Original Article

Diabetes Mellitus

Incidence of Orthostatic Hypotension and Postural Dizziness in Patients with Type II/Non–Insulin-Dependent Diabetes Mellitus

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ABSTRACT

Objective: To evaluate the association between orthostatic hypotension and postural dizziness, and determined the factors most likely related to orthostatic hypotension in patients with diabetes.
Study Design: Comparative study.
Place and Duration of Study: This study was conducted at the Hamdard University Hospital, Karachi between October 2010 and September 2012.
Materials and Methods: The subjects were 102 consecutive non–insulin-dependent patients with diabetes and 204 age- and sex-matched control subjects. Orthostatic hypotension was defined as a decline of 20 mm Hg or more in systolic blood pressure 1 minute after standing. Postural dizziness was any feelings of dizziness, light-headedness, or faintness that occurred while standing during the examination.
Results: The prevalence of orthostatic hypotension and postural dizziness in patients with diabetes was higher than in control subjects. Those patients with both diabetes and orthostatic hypotension were older and had higher supine systolic blood pressures and higher plasma glycosylated hemoglobin and fasting glucose levels. They had higher prevalence of postural dizziness, hypertension, and cerebrovascular disease, and lower standing systolic blood pressures than those without orthostaticl hypotension. They also were more often being treated with antihypertensive agents. Only 30.8% of patients with diabetes with orthostatic hypotension suffered from postural dizziness. Postural dizziness, hypertension, cerebrovascular disease, and plasma glycosylated hemoglobin levels were independently associated with orthostaticl hypotension in patients with diabetes.
Conclusion: Postural dizziness, glycemic control, hypertension, and cerebrovascular disease were important determinants of orthostatic hypotension in patients with diabetes. Orthostaticl hypotension was associated with postural dizziness, but it cannot be determined clinically just from the presence of postural dizziness because the sensitivity for diagnosis of orthostatic hypotension is low.
Key Words: Orthostatic Hypotension, Postural Dizziness, Diabetes Mellitus

INTRODUCTION

Orthostatic hypotension is considered the most dramatic clinical manifestation and hallmark of diabetic autonomic neuropathy.[1-2] In patients with diabetes, autonomic neuropathy with abnormal cardiovascular reflex tests has been associated with increased mortality from unexpected sudden death and renal failure.[3-4] However, there is no uniform criterion for postural hypotension that may be symptomatic or asymptomatic[5] Although orthostatic hypotension is most commonly defined as a drop of 20 mm Hg or more in systolic blood pressure from the lying posture to the upright posture,[6-11] the lack of symptoms associated with orthostaticl hypotension raises a question about the clinical value of this definition. It is reasonable to define orthostatic hypotension as a particular decline in blood pressure that can predict a poor outcome.[10] A study of the Hypertension Detection and Follow-up Program6 revealed that a decline of 20 mm Hg or more in systolic blood pressure after standing was associated with a high 5-year mortality rate, which indicated a poor prognosis for patients with diabetes complicated with hypertension. Epidemiological evidence also suggested that postural change with a decrease of 20 mm Hg or more in systolic blood pressure was a significant risk factor for fall and syncope.[7-8] Furthermore, a drop of more than 20 mm Hg in postural systolic blood pressure was a risk factor for symptomatic occlusive cerebrovascular disease[9]. Therefore Lipsitz[10] thought that orthostatic hypotension with a decline of 20 mm Hg or more in systolic blood pressure on standing should be used to define a potentially dangerous hypotensive response.

Postural dizziness was believed to be due to reduced cerebral perfusion.[8,12-13] However, Ohashi et all [4] used single photon emission computed tomography to examine cerebral blood flow and showed that regional cerebral autoregulation was not associated with postural dizziness. Thus, the mechanism of postural dizziness may be heterogeneous.[15] Clinically, postural dizziness is often strongly associated with orthostatic hypotension, but the evidence is conflicted.[11,16-18] Some people with minor drops in systemic blood pressure develop clinical signs of cerebral ischemia and complain of dizziness or faintness on standing, whereas

others with greater drops in blood pressure remain asymptomatic. 12 Thus, some reports indicate that orthostatic hypotension is related to postural dizziness,[16,18] while others show that there is no association between orthostatic hypotension and postural dizziness.[11,17]

Certain medications, normal aging, and some pathological changes such as diabetes mellitus, hypertension, and cerebrovascular disease are believed to be associated with orthostatic hypotension.[10,19-20] Similarly, postural dizziness is also associated with age, medication use, and comorbid diseases such as diabetes and stroke.[16,21-22] Some of these associated factors are interrelated and interdependent, which may confound the relationship between orthostatic hypotension and postural dizziness.

MATERIALS AND METHODS

The subjects were 102 consecutive non–insulin-dependent patients with diabetes and 204 age- and sex-matched nondiabetic control subjects who underwent physical examinations for preventive reasons at the Hamdard university Hospital between October 2010 and September 2012. Subjects were excluded from the study for anemia, thyroid disorder, pregnancy, chronic liver disease, andcongestive cardiac failure. The subjects with diabetes included 57 men and 45 women with a mean age ± SD of 57.9 ± 10.5 years. The nondiabetic control subjects were 228 men and 180 women with a mean age ± SD of 57.1 ± 9.5 years.

Demographic characteristics, medical history, and use of medications were assessed using a standard structured questionnaire. All the subjects received a complete physical examination, measurement of seated blood pressure, body weight, height. The laboratory tests included blood chemistry analysis,Lipid profile, fasting blood sugar and random bood sugar.

Blood pressure and heart rate were measured based on the American Heart Association recommendations[26] with a vital sign monitor . Measurements were obtained at least 3 hours after a meal in a quiet room. The appropriate-sized cuff was wrapped around the right upper arm and blood pressure and heart rate were recorded after the subject had rested in a supine position for at least 5 minutes. The subject was then asked to stand, with the entire forearm relaxed and supported at the heart level (fourth intercostal space) on an adjustable table; measurements of blood pressure and heart rate were repeated after 1, 2, and 3 minutes of standing.[5,26] The subjects were asked about any feelings of dizziness, light-headedness, or faintness during the standing procedure and a positive or negative response was recorded.

Clinical diagnoses and definitions were determined as follows: (1) Diabetes mellitus was diagnosed with a fasting plasma glucose measurement of 7.8 mmol/L (140 mg/dL) or greater or 11.1 mmol/L (200 mg/dL) , when a history of diabetes was reported, or if the subject currently used insulin or an oral hypoglycemic agent.[27] (2)Orthostatic hypotension was defined as a drop in systolic blood pressure from the lying position to the upright position of 20 mm Hg or more after 1 minute of standing.[11,16,25] (3) Postural dizziness was defined as any feelings of dizziness, light-headedness, or faintness while standing during the examination.[11,16,25]

Comparisons of categorical variables were analyzed using the χ^2 test. Comparisons of continuous variables between the 2 groups were carried out using the Student *t* test or the Mann-Whitney *U* test, where appropriate. Analysis of variance was used for comparisons of blood pressure and levels of fasting plasma glucose, glycosylated hemoglobin, cholesterol, and triglycerides with covariance of age and BMI between the 2 groups. Stepwise multiple logistic regression analysis was used to assess the association of clinical variables with postural hypotension. *P* values of .05 or lower indicated statistical significance.

RESULTS

Table 1 shows the clinical characteristics of subjects with diabetes and nondiabetic control subjects. Subjects with diabetes had significantly higher BMI, seated blood pressure, and heart rate; they had significantly higher plasma creatinine, cholesterol, triglyceride, fasting glucose, and glycosylated hemoglobin levels, and a significantly higher prevalence of hypertension and use of antihypertensive agents than nondiabetic control subjects. However, there were no significant differences between subjects with diabetes and nondiabetic control subjects in age, sex, prevalence of cerebrovascular disease, or left bundle-branch block or ischemic patterns on electrocardiograph.

Table No.1: Clinical characteristics of subjects with diabetes and nondiabetic control subjects

Variable	Subject with diabetes (t=102)	Control subject (t=204)	p
Age y	56 ±11	55±8	36
Men %	26	26	≥99
BMI kg/m^2	26	25.5	≤.001
Heart rate beats per min	76±7	80±9	≤.001
Seated blood pressure mm Hg			
Systolic blood pressure	140±10	120±9	≤.001
Diastolic blood pressure	90 ±10	80 ±6	≤.001
Fasting blood glucose mg/dl	184±60	104±30	≤.001
Glycosylated haemoglobin %	8±2	5.6±2.5	≤.001
Triglyceride mg/dl	160±120	153±80	≤.001
Cholesterol mg/dl	220±55	170±40	≤.001

Figure 1 reveals the prevalence of orthostatic hypotension and postural dizziness in subjects with diabetes and nondiabetic control subjects. Subjects with diabetes had a significantly higher prevalence of orthostaticl hypotension and postural dizziness than nondiabetic control subjects (subjects with diabetes vs those without:orthostatic hypotension, 27.4% vs 15.4%, *P*<.001; postural dizziness, 22.5% vs 15.3%, P=.03).

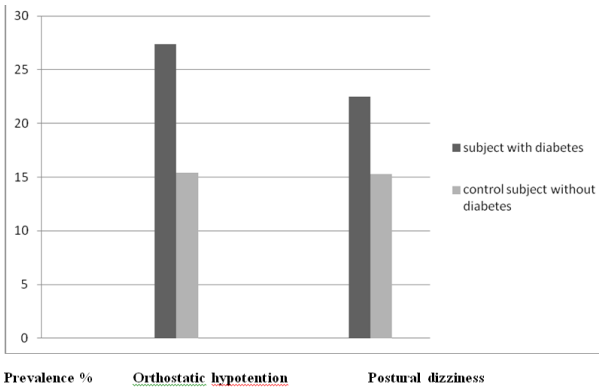

Figure No.1: Prevalence of orthostatic hypotension and postural dizziness in subjects with diabetes and nondiabetic control subjects.

Figure 2 illustrates the prevalence of postural dizziness in subjects with diabetes and nondiabetic control subjects with and without orthostatic hypotension. Among subjects with diabetes, those with orthostatic hypotension had a higher prevalence of postural dizziness than those without. However, only 30.8% of 18.5% subjects with both diabetes and orthostatic hypotension suffered from postural dizziness. Among nondiabetic control subjects, there was no significant difference in the prevalence of postural dizziness between those with and those without orthostatic hypotension.

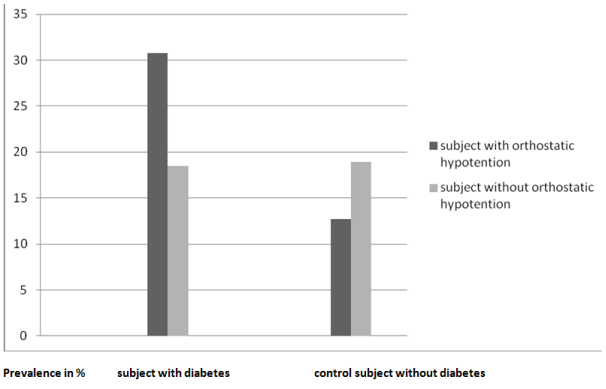

Figure No.2: Prevalence of postural dizziness in subjects with diabetes and nondiabetic control subjects with and without orthostatic hypotension

To examine the relationship between orthostatic hypotension and postural dizziness, the outcome variable was orthostatic hypotension and the predictor variables included postural dizziness and other clinical variables in multiple logistic regression analysis . For total study populations, the predictor variables included postural dizziness, age, BMI; plasma cholesterol, triglyceride, and creatinine levels; and diabetes mellitus, hypertension, cerebrovascular disease, and use of insulin or oral hypoglycemic and antihypertensive agents. The results show that an independently positive correlation existed between orthostatic hypotension and the following variables: age (*P*=.005), diabetes mellitus (*P*=.005), and hypertension (*P*=.001). An increase in the number of these independently associated factors increased the likelihood of orthostatic hypotension. In subjects with diabetes, the predictor variables of multiple logistic regression included postural dizziness, age, BMI; plasma cholesterol, triglyceride, creatinine, and glycosylated hemoglobin levels; and duration of diabetes, diabetic retinopathy, hypertension, cerebrovascular disease, and use of insulin or oral hypoglycemic and antihypertensive agents. The results demonstrated that postural dizziness (*P*=.02), glycosylated hemoglobin levels (*P*=.002), hypertension (*P*=.002), and cerebrovascular disease (*P*=.04) were independently associated with postural hypotension. In nondiabetic control subjects, the predictor variables included postural dizziness, age, and BMI; plasma cholesterol, triglyceride, creatinine, and glycosylated hemoglobin levels; and hypertension, cerebrovascular disease, and use of antihypertensive agents. The results indicated that age (*P*=.01) and hypertension (*P*=.01) were independently related to orthostatic hypotension.

DISCUSSION

Diabetes mellitus was an independently associated factor of postural hypotension in our study, which is consistent with the literature.[1,3,19,32] Regarding the mechanism of orthostatic hypotension in diabetes, there is more commonly a neurogenic cause usually associated with efferent involvement of the baroregulatory reflex arc with damaged sympathetic vasoconstrictor fibers in the splanchnic bed, muscle, and skin.5 In contrast, diminished cardiac acceleration may play a lesser role in the development of orthostatic hypotension.[33-34]

Our patients with diabetes had a higher resting heart rate than nondiabetic control subjects, which is consistent with other reports. A higher resting heart rate is often observed in patients with diabetes, and this is due to cardiac vagal neuropathy. With progression of diabetic autonomic neuropathy, some patients experienced initial tachycardia that may be followed by a decreased heart rate and, ultimately, a fixed heart rate due to the progression of cardiac sympathetic nerve dysfunction. The increase in heart rate on standing results from the dual effects of inhibition in cardiac vagal tone and increase in sympathetic tone. The heart

rate change after standing in those subjects with orthostatic hypotension was lower than in those without because sympathetic abnormalities in patients with diabetes are detectable almost exclusively after cardiac vagal neuropathy is impaired. Although all of our subjects with postural hypotension, both with and without diabetes, had lower heart rate changes than those without orthostatic hypotension, the difference was not significant. This may be due to the high fatality rate in subjects with orthostatic hypotension[3 - 4] and the minor role of diminished cardiac acceleration in the development of orthostatic hypotension,[33 - 34] thus causing and underestimate in the relationship between orthostatic hypotension and heart rate change after standing.

Reported studies have revealed that poor glycemic control of diabetes mellitus, which is shown by increasing plasma glycosylated hemoglobin levels, was vulnerable to orthostatic hypotension.[23 - 24] In our patients with diabetes, plasma glycosylated hemoglobin was an independently positive factor correlated with orthostatic hypotension. Therefore, good glycemic control is important in the prevention of orthostatic hypotension in subjects with diabetes, which is also suggested in other reports.[1 ,23 - 24]

Duration of diabetes has often been perceived as an associated factor of orthostatic hypotension, but the evidence was sparse. The prevalence of orthostatic hypotension (the criteria of orthostatic hypotension with a systolic blood pressure change of 30 mm Hg or more) increased with duration of diabetes in a young group (aged 18-34 years).[24] However, our study and another report[23] showed that duration was not independently associated with orthostatic hypotension. Because porthostatic hypotension was associated with increased mortality,[3 - 4] the prevalence of orthostatic hypotension in survivors would be diminished.[24] This may be the partial explanation for the discrepancy between the prevalence of orthostatic hypotension and duration of diabetes.

The prevalence of orthostatic hypotension was 27.4% in our subjects with diabetes. Hilsted and Low[1] reported 2 studies on diabetes mellitus complicated with orthostatic hypotension in 19 (26%) of 73 patients and 7 (43%) of 16 patients. Tsutsu et all[23] reported on 157 (18%) of 886 cases of patients with diabetes. The variation was considered to be due to the referral bias.[1]

The literature has revealed that cerebrovascular disease is a risk factor associated with orthostatic hypotension,[10 - 11 ,19] because it may interrupt the central nervous system pathways that control autonomic reflexes.[32] Cerebrovascular disease was an independently associated factor of postural hypotension in our patients with diabetes. Our results suggest that hypertension is associated with orthostatic hypotension in subjects with diabetes and in nondiabetic control and total subjects as well, which is consistent with the findings of other studies[11,16,18,25]. Hypertension has been shown to be associated with impaired baroreflex sensitivity, which may be due to a decrease in vascular compliance and consequent diminution of baroreceptor stretch and relaxation during blood pressure changes. Moreover, an increase in blood pressure and the duration of hypertension may exacerbate the decline in baroreflex sensitivity, in part, causing orthostatic hypotension[20] Although the literature has shown that antihypertensive medication was related to orthostaticl hypotension,[10 ,19] our study and another report revealed that there was no significant association between orthostatic hypotension and antihypertensive medication. Masuo et al[35] showed that the incidence of orthostatic hypotension decreased significantly followed by decreasing blood pressure and normalizing blood pressure with the use of antihypertensive drugs (especially calcium channel blockers, β-blockers, and angiotensin-converting enzyme inhibitors) in elderly patients with hypertension. This may be a partial explanation for the dissociation between orthostatic hypotension and antihypertensive medication. Another factor could be due to an underestimation in a cross-sectional study if a past occurrence of a treatment adverse effect or related symptom led to an adjustment of the treatment regimen.

The mechanism of postural dizziness remains obscure and may be heterogeneous.[12] Some reports have suggested orthostatic hypotension or cerebral ischemia may be involved in postural dizziness,[12- 13] and others have suggested vestibular dysfunction, vision impairment, and disorders in the proprioceptive system may be also involved.[15,] Thus, orthostatic hypotension is just 1 of the causes of postural dizziness, and it is not surprising that only 19 (32.8%) of 58 subjects with diabetes and orthostatic hypotension suffer from postural dizziness. This is consistent with other reports suggesting that orthostatic hypotension may be a cause of postural dizziness, but most subjects with orthostatic hypotension in the studies of the elderly[16 ,18] did not suffer from postural dizziness. Thus, the sensitivity was low for the diagnosis of orthostatic hypotension based solely on the presence of postural dizziness relative to the diagnosis based on the orthostatic blood pressure changes. Therefore, orthostatic hypotension cannot be clinically determined just from the presence of postural dizziness.

CONCLUSION

The prevalence of orthostatic hypotension and postural dizziness in patients with diabetes was higher than in nondiabetic control subjects. Only 32.8% of subjects with both diabetes and orthostatic hypotension suffered from postural dizziness. Age, diabetes mellitus, and hypertension were independently associated with orthostatic hypotension. Plasma glycosylated hemoglobin levels, postural dizziness, hypertension,

and cerebrovascular disease are independent determinants of orthostatic hypotension in subjects with diabetes. Clinically, older adults and patients with diabetes mellitus or hypertension should receive regular monitoring of supine and upright blood pressure changes. Good glycemic control is important in preventing orthostatic hypotension in patients with diabetes. Orthostatic hypotension was associated with postural dizziness in subjects with diabetes, but it cannot be diagnosed clinically just from the postural dizziness because of the low sensitivity in the diagnosis of orthostatic hypotension based only on postural dizziness relative to the diagnosis based on postural systolic blood pressure changes.

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