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## Fibromyalgia in diabetes mellitus

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**Abstract** *Objective* The aim of this study was to evaluate the prevalence of fibromyalgia (FM) in patients with diabetes mellitus (DM). *Subjects* The study included 100 consecutive unselected patients with DM attending our diabetes clinic. Patients were divided into two groups: 45 patients with type 1 diabetes and 55 patients with type 2 diabetes. A group of 50 healthy hospital staff members served as controls. The FM was diagnosed according to the 1990 American College of Rheumatology criteria. Counts of 18 tender points were performed by thumb palpation and assessed by dolorimeter. Routine biochemical tests and levels of HbA<sub>1c</sub> were recorded in each patient. *Results* The main outcome measure was the association of FM with DM. Fibromyalgia was diagnosed in 17 patients (17%) with DM and in only one (2%) healthy control ( $P=0.008$ ). No differences in patients were noted in the prevalence of FM between type 1 and type 2 diabetes (18.5% vs 15.5%, respectively). Patients with both FM and DM had significantly higher levels of HbA<sub>1c</sub> than DM patients without FM ( $9.2 \pm 1.1\%$  vs  $6.4 \pm 1.5\%$ ) ( $P < 0.05$ ). Similarly, the numbers of tender points, pain scores, and the prevalence of sleep disturbances, fatigue, and headaches were higher in this group of patients. A significant correlation was observed between the numbers of tender points and HbA<sub>1c</sub> levels in the DM patients with FM ( $r=0.72$ ,  $P=0.027$ ). *Conclusion* Fibromyalgia is a common finding in patients with types 1 and 2 diabetes,

and its prevalence could be related to control of the disease. As with other diabetes complications, FM might be prevented by improved control of blood glucose levels.

**Keywords** Diabetes mellitus · Fibromyalgia · HbA<sub>1c</sub>

### Introduction

Fibromyalgia (FM) is a common disorder with cardinal symptoms of diffuse chronic pain associated with muscle stiffness and tenderness of specific points on examination [1]. This condition affects mainly women, with a female-to-male ratio of 9:1, and its estimated prevalence in various populations varies between 0.2% and 4.4% [2]. The currently accepted criteria of most investigators are those proposed by the American College of Rheumatology in 1990 and include a combination of chronic widespread pain with tenderness in at least 11 of 18 specific tender points [3].

Despite extensive research, the etiology and pathogenesis of FM still remains unclear. The disorder has been associated with various rheumatic diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), Sjögren's syndrome (SS), and osteoarthritis (OA) in up to 22% of patients [4]. A high prevalence of FM was also observed in a number of infectious diseases, including human immunodeficiency virus, Lyme disease, and hepatitis C virus infections [5, 6].

Diabetes mellitus (DM), a metabolic disease, affects the connective tissue in a variety of ways. Many rheumatologic disorders have been described in patients with DM, including diabetic osteoarthropathy, stiff hands syndrome, osteoporosis, neuropathic joints, and calcific periartthritis [7,8]. Nevertheless, no association between FM and DM could be found in an extensive literature survey. The aim of the present study was to evaluate the frequency of FM and the factors contributing to its presence in patients with DM.

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## Patients and methods

### Patients

One hundred consecutive, unselected patients with DM attending the Diabetes Clinic at the Souraski Medical Center in Tel Aviv, Israel, were included in the study. These patients had been regularly treated in this clinic, which acts as a tertiary referral center. They were divided into two groups: those with type 1 diabetes (group A) and those with type 2 diabetes (group B). A control group of 50 healthy subjects was randomly recruited from hospital staff on a voluntary basis.

### Assessment

Each patient was interviewed, and detailed questionnaires concerning the use of various medications, sleep disturbances, concomitant diseases, the presence of fatigue, and specific questions regarding rheumatic symptoms were filled out. A count of 18 tender points at nine symmetrical sites was performed in all subjects by thumb palpation and assessed by dolorimeter (model 719–20, Chatillon) using a pressure of 4 kg/cm<sup>2</sup> [9]. Definite tenderness of any of the points was considered to be present if some involuntary verbal or facial expression of pain occurred. Thumb palpation and pressure were also done at four control sites, and patients were not told which were the tender or control points [10]. All dolorimeter measurements and total point counts were done by the same observer (TS), who was not blinded to the assessed status before interviewing the patients.

Subjects were diagnosed as having FM if they fulfilled the American College of Rheumatology criteria [3]: (1) widespread pain for more than 3 months and (2) tenderness of 11 or more specific tender points. Widespread pain was diagnosed if the pain were experienced in all of the following areas: (1) the left side of the body, (2) the right side of the body, (3) above the waist, (4) below the waist, and (5) axially. In each patient, levels of hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>), the measuring of which is an established procedure for evaluating long-term control of diabetes, were recorded. The means of the final three measurements in each patient were collected, reflecting the period of 1.5–2 years prior to the study. Sleep disturbances were assessed using a ten-point mini sleep questionnaire [11]. Current levels of pain and fatigue were evaluated using a visual analog scale scored from 0 to 10, featuring 10 as the worst possible condition. The frequency of headaches, evidence of peripheral neuropathy, and symptoms attributed to inflammatory bowel syndrome (IBS) were recorded in all patients. The use of antidepressive medications was also recorded, but no patient or control admitted to using them.

### Statistical analysis

Student's *t*-test was used to compare tenderness results in the study groups and controls, while prevalence rates of FM in the various groups were compared using Fisher's exact test.

## Results

Of the 100 patients with DM, 45 had type 1 diabetes and 55 had type 2. No significant statistical differences concerning sex, disease duration, or HbA<sub>1c</sub> levels were noted between the study groups. As expected, patients with type 1 diabetes were generally younger than those in the other groups.

Fibromyalgia was diagnosed in 17 DM patients (17%) (two males and 15 females) and in only one (2%)

healthy control ( $P=0.008$ ). No differences were noted in the prevalence of FM between types 1 and 2 diabetes (18% vs 15.5%, respectively) (Table 1). Fibromyalgia in DM was associated with elevated levels of HbA<sub>1c</sub>: DM patients with FM had significantly higher levels of HbA<sub>1c</sub> than those without FM ( $9.2 \pm 1.1\%$  vs  $6.4 \pm 1.5\%$ , respectively) ( $P<0.05$ ). These differences remained unchanged when analyzing the subgroups of DM (type 1 vs type 2). As expected, patients with FM had more tender points than those without FM ( $12.8 \pm 1.4$  vs  $3.1 \pm 2.2$ ,  $P=0.01$ ) and higher levels of pain ( $7.1 \pm 2.2$  vs  $1.1 \pm 1.8$ ,  $P<0.001$ ) (Table 2). The prevalence of sleep disturbances, fatigue, and headaches was significantly higher among patients with both FM and DM, while the occurrences of peripheral neuropathy and IBS did not differ between the groups. A significant correlation was observed between the numbers of tender points and HbA<sub>1c</sub> levels in the FM group ( $r=0.72$ ,  $P=0.027$ ).

## Discussion

Fibromyalgia is a clinical syndrome having a common group of symptoms that can be reliably identified in medical clinics and in the community, with prevalence ranging from 0.2% to 4.4% in varying populations [2]. There is no single etiologic factor, though physical and emotional trauma may trigger its appearance. Although it is seen as a disorder of pain perception involving neurohormonal dysregulation, it has been associated with various rheumatic and infectious diseases [4, 5, 6]. Certain nonrheumatic illnesses such as depression, IBS, and hypothyroidism have been associated with it [12].

Diabetes mellitus is a metabolic disease affecting more than 8% of the general population, and its complex metabolic disturbances cause a variety of alterations in the musculoskeletal system. Bone and joint alterations that have been associated with DM include hyperostosis, OA, and osteoarthropathy [13]. Soft-tissue involvement has also been described in DM and can be manifested by calcific periartthritis of the shoulder and diabetic hand syndrome, characterized by the presence of contractures involving the small joints of the hands [14].

Although FM and DM are both common, no association between them has been reported. In our study, FM was detected in 17% of DM patients, with no preference for type 1 or type 2 disease. This prevalence was significantly higher than in our control group (2%), which result is no different from that reported in other healthy populations [2]. Although these figures seem high, they do not differ from those reported in various rheumatic and chronic infectious diseases such as Lyme disease and hepatitis C virus infection [5, 6].

The most important finding in this study is the association between FM and higher levels of HbA<sub>1c</sub>, which is further emphasized by the correlation between numbers of tender joints and HbA<sub>1c</sub> levels. Usually these levels most accurately reflect the previous 2–3 months of

glycemic control [15]. For our study, we chose the means of the previous three HbA<sub>1c</sub> measurements, which reflect the metabolic control of these patients for 1.5–2 years prior to the study. Moreover, several studies have shown that elevated HbA<sub>1c</sub> levels sharply raise the likelihood of having or developing micro- and/or macrovascular disease [15, 16]. On the other hand, we cannot rule out that the high prevalence of FM in DM could correlate with the psychiatric effect deriving from chronic and often crippling diseases such as diabetes. The detection of similarly high prevalences of FM in many other pathologic conditions with completely different pathogenesis, such as rheumatic and chronic infectious diseases, supports this observation.

The detection of FM in patients with DM is important, since muscle aches and stiffness can be erroneously attributed by many physicians to the diabetes alone. One might argue that DM patients simply have more myalgias or altered pain sensation due to neuropathy rather than FM. Nevertheless, the clinical findings of specific tender points, fatigue, and sleep disturbances support the diagnosis of FM in our patients. Furthermore, the prevalence of peripheral neuropathy did not differ between FM patients with and without DM.

It is important to emphasize that the diagnosis of FM, which could be made by any physician in a simple physical examination, also has a therapeutic implication. Better control of diabetes may reduce the incidence of FM, as shown by our study results. Fibromyalgia can therefore be added to the list of complications associated with DM. An intervention study is recommended to address the question of whether reduced HbA<sub>1c</sub> levels in DM patients with FM can lead to decreases in FM symptomatology.

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