# Transcranial Doppler ultrasound assessment of intracranial hemodynamics in patients with type 2 diabetes mellitus

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BACKGROUND: Diabetics have a 3-fold risk for cardiovascular diseases compared with non-diabetics. This study was designed to evaluate cerebral hemodynamic changes related to type 2 diabetes mellitus (DM) with transcranial Doppler ultrasonography (TCD). TCD is a highly sensitive and specific method of quick bedside assessment of cerebrovascular circulation hemodynamics.

PATIENTS AND METHODS: In a prospective study, we compared a group of 100 patients with the diagnosis of type 2 diabetes mellitus (aged 48 to 67 years) and an age- and sex-matched control group of 100 healthy subjects without diabetes mellitus. We measured flow velocities (Vm) and the Gosling pulsatility index (PI) of the middle cerebral artery (MCA).

RESULTS: The rate of TCD abnormalities was significantly higher in diabetic patients than in healthy control subjects (55% vs. 11%, $P<0.05$). The PI was significantly higher in diabetic patients than in healthy controls ($P<0.001$). Atherosclerotic changes were found in 34.0% and 71.4% of patients suffering from diabetes for <5 and ≥5 years, respectively.

CONCLUSION: This study suggests that TCD is a useful marker for the detection of diabetic cerebrovascular changes. The duration and type of diabetes were found to have an impact on the development of pathologic cerebrovascular changes.

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*Accepted for publication*
*May 2005*

Ann Saudi Med 2005;25(6):486-488

Diabetes mellitus is a major independent risk factor for cerebrovascular disease (CVD), especially for ischemic stroke. After adjustment for age, blood pressure, cigarette smoking and cholesterol level, diabetics have a 3-fold risk for cardiovascular diseases compared with non-diabetics. This also applies to cardiovascular death, coronary heart disease and stroke.[1-5] Transcranial Doppler sonography (TCD) is a modern and sophisticated diagnostic procedure that enables visualization of hemodynamic changes in the basal cerebral arteries in real time and the recording of changes in cerebral perfusion in various physiological and pathophysiological states.[6-11] TCD is a highly sensitive and specific method for quick bedside assessment of cerebrovascular circulation hemodynamics.[12] Hemodynamic disturbance worsens brain artery autoregulation and disturbs development of collateral circulation and compensatory flow. The aim of the study was to evaluate the Doppler characteristics of patients with diabetes mellitus compared with healthy control subjects.

## Patients and Methods

This prospective study was carried out at the General Hospital Slavonski Brod between January to December 2003. The study included a group of 100 patients aged 48-67 years, with the diagnosis of diabetes mellitus, and an age- and sex-matched control group of 100 healthy subjects. Diabetic patients were divided into two subgroups according to the duration of diabetes (<5 and ≥5 years). Study patients had no risk factors for cerebrovascular disease other than type 2 DM. Healthy controls had no risk factors for cerebrovascular disease, including smoking, hypertension, dyslipidemia, obesity and diabetes. Study patients were treated with oral antidiabetic drugs. Study patients had no signs of cerebrovascular disease and were without anatomic variation of the circle of Willis at enrollment. TCD was performed by leaning a pulsating ultrasound 2 MHz (Transscan 30 EME, Uberlingen, Germany) probe against the temporal windows, and screening the flow in the blood vessels of the circle of Willis according to standard criteria. A hemodynamic chart was designed, the frequency of the mean blood flow velocity spectra (MBFV; systolic, diastolic and mean) was analyzed, and sound phenomena and flow disturbances in terms of turbulence, stenosis or occlusion were recorded. We measured flow velocities (Vm) and the Gosling pulsatility index (PI) of the middle cerebral artery (MCA) in patients and healthy controls.[13,14] The normal value of the PI is from 0.6 to 1.1; arterial stenosis is less than 0.6 and a value above 1.1 indicates attenuation of flow. Criteria for stenosis of the MCA are a significant focal mean flow velocity increase (MFV >80 cm/s), and/or a peak systolic velocity increase (PSV <140 cm/s), and/or a interhemispheric MBFV difference >30 cm/s in adult. Additional findings may include turbulence or disturbed flow distal to the stenosis, increased unilateral anterior cerebral artery (ACA) MFV indicating compensatory flow diversion. This finding may also indicate A1 ACA or an internal carotid artery (ICA) bifurcation stenosis with a side-to-side ACA MFV ratio >1.2, a low-frequency noise produced by nonharmonic covibrations of the vessel wall and musical murmurs due to harmonic covibrations producing pure tones.[6] On statistical analysis, the proportion test was used.

## Results

In the study population of 100 patients (46 men, 54 women) with diabetes mellitus type 2 (aged 48 to 67 years, mean 58±2 years) and an age- and sex-matched control group of 100 healthy subjects without diabetes mellitus, TCD investigation showed two specific types of hemodynamic changes in diabetic patients. One was attenuation of the cerebral spectra and deceleration of MBFV in all or most of the arteries of the circle of Willis, which indicates cerebral microangiopathy. The other change was acceleration of MBFV, turbulence and a pathologic sound phenomena in some arteries of the circle of Willis, which indicates atherosclerotic plaques and stenosis of arteries of the circle of Willis or macroangiopathy. We found a statistically significantly higher rate of abnormalities in diabetic patients than in the control group of healthy subjects (55% vs. 11%; $P<0.05$), (Table 1). The PI was significantly higher in diabetic patients than in healthy controls ($P<0.001$).

Table 1. Transcranial Doppler ultrasound (TCD) examination of diabetic patients and healthy control subjects.

| | Healthy controls (n=100) | Diabetic patients (n=100) |
|---|---|---|
| Normal TCD (%) | 89 | 45 |
| Abnormal TCD (%) | 11 | 55 |

$P<0.001$ healthy controls vs. diabetic patients

The type of diabetes plays a prominent role in the development of cerebrovascular disease in diabetic patients as well as in the character of these lesions. Comparison of the duration of diabetes and changes in cerebral hemodynamics in diabetic patients produced interesting results as well. In the group of 44 diabetics with diabetes duration of up to 5 years, signs were observed in 34% of patients. In the group of 56 diabetics with diabetes duration of ≥5 years, angiopathy was present in 71.4% of patients. Pathologic atherosclerotic lesions of cerebral arteries were found in 34% of diabetic patients with diabetes duration of <5 years and in 71.4% of those with diabetes duration of ≥5 years. These results yielded a statistically significantly higher rate of pathologic cerebral artery changes in patients with diabetes duration of ≥5 years ($P<0.05$). In the control group, angiopathy was detected in 11% of the subjects (Table 2).

## Discussion

Diabetes mellitus is one of the most important risk factors for CVD.[1,15] In the Framingham study, the incidence of stroke in diabetic patients aged 45-74 years was 2.5- to 3.5-fold that found in nondiabetics.[15] In diabetics, the risk of stroke is twofold that in nondiabetics[16] and diabetic patients are at a higher risk of stroke recurrence.[17] Diabetes mellitus is a

Table 2. Proportion of patients with cerebral hemodynamic impairments according to duration of diabetes mellitus.

| | Angiopathy (%) |
|---|---|
| DM <5 years (n=44) | 34 |
| DM ≥5 years (n=56) | 71.4 |
| Healthy controls (n=100) | 11 |

*P*<0.05 DM <5 years vs. DM ≥5 years

metabolic disease involving all arteries and is frequently associated with stroke development along with peripheral vasculopathy and coronary disease.[15-18] The mechanism of atherosclerotic changes in diabetic patients has not been fully elucidated, but the following causes have been proposed: a decrease in HDL cholesterol, proliferation of smooth muscle cells, changes in the metabolism of glucosaminoglycans, increased level of thromboxane, decreased prostacyclines, and blood coagulation impairment. Insulin stimulates smooth muscle cell proliferation in the arterial wall and the activity of LDL receptors.[19] In our study, we found a significant relationship between the duration of diabetes and cerebral hemodynamic disturbances. In the group of diabetic patients with a disease duration of <5 years atherosclerotic changes were more common than in patients with a duration ≥5 years (71.4% vs. 34.0%).

The results of our study showed that the prevalence of cerebral hemodynamic abnormalities was statistically significantly higher in diabetic patients as compared with healthy control subjects without DM. The duration of diabetes play an important role in the development of pathologic changes in cerebral vessels. On the other hand, duration of diabetes was found to predict the development of atherosclerotic processes in brain vessels. In all our diabetic patients, the signs of cerebral angiopathy, affecting cerebral perfusion and probably gradually leading to collapse of cerebral autoregulation, were seen in these patients. Compared to Elmore and al.[20] we studied a younger population without risk factors other than type 2 DM for development of cerebrovascular disease. The duration of type 2 DM reflected significantly on hemodynamic disturbance and confirms the importance of DM as a main risk factor for development of cerebrovascular disease.

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