The Relationship between Frequency of Restless leg Syndrome and Type 2 diabetes

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Abstract

Objective: Diabetes Mellitus (DM) is one of the most common metabolicdisorders . It is assumed that restless leg syndrome (RLS) occur more in diabetics. Our study aims to investigate the relationship between DM and restless leg syndrome.

Materials and Methods: Our study conducted as a Case-control study, containing 180 patients as the cases and 201 as the controls from June 2016 to March 2017, at Ziyaiyan hospital, Tehran. All participants aged above 18 years. Data was collected by filling the pre-prepared checklists, complementary laboratory tests and precise physical examination by a single medical doctor.

Results: The study was carried out with 318 participants, 163 (42.8%) were male and 218 (57.2%) female, total mean age was 52.2 $\pm$ 16.3 years, BMI in case group and control group was 28.6 $\pm$ 4.9and28.6 $\pm$ 4.1 respectively. There was no statistically significant difference between the genders, mean age and BMI in two groups (*P*-value= 0.14, 0.14 and 0.56). RLS had a higher prevalence in Diabetic mans (*P*=value 0.04) with no significant difference in non-diabetics (*P*-value=0.21). RLS was more common in Diabetics (p-value=0.001) and they have 1.79 –fold higher risk of RLS (*P*-value<0.052).

Conclusion: According to our findings, diabetic patients have increased risk of RLS. Diabetes can be considered as one of its risk factors; besides, the signs resemble diabetic neuropathy; therefore, we recommend accurate screening tests and immediate diagnosis and treatment perform in all diabetic patients.

Keywords: Diabetes mellitus, Restless leg syndrome

Introduction

Considering one of the most common endocrine disorders, the prevalence of Diabetes Mellitus(DM) is expected to increase to 366 million in 2030 with greater portion of the developing countries (77.6%) consisting 90-95% of type 2 DM (1). These patients encounter many complications, such as restless leg syndrome (RLS) (2). Abnormal sensation and abnormal limbs movements occur as a result of this syndrome. The symptoms emerge during the rest, especially at nights and decrease by moving the affected

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limb. This can lead to sleep disturbances and decreased patients' quality of life (3). The pathophysiology of this syndrome remains unknown but it is assumed that dopaminergic system play a part, as symptoms relive using low doses of Levo- dopa (4). Regularly the patients receive no treatment in case the signs are minor; however, in the more severe conditions, medical therapy can relive the complaints primarily but the complaints will reappear after a short while. In the general population, the prevalence is estimated to be 5-12%, more common in female and only 25% of patients are diagnosed accurately (5). Respecting the higher prevalence of this syndrome among diabetic patients and erroneous signs with diabetic neuropathy, our study aims to evaluate the prevalence of RLS among the diabetic patients and obtain insight into the necessity of early medical therapy.

Materials and Methods

Study design

Our study conducted as a Case- control, with total number of 318,containing 180patients as the cases and 201 as the controls between June 2016 and March 2017. All the patients were selected consecutively among the both clinic and hospital-admitted patients, at Ziyaiyan hospital, Tehran, Iran. We defined the inclusion criteria as the all patients diagnosed with type 2 DM, aged more than 18. The exclusion criteria were defined as all patients with type 1 DM, pregnancy, using Tricyclic Anti Depressions (TCAs), neuroleptic and antipsychotic drugs, history of Alcohol use, Iron, vitamin B12 and folate deficiency, ferritin level under 14, hypothyroidism and glomerular filtration rate (GFR) under 60 (calculated by MDRD method). Ethical approval of the study was obtained from the Institutional Review Board, besides the consent form signed by the patients enrolled in our study.

Data collection

Data were collected by the pre-prepared checklist and complementary laboratory tests. Checklist included information aboutage, gender, body mass index, family history of DM, weight, height, history of renal, cardiac disease, hyperlipidemia and stroke, history of DM, length between the time of DM diagnosis and time of the visit, history of any anti-depressant drug. Complementary tests included HbA1C, FBS, BS 2hpp, BUN, plasma creatinine, TSH, T4, Cobolamine, folate and Ferritin. RLS was diagnosed by a single medical doctor by use of developed standardized criteria of RLS (3).

1-Desire to move the extremities because of the unpleasant sensation

2-Unpleasant sensation during extremities' movements, such as walking (Motor RLS patients)

3-Aggravation of the signs during the rest

4-Aggravation of the signs at nights or at the end of the day

The patients were referred to specialists for further investigations, if there were any signs and symptoms for iron deficiency, folate deficiency and hypothyroidism. The control group was chosen among the non-diabetic patients (FBS<100 mg/dl and HBA1C <5.6%) and patients were matched by the gender and age with patients in the case group.

Statistcal analysis

Data are displayed in tables. Qualitative variables were expressed by number and percentage and quantitative variables were expressed by mean and standard deviation (SD). *P*-value of less than 0.05 was considered statistically significant. Binary logistic Regression was performed to adjust for confounders and establish the RLS risk in diabetic patients and in different genders.

A *P*-value<0.05 was considered statistically significant. Statistical analysis was carried out using the SPSS 21 software (SPSS, Inc., Chicago).

Results

The study was carried out with 318 participants, 163 (42.8%) were male and 218 (57.2%) female, total (± SD) age was 52.2

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±16.3, mean (± SD) age in case group was 50.8±17.5 and in control group, BMI in case group and control group was 28.6±4.9and28.6 ±4.1and in the patients with and without RLS was 28.96±12 and 28.56±4.1, that BMI did not change significantly between them (*P*-value=0.397). Additionally, there was no statistically significant difference between the genders, mean age and BMI in groups (*P*-value= 0.14, 0.14 and 0.56) (Table 1). Length of unpleasant sensation in diabetic and non-diabetic patients were 2.44 ± 1.49 and 3.35 ± 1.14 year with no significance (*P*-value=0.257). 54.4% of the diabetics and 30.3% of non-diabetics had RLS (*P*-value=0.001). There was no relationship between RLS and age in both diabetics and non-diabetics (*P*-value=0.73 and 0.12); however, RLS had a higher prevalence in diabetic mans (*P*=value 0.04) with no significant difference in non-diabetics (*P*-value=0.21). We found no relationship between RLS and HbA1c, FBS and 2hpp (*P*-value=0.14, 0.39 and 0.79) and there was a significant relation between RLS and diabetes duration (Table 2). RLS was more common in diabetics (*P*-value=0.001) and they have 1.79 fold higher risk of RLS (*P*-value<0.052). Binary logistic regression showed 2.87-fold increased risk of RLS in diabetics (*P*-value<0.05, CI95% =1.8-4.4) and women had a 1.7-fold higher risk of RLS (*P*-value=0.022, CI95% =1/08- 2.67).

Discussion

DM, one of the most common metabolic disorders, can lead to impaired glucose metabolism, as a result of Insulin resistance (type 2 DM) or lack of insulin (type 1 DM). Type 2 DM is the most common type with 90% of prevalence (1). These patients may encounter many complications such as diabetic foot, cardiovascular complications, renal disorders, retinopathy, neuropathy and etc. as a result of systemic organ involvement due to impaired glucose metabolism and elevated glucose plasma level.

RLS was described by Karl-Axel Ekbom (6) which is diagnosed clinically, but excessive laboratory tests are useful to differentiate between other causes like, iron, folate, vitamin B12 deficiency (usually occurred alcohol abuse), hypothyroidism, renal, cardiovascular and neurologic disorders. 5-15% of general population suffer from RLS (7). Clinical signs of RLS include having unpleasant sensation of lower and sometimes upper extremities (like itchy, pins and needles sensation), urge to move the extremities, the signs worsen by rest and relive by activity and aggravate during the nights and paresthesia of the limbs (8). Precise history taking and physical examinations in addition to further laboratory tests can be useful for its accurate diagnosis.

This syndrome is considered one of the complications of DM (2) and 18% of the diabetics experience RLS, compared to 5.5% of non-diabetics(9). Causes of RLS, other underlying disease included: hypertension, cardiovascular diseases and osteoporosis. Merlino et al had shown that polyneuropathy accompany RLS but it cannot justify all signs occurred in RLS (10). Sleep disturbance and daily drowsiness occur due to insomnia caused by RLS and all together lead to decreased quality of life in addition to increased risk of cardiovascular disease, depression, anxiety disorders and social isolation (11). According to Skomro et al sleep disturbances and RLS are more common in diabetic population (12) and Lopes et al showed 27 % of the diabetics suffer from RLS (13). Interestingly, Norma et al found that RLS can cause higher FBS level (14) but our study did not show any relationship between RLS and FBS. According to a study done by Innes et al, there is a significant relationship between RLS and gestational diabetes mellitus (GDM) (15). Similar to our study, Jennings et al showed RLS diabetic females have a greater risk of RLS; in contrast to us, they found relationship between BMI and RLS occurrence (16).

Sabic et al, in 2016, studied 90 patients with hypertension and DM to determine the

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Table 1. Comparison between means of age, duration of un-unpleasant sensation in foot and body mass index in diabetic and non- diabetic patients

Variable	Number		Mean		Standard Deviation		*P*-Value
	Diabetic	Non- Diabetic	Diabetic	Non- Diabetic	Diabetic	Non- Diabetic	
Age (years)	180	201	50.8	53.2	17.5	15.1	0.14
Length of unpleasant sensation in foot (years)	180	201	1.5	1.1	2.4	3.3	0.25
Body Mass Index (Kg/m2)	180	201	28.8	28.6	4.9	4.1	0.56

Table 2. Correlation between restless leg syndrome and duration of diabetes

RSL	Number	Percent	Duration of Diabetes	Standard Deviation
Present	98	54.5	8.6	7.3
Absent	82	45.5	5.9	5.5

P-Value=0.01

prevalence of RLS among them. 30 patients were diabetic (aged63.9 ±7.49 years), 30 were hypertensive (aged 58.7 ±9/07years) and 30 healthy individuals (aged52.76 ± 14.83years) were enrolled as the control group. 21% of patients with hypertension and 30% with DM had RLS; one the other hand, 30% of whom suffered from RLS, had both of the hypertension and DM. their result showed no significant difference between hypertensive and control group (*P*-value=0.0012) and between DM patients and control group (*P*-value=0.0012) (14).

Conclusions

According to our findings, diabetic patients have increased risk of RLS and DM can be considered as the one of its risk factors, beside other causes such as iron, folate or vitamin B12 deficiencies, hypothyroidism and renal, neurological or muscular disorders. As it can lead to decrement in patients' quality of life and adverse long term outcomes, like cardiovascular disease, we recommend precise physical examination for any patients with RLS complaints, further laboratory tests for detecting curable causes and finally treating patients as soon as possible.

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