

Original article:

Are diabetes mellitus, restless syndrome, and fibromyalgia related?

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ABSTRACT

Introduction: Diabetes mellitus can lead to a secondary restless syndrome, the later together with fibromyalgia disturb sleep, thus may affect diabetes control.

Objectives: This study aimed to study the effect of the restless syndrome and fibromyalgia on diabetes control.

Material &Methods: This cross-sectional study of one hundred consecutive type2 diabetic patients attending an outpatient diabetes clinic, Sudan. Participant signed a written informed consent then interviewed using the American College of Rheumatology and International Restless Leg Syndrome Study Group criteria for the diagnosis of fibromyalgia and the restless syndrome. A blood sample was taken for glycated hemoglobin then a comparison between accepted and poor control diabetic patients with and without fibromyalgia and restless syndrome was undertaken

Results: Out of 100 type2 diabetic patients, restless leg syndrome, and fibromyalgia were reported in 23% and 21% respectively. A significant statistical difference was evident between accepted and poor control patient regarding restless syndrome rate P-value<0.05, no difference was noted regarding fibromyalgia. Restless syndrome patients had more rates of fibromyalgia and peripheral neuropathy. Also, higher rates of the restless syndrome and peripheral neuropathy were observed in fibromyalgia patients P-value<0.05.

Conclusion: Restless leg syndrome and fibromyalgia were prevalent among diabetic patients, and the former was more common among those with poor control. A strong relation between fibromyalgia and restless syndrome was observed. Peripheral neuropathy seems to link these common and morbid disorders.

Keywords: Diabetes, Restless, Fibromyalgi

1-Introduction

Fibromyalgia is a common disorder characterized by widespread pain, abnormal perception of pain, fatigue, sleep, and somatic disorders. Also, patients may have morning stiffness, irritable bowel syndrome and cognitive problems sometimes referred as to Fibro Fog [1,2].

The prevalence ranged from 0.5% in men to 3.5% in women; it is estimated that about 5 millions of people were affected by the disease in the year 2005. Fibromyalgia is associated with low level of quality of

life, especially among females. Furthermore, the total days lost per year is double among patients with fibromyalgia [3,4]. Death rates from suicide and injury are higher among patients with fibromyalgia [5].

Doctors awareness of this common disease lacks, so it is not uncommon for patients to visit many doctors and underwent multiple diagnostic tests before reaching the diagnosis, making fibromyalgia the third most common cause for appointments in rheumatic clinics [6-8].

The diagnosis of fibromyalgia is based on: Widespread Pain Index (WPI) ≥ 7 and a symptom severity scale

(SS) ≥ 5 or WPI 3-6 and SS ≥ 9 , and the patient does not have a disorder that would otherwise explain the pain^[9].

Diabetes mellitus is common worldwide and due to obesity and sedentary lifestyle the level is rising. Through its effects on microvascular circulation, diabetes can lead to blindness, renal failure, and peripheral neuropathy, patients, also may have macrovascular complications (myocardial infarction, Stroke, and peripheral arterial disease) with deleterious health consequences and impairment in quality of life^[10-12].

Restless leg syndrome (RLS) is a common sleep disorder characterized by the urge to move limbs accompanied by the unpleasant sensation that increase at night and relieved by movement. RLS can be primary or secondary to many disorders including iron deficiency anemia, rheumatoid arthritis, uremia, pregnancy, and polyneuropathy. The presence of at least the later condition leads to the suspicion of the relationship between diabetes mellitus and RSL^[13-18].

Diabetes mellitus can affect the connective tissue giving rise to stiff hands syndrome, neuropathic joints, and diabetic osteoarthropathy^[19]. Fibromyalgia can lead to pain and sleep disorder. Thus, there may be a relationship between these three disabling disorders.

To our knowledge, this is the first research to assess fibromyalgia and restless syndrome among patients with type2 diabetes in Sudan.

Aims and objectives: In this study, we thought to study the prevalence of these disorders and investigate their relationship to diabetes complications and degree of glycemic control.

2-Material & methods:

This comparative cross-sectional study was conducted at an outpatient endocrine clinic in Omdurman Teaching Hospital Sudan, during the period from June to August 2015.

One hundred consecutive patients were reviewed by the principal researcher using The American College of Rheumatology Criteria^[9], a well-validated scale for fibromyalgia diagnosis. The diagnosis of restless syndrome was based on the four minimal standardized criteria for the diagnosis validated by the International Restless Leg Syndrome Study Group (an urge to move the legs accompanied by or caused by unpleasant sensations, these become worse during periods of rest or inactivity and totally or partially relieved by movement, and become worse in the evening or night or occur only during the evening or night than during the day). Exclusion criteria included patients with rheumatoid arthritis, pregnant ladies, anemia, patients with dialysis, parkinsonism, and those diagnosed with L 4,5 S1 myelopathy.

The fibromyalgia criteria includes the Wide- Spread Pain Index (WPI): in which the patient reports pain during the last week in different 19 areas of the body including shoulder, upper arm, and lower arm(right and left), hip, upper leg, and lower leg (right and left), jaw right and left, back upper and lower, neck, chest and abdomen, and Symptom Severity Scale (SS) which asks about fatigue, waking un-refreshed, cognitive symptoms, and somatic symptoms each with a score from 0-3with 3 indicating the greatest dysfunction.

The diagnosis of fibromyalgia was based on: Widespread pain index (WPI) ≥ 7 and symptom severity (SS) scale score ≥ 5 , or WPI 3-6 and SS scale score ≥ 9 , and symptoms have been present at a similar level for at least 3 months, and the patient does not have a disorder that would otherwise explain the pain.

A blood sample was taken for the renal function test, and glycated hemoglobin was measured using reagent set from Pointe Scientific Inc^[20]. Patients with HbA1c of < 8 were regarded as accepted diabetes control^[21].Urine analysis for proteinuria was undertaken.

Information collected also included diabetes macrovascular (myocardial infarction, stroke, and peripheral arterial disease), and microvascular (neuropathy, nephropathy, and retinopathy) complications. Sensory function, distal muscle strength, and deep tendon reflexes were assessed by the first author, and the diagnosis of peripheral neuropathy was based on the presence of sensory, motor signs and paresthetic symptoms having a symmetric glove and stock distribution [22]. Diabetic retinopathy was diagnosed by fundoscopy after full dilatation, test for microalbuminuria was not done, and the diagnosis of proteinuria was based on the presence of albumin in the early urine sample.

Comparison was then undertaken for:

- Type2 diabetic patients with good control (HbA1c%<8) and those with poor control (HbA1c%≥8)
- Diabetic patients with and without restless syndrome and fibromyalgia were compared regarding diabetes complications and state of control.

Analysis:

Data was analyzed by using statistical software (SPSS version 20); Chi-square was used for testing the statistical significance, data were presented as percentage or mean ±SD unless otherwise specified, and P- a value of< 0.05 was considered as statistically significant.

3-Observation &Results:

They were 100 diabetic patients with a mean age of 50.5±0.29 years. The restless syndrome was found in 23% of diabetic patients while fibromyalgia was evident in 21%, the HbA1c was 9.7±2.58, the WPI score was 3.58±3.26, and the somatic score was 5.52±2.3 (Table1).No significant statistical difference in prevalence of fibromyalgia between the poor and accepted diabetes control (25.3% vs.21.1% P value=0.191), Table (2) illustrates the different

components of fibromyalgia among diabetic subgroups. Table (3) depicted the relationship of the restless syndromes to diabetes control in which: Restless leg syndrome was reported in 21% of poor control group vs.2% of accepted control with a statistically significant difference (P value=0.005). Significant statistical differences were evident between poor and accepted controlled diabetic patients as regarding all the components of the restless components (the urge to move the legs: 37 vs.8 (P value 0.002), complaints of RLS arise or worsen during the night: 26 vs.5 (P value=0.021), Complaint relieved by movement: 24 vs.4 (P value=0.017), and Complaints increase during periods of rest 29 vs.5 (P value=0.007).

Table (4) illustrated diabetes complications in 100 patients with diabetes mellitus in which peripheral neuropathy was found in 15 patients of poor control while it was not evident in good control patients P value=0.002; retinopathy was observed in 29 and six patients among poor and good control patients respectively P value=0.015. Proteinuria was observed in 13 patients with poor control while it was found in 2 patients in the good control, renal impairment was detected in 5 patients in the poor control and not found among good control, and macrovascular complications were concluded in 8 patients of poor control and not observed in good control patients.

The outstanding result of this study is the significant statistical difference between patients with and without restless syndrome as regarding the rate of fibromyalgia, (43.4%vs.14.2) P-value=0.005, peripheral neuropathy (39.1%vs.7.8%) P-value=0.001

Table (5) showed other features of patients with and without the restless syndrome.

Table (6) showed the strong relation between peripheral neuropathy and fibromyalgia ((61.95vs.2.5%) in patients with and without fibromyalgia respectively P-

value=0.000. Restless leg syndrome was evident in (47.6% and 16.4%) of patients with and without fibromyalgia P-value=0.005

No significant statistical difference between gender as regarding restless syndrome and fibromyalgia Table (7)

Table (1): characteristics of 100 type2 diabetic patients

Character	Mean±SD
Age	50.5±0.29
HbA1c	9.7±2.58
WPI Score	3.58±3.26
Somatic Score	5.52±2.3

Table (2): Fibromyalgia relation to HbA1c

Character	HbA1c%<8 no=33	HbA1c%≥8 no=67	P-value
WPI mean±SD	3.1±3.2	3.8±3.3	0.296
Somatic score	5±2.5	5.8±2.1	0.113
Fibromyalgia %	12.1	25.3	0.191

Table (3): Restless leg syndrome among accepted and poor control diabetic patients.

Character (No%)	Total	HbA1c%<8 no=33	HbA1c%≥8 no=67	P-value
The urge to move the legs	45	8	37	0.002
complaints of RLS arise or worsen during the night	31	5	26	0.021
Complaint relieved by movement	28	4	24	0.017
Complaints increase during rest	34	5	29	0.007
Positive restless leg syndrome	23	2	21	0.005

Table (4): Comparison between accepted control and poor control type2 diabetic patients as regarding diabetes complications

Character (No%)	Total no=100	HbA1c%<8 no=33	HbA1c%≥8 no=67	P-value
Sex				0.509
Males	29	10	19	
Females	71	23	48	
Retinopathy	35	6	29	0.015
Neuropathy	15	0	15	0.002
Protienuria	15	2	13	0.079
Renal impairment	5	0	5	0.168
Macrovascular complications	8	0	8	0.50

Table (5): relationship of restless syndrome to fibromyalgia and diabetes complications

Character	Restless syndrome present n=23	Restless syndrome not present n=77	P-value
Macro vascular complications	4 (17.3%)	4 (5.2%)	0.079
Proteinuria	4 (17.3%)	11 (14.2%)	0.743
Retinopathy	12 (52.1%)	23 (29.8%)	0.044
Peripheral neuropathy	9 (39.1)	6 (7.8%)	0.001
Fibromyalgia	10 (43.4%)	11 (14.2%)	0.005

Table (6): relationship of fibromyalgia to the restless syndrome and diabetes complications

Character	Fibromyalgia present n=21	Fibromyalgia not present n=79	P-value
Macro vascular complications	3 (14.2%)	5 (6.3%)	0.359
Proteinuria	4 (19.0%)	11 (13.9%)	0.521
Retinopathy	11 (52.3%)	24 (30.3%)	0.054
Peripheral neuropathy	13 (61.9)	2 (2.5%)	0.000
Restless leg syndrome	10 (47.6%)	13 (16.4%)	0.005

Table (7): sex differences of restless syndrome and fibromyalgia

Character	Males n=29	Females n=71	P-value
Restless syndrome%	17.2	25.3	0.257
Fibromyalgia%	20.6	25.3	1.00

4-Discussion:

In the present study, fibromyalgia was evident in 21% of type2 diabetic patients in accordance with Tishler et al. who reported fibromyalgia in 17% of patients with diabetes mellitus [23]. The restless syndrome was found in 23% of diabetic patients similarly Merlino et al. observed restless syndrome in 17% of diabetic patients [24]. The present data observed a higher prevalence of fibromyalgia and restless syndrome among women in accordance with the previous studies.

It is interesting to show that restless leg syndrome was more prevalent in patients with fibromyalgia than those without (47.6%vs.16.4%) P- value 0.005 confirming previously described association (33%vs.3.1%) [25]

Although the prevalence of fibromyalgia is high among patients with type2 diabetes mellitus, it is not higher than the observed prevalence of other chronic diseases with different pathogenesis like Lyme disease, rheumatic disorders, and hepatitis C virus, this may correlate fibromyalgia to psychiatric manifestations of diabetes mellitus as life lasting crippling disease and altered pain perception due to peripheral neuropathy [23]. The current finding of high peripheral neuropathy rate ((61.9%) among patients with fibromyalgia could support this observation: The current study showed no significant statistical difference (P value=0.191) in fibromyalgia rate between poor and accepted control diabetic patients. Previous studies [23] confirmed the association of fibromyalgia and diabetes control, but the researchers have not studied the effects of peripheral neuropathy.

Polyneuropathy is a risk factor for the restless syndrome, but diabetes mellitus is strongly associated with restless

legs syndrome even after controlling for neuropathy, on the other hand, increased risk of restless leg syndrome among diabetics may reflect partial consequences of polyneuropathy [26,27]. The Association of the restless leg syndrome with peripheral neuropathy had been previously documented. From the above the overlap between diabetes mellitus, restless syndrome, and fibromyalgia is obvious.

The outstanding finding in the present study is the high prevalence of the restless syndrome among patients with poorly controlled diabetes mellitus as compared to those with good control (21%vs.2% P value=0.005), reportedly restless syndrome may impair glycemic control of diabetic patients through the negative impact on sleep and psychological effects (depression and anxiety) [29].

The role of tight glycemic control in preventing microvascular diabetes complications had been previously documented [28], in the present data peripheral neuropathy was confirmed in 15% in diabetic patients with poor control while it is not observed in good control patient P value=0.002

5-Conclusion:

Both restless leg syndrome and fibromyalgia were prevalent in patients with type2 diabetes mellitus, but restless leg syndrome and peripheral neuropathy were more prevalent in patients with poor diabetes control. This observation call for further larger researches to study poor sleep, depression, and anxiety among patients with the restless syndrome and fibromyalgia and their impact on diabetes control.

Limitation of the study were the small sample size and the fact that the study was conducted at a single diabetes

clinic, so generalization cannot be insured. The reliance on a self-reported questionnaire is more prone to

subjectivity. Also, we cannot control for confoundable variables like obesity.

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