (OR 7.3, CI [1.78 - 41], $p = 0.005$). **Conclusion:** Compared to a chronic disease, devastating in Africa and evolving over the long term, autoimmune diseases are more strongly and more frequently associated with anxiety and depression. This is a factor to be taken into account in the holistic management of these patients.

Keywords

Connective Tissue Disease, Lupus, Rhumatoid Arthritis, Diabetes, Depression, Anxiety, Disability

1. Introduction

Connective Tissue Diseases (CTD) are a variety of heterogeneous autoimmune and/or autoinflammatory diseases and syndromes, usually affecting several systems [1]. They result from dysregulation of the immune system, leading to an inappropriate immunological response of the body against self-antigens [2]. They are often associated with numerous repercussions due to their chronic and recurrent nature, associated comorbidities, multi-organ damage and severe complications. At an individual level, these disabilities can be physical, socio-professional and psychological [3] [4]. Thus, patients with CTD may have a unique temperament profile, making them susceptible to psychosomatic pathologies [5]. The literature indicates that stress can have an impact on the immune system, potentially contributing to the development of CTD and disease flare-ups [6]. This can lead to significant complications and repercussions at both individual and societal levels [4] [7].

Although the psychosomatic aspect of CTD is widely recognized, few studies have examined the impact of psychological interventions on disease progression.

We evaluated risk factors for depression and anxiety in a CTD cohort compared with diabetic patients.

2. Patients and Methods

We conducted an observational, cross-sectional, case-control survey comparing two groups: individuals with CTD and diabetic controls who were followed within three Dakar university hospitals during the period from April to June 2023. The study involved 106 participants, 51 of whom were being treated for CTD at the Dakar University Hospital (Abbas Ndao Hospital, Aristide Le Dantec Hospital, Ouakam Military Hospital) and 55 other type 2 diabetics selected as a matched control group. Patients in the two groups were not matched for age and sex. The patients included were aged 18 or over, had given their consent and had a complete file.

Data were collected using a form designed via Koobotoolbox. This included questions assessing patients' quality of life and psychological state, using the SF-36 and Hamilton Depression and Anxiety Scale (HADS) questionnaires. These two questionnaires were chosen for their ease of completion and applicability to our population.

Statistical analyses were performed using R software version 4.3.0. This analysis was both descriptive and multivariate. Logistic regression was used to perform multivariate analyses. Three logistic models were developed: one to assess

the risks associated with autoimmune diseases, another to assess the risk factors associated with anxiety, and a third to examine the risk factors associated with depression as a function of various socio-demographic variables. An initial baseline regression was used to identify the variables to be incorporated into the multivariate model. Only variables with a significance level above 0.25 were retained for inclusion in the multivariate models. The significance level for the final analyses was set at 0.05.

3. Results

3.1. Epidemiological Data

The sample included 106 participants, 51 (48%) had CTD and 55 (52%) were the diabetic group controls. In the CTD group, the majority had lupus (19) and rheumatoid arthritis (23). The other patients had inflammatory myopathie, Sjogren syndrom, Behcet disease and scleroderma. The CTD patients had a mean age of 41.0 years (SD 16.9), while the diabetic patients had a mean age of 55.9 years (SD 11.7), with a significant difference observed ($p < 0.001$). The results show that diabetics outnumber CTD patients in subjects under 30 and over 60 years of age. However, CTD predominate in patients under 30 ($p = 0.001$). Comparing age groups, it is clear that a greater proportion of diabetic subjects were over 60 years of age than of patients with AIS (76% vs. 24%). On the other hand, subjects under the age of 30 were more likely to have CTD than diabetes (94% vs. 6%). However, in the 30 - 60 age group, CTD patients and diabetics were equally represented (52% vs. 48%). In terms of gender distribution, there was no significant difference between the group of CTD patients and the diabetic control group ($p = 1$). However, a higher proportion of women was observed in both groups, with sex ratios of 2 and 2.18 for diabetic and CTD patients respectively (**Figure 1**).

Diabetic patients had a longer duration of illness than CTD patients. The majority of CTD patients (64.7%) had been ill for less than five years, whereas most diabetics had been ill for more than ten years ($p = 0.01$). With regard to therapeutic education, less than half of the CTD patients reported having received therapeutic education as part of their disease management. In addition, diabetic controls showed a significantly higher rate of 85% ($p < 0.001$). The prevalence of satisfactory diabetic disease management was significantly higher (98%) than in CTD patients (80%) ($p = 0.007$).

3.2. Prevalence of Anxiety and Depression

The prevalence of anxiety was higher in patients with CTD (37%) than in those with diabetes (5%) ($p < 0.001$). Of all anxious patients in both groups, 86% had CTD and 14% diabetes.

In the case of depression, CTD patients had a higher prevalence 6 patients vs. 4, but the associated difference was not significant ($p = 0.647$). In fact, 60% of depressed patients in our study had CTD (**Table 1** and **Figure 2**).

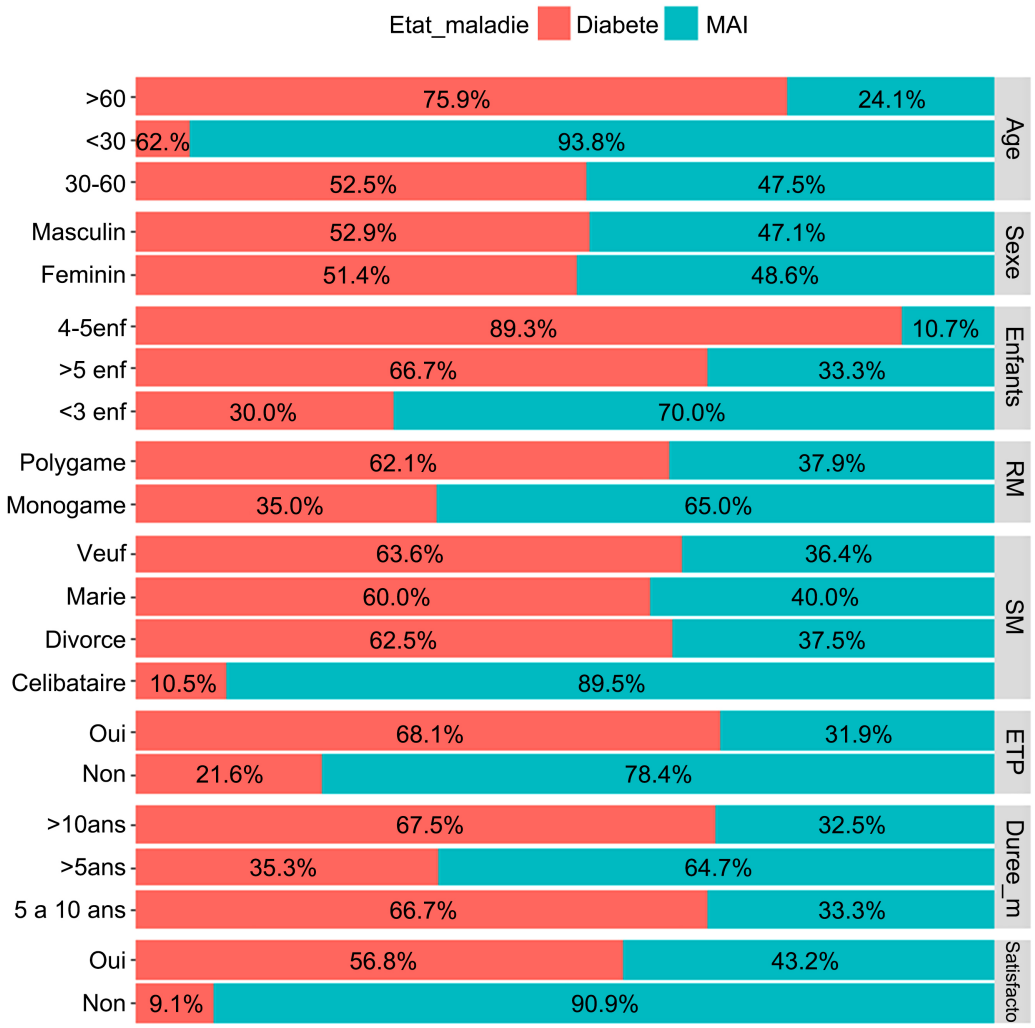

Figure 1. Comparison of socio-demographic parameters in AID vs Diabetic. RM = matrimonial regimen; SM = marital status.

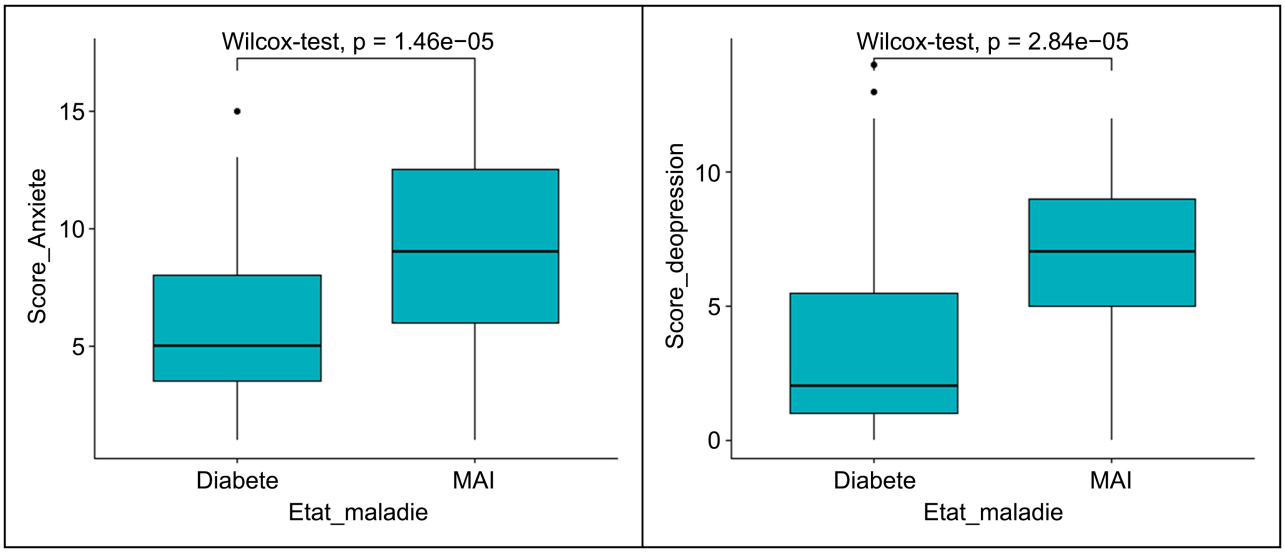

Figure 2. Moustache plots comparing HADS scores in AID vs Diabetes.

Table 1. Comparison of HADS score frequencies in AID vs. diabetics.

		Diabètes (%)	AID (%)	p-value
Anxiety	No	52 (94.5)	32 (62.7)	<0.001
	Yes	3 (5.5)	19 (37.3)	
Depression	No	51 (92.7)	45 (88.2)	0.647
	Yes	4 (7.3)	6 (11.8)	

4. Discussion

4.1. Epidemiological Data

The results indicate a higher prevalence of CTD in individuals under the age of 30, while a greater number of diabetics appear in those over 60. This observation is attributed to the fact that CTD are more likely to appear at an early age, whereas type 2 diabetes is a late-onset disease. It is therefore reasonable to deduce that diabetics aged 60 and over are better represented because of this "causal link". Age diversity represents a challenge for the life expectancy of autoimmune disease patients in our region. In our series, the mean age was 41.0 years (standard deviation 16.9). In their study on the prevalence of CTD, N. Cardinez *et al.* [8] reported a mean age of 53 years, with a maximum age of 58 years. The African series reported by B.S. Kane *et al.* [1] observed an even lower mean age of 43.76 years.

No difference was found between the two groups in terms of gender. In their research on diabetics, Svenningsson *et al.* [8] found that women predominated. S.T. Ngo *et al.* [9] reported that there are clear gender differences in prevalence for most CTD, with women generally more frequently affected than men. Unlike these two studies where intragroup comparisons were made, our series made an intergroup comparison. The within-group comparison shows that the sex ratio, in favor of women in both groups, is greater than two, which is consistent with the findings in the literature.

Our results indicate a significant number of unmarried patients with CTD, which may be attributed to the disease manifesting at a younger age, coinciding with the age of first marriage. In Senegal, according to the 2019 Demographic and Health Survey (DHS), the median age of first marriage is around 18 for women with no education, while it rises to 22 for those with primary schooling [10]. The manifestations of the disease, combined with a treatment plan that coincides with the age of marriage, mean that people diagnosed with CTD have very few plans to pursue a married life. Various other factors may also play a role, including partner prejudice, for example, the impact of the disease, the expenses associated with treatment, etc.

On average, diabetics have four children, while people with CTD have only one. M. Pons and A. Molto [11] have observed that the fertility of young women can be impaired not only by the consequences of CTD, but also by the ongoing

activity of the disease and the treatments used. Subfertility is maintained both by the emotional impact of the disease and by the gonadotoxic molecules used in the treatment of CTD.

4.2. Prevalence of Anxiety and Depression

We also found that people with diabetes had higher mental health scores. This suggests that patients with CTD are more prone to depression and anxiety. In a meta-analysis [12], the authors reported that patients with systemic lupus erythematosus were at high risk of depression and anxiety. The prevalence of major depression and anxiety in this series was 24% (95% CI, 16%-31%, I2 = 95.2%) and 37% (95% CI, 12%-63%, I2 = 98.3%) respectively. The authors used several methods to assess psyche, and all the results point in the same direction. Authors K. M. Fiest *et al.* [13] and M. S. Soósová *et al.* [14] have similarly demonstrated, on the basis of a meta-analysis, that depression and anxiety are very common in people with rheumatoid arthritis and can have harmful consequences. It should be noted that these symptoms persist for an average of 30.9 months (standard deviation: 13.0) [15]. All specialists involved in the management of autoimmune diseases, including internists, rheumatologists and psychiatrists, need to be aware of the existence of these psychiatric manifestations and react promptly to any clinical signs.

Furthermore, our results indicate that CTD patients of advanced age are less likely to develop depression than younger patients, but are at higher risk of anxiety. Good mental health and a high physical activity score are preventive measures against depression in this patient population. It has been observed that male patients suffer more from depression than female patients, and vice versa for anxiety. Y. M. El-Miedany and A. H. E. Rasheed [16], and M. Uda *et al.* [17], carried out a study on populations suffering from rheumatoid arthritis and lupus respectively, and reported results in line with our own.

Several studies suggest that pro-inflammatory cytokines play a primary role in mediating the pathophysiological features of major depression, in which an inflammatory process can be induced by external and internal stressors, such as psychological and inflammatory diseases, respectively. The higher prevalence of depression, particularly in patients with connective tissue disease (CTD), suggests that depression may present a dysfunctional cytokine-induced adaptation of the disease, which could manifest itself in times of exacerbated activation of the innate immune system. Thus, inflammation may contribute to the development of clinical depression through its ability to induce pathological behaviors corresponding to the neurovegetative features of depression, through deregulation of the hypothalamic-pituitary-adrenal axis, through alterations in neurotransmitter synthesis and reuptake, and through its involvement in neuroprogressive pathways [18].

Apart from inflammation, other ethiopathogenic hypotheses have been put forward: direct activity of the disease on the central nervous system via autoan-

tibodies, side effects of glucocorticoids and hydroxychloroquine, or anxious reactions to a chronic and potentially fatal disease. For others, psychiatric disorders may be associated with vasculitis and the non-inflammatory vasculopathy of small cerebral blood vessels that can occur with some of these CTD [19].

5. Limitations of our Study

One of the main limitations of our study is the absence of age and sex matching. This would minimize bias. In fact, there was a significant difference in age and sex between the two groups. In addition, multivariate analysis showed that age was a protective factor, reducing the probability of suffering from depression in later life, and that the risk of depression was 1.8 higher in men than in women.

6. Conclusion

Compared to a chronic disease, devastating in Africa and evolving over the long term, CTD is more strongly and more frequently associated with anxiety and depression. This is a factor to be taken into account in the holistic management of these patients.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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