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Comparison study of clinical presentation and risk factors for cerebrovascular stroke in diabetic versus nondiabetic patients

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Abstract

Background: Diabetes and stroke prevalence rates are increasing worldwide, and both are major human health threats causing disability and death. Diabetes is a well-known independent risk factor for stroke. In addition, diabetes increases the prevalence of other stroke risk factors; however, few studies evaluate whether diabetes may influence stroke presentation.

Aim of the work: This study was conducted to assess the risk factors and clinical presentation of stroke in patients with and without diabetes.

Patients and methods: This cross-sectional study was conducted on 200 patients with radiologically confirmed acute cerebrovascular stroke, selected from tertiary care hospitals in Alexandria, Egypt. They were divided into 2 groups: group 1: 100 patients with diabetes for more than 5 years and group 2: 100 nondiabetic patients. All patients were evaluated for risk factors, stroke types, and clinical presentation.

Results: Compared with nondiabetic patients, diabetic patients with stroke had a significantly higher prevalence of hypertension ($p = 0.031$) and dyslipidemia ($p = 0.016$) and higher incidence of ischemic stroke ($p = 0.030$), and they were more likely to present with motor deficit ($p = 0.045$) and dysarthria ($p = 0.048$). There was a modest difference between diabetic and nondiabetic group regarding OCSP ischemic stroke subtypes, but it was non-significant.

Conclusion: There was a significant difference in stroke risk factors, pathological types, and presentation between diabetic and nondiabetic patients, but not in ischemic stroke anatomical subtypes.

Keywords: Diabetes, Cerebrovascular stroke, Dyslipidemia

Introduction

There has been a significant increase in diabetes worldwide. Diabetes increases the risk for stroke about 4 times [1]. How diabetes leads to stroke is multifactorial. The oxidative stress, inflammatory condition, endothelial dysfunction, accelerated atherosclerosis, and hypercoagulability caused by hyperglycemia contribute to micro and macro-vascular damage which therefore enhance the risk for different stroke subtypes [2]. Besides the well-recognized independent effect of diabetes in developing stroke, diabetes also is usually associated with other stroke risk factors such as hypertension, hyperlipidemia, and obesity [1]. Effective prevention strategy is a must as long as diabetic patients are at higher risk for developing stroke and subsequent consequences of disability and mortality.

Although the well-established risk of diabetes for cerebrovascular stroke, it is not clearly known whether people with diabetes are more vulnerable to suffer specific stroke pattern or different clinical presentations compared to nondiabetic people.

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Several studies demonstrated that diabetic patients have higher prevalence of ischemic stroke and the same or lower prevalence of hemorrhagic stroke in comparison with patients without diabetes [3–5]. Studies also revealed diabetic patients have a higher prevalence of strokes in the posterior circulation [4–6]. Other studies found lacunar infarctions prevalence as a whole was not different between diabetic and nondiabetic, but diabetic patients may have higher incidence of multiple lacunar infarctions [7, 8].

These differences in stroke types and anatomic location may happen due to different stroke pathophysiologies and may be associated with particular clinical presentations of stroke in diabetic patients which requires special attention for early diagnosis and treatment.

Aim of the work

To evaluate the risk factors and clinical presentation of stroke in patients with and without diabetes

Patients and methods

This prospective study was conducted on 200 patients divided into two groups: group 1: 100 patients with diabetes of more than 5-year duration and group 2: 100 nondiabetic patient's age and sex matched. All patients above 18 years old were diagnosed with radiologically proved acute cerebrovascular stroke either ischemic or hemorrhagic and were admitted to tertiary care hospitals.

Informed consent was taken from all patients, and all patients were assessed for age, history of previous diagnosis of diabetes and intake of antidiabetic medications, duration of diabetes in the diabetic patients, modalities of stroke presentation, and stroke risk factors including smoking, AF, dyslipidemia, family history of cardiovascular events, and history of hypertension and its duration. Full clinical and neurological examination were done, and laboratory investigations including lipid profile, random blood glucose, HbA1c, blood urea, and serum creatinine were performed for all patients.

Clinical classification for stroke patients was performed using the Oxfordshire Community Stroke Project (OCSP) classification [9], which is a simple method that is widely used to categorize clinical stroke syndromes and proved helpful to predict the risk of neurological complications (Table 1).

Exclusion criteria

Patients with end-stage organ failure, severe acute infection or inflammation, and severe chronic illness, patients known to have severe uncontrolled hypertension, and patients with stress hyperglycemia at presentation (*RBG* > 200 mg/dl, HbA1c < 6.5%) were excluded.

Ethical approval was obtained from our institution research ethics committee. Ethical approval serial number is 0105519 (date of approval 16 May 2018). Informed consent was obtained from all participants included for participation in our study.

Methods

Patient's demographics and medical history were obtained from the patients file during the patient's hospital stay.

Laboratory assessment

Whole blood samples were collected after an overnight fast from all 200 patients. The blood collected was split into three portions: the first portion was used to measure random blood glucose and collected in Na fluoride containing vacutainer tubes. The second portion was collected on EDTA containing vacutainer tubes to measure glycated hemoglobin (HbA_1c %). The third portion of blood was centrifuged to separate serum for the measurement of lipid profile.

Table 1 Oxfordshire Community Stroke Project classification

OCSP term	Clinical features	Vascular basis
Total anterior circulation syndrome (TACS)	•Hemiparesis AND •Higher cortical dysfunction (dysphasia or visuospatial neglect) AND •Homonymous hemianopia	Usually proximal middle cerebral artery (MCA) or ICA occlusion
Partial anterior circulation syndrome (PACS)	•Isolated higher cortical dysfunction OR •Any two of hemiparesis, higher cortical dysfunction, hemianopia	Usually branch MCA occlusion
Posterior circulation syndrome (POCS)	Isolated hemianopia (posterior cerebral artery (PCA)) brainstem or cerebellar syndromes	Occlusion of vertebral, basilar, cerebellar, or PCA vessels
Lacunar syndrome (LACS)	• Pure motor stroke OR • Pure sensory stroke OR • Sensorimotor stroke OR • Ataxic hemiparesis OR • Clumsy hand-dysarthria	Small penetrating artery occlusion, usually in lenticulostriate branches of MCA, or supply to brainstem or deep white matter

All routine work analyses were measured in the same day of the blood collection.

Statistical analysis

Collected data were analyzed by using IBM SPSS software package version 20.0. (Armonk, NY, USA: IBM Corp.) Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution, and quantitative data were described using range (minimum and maximum), mean, standard deviation, median, and interquartile range (IQR). Significance of the obtained results was judged at the 5% level.

Results

The baseline characteristics for the two studied groups are shown in Table 2. Dyslipidemia and hypertension were significantly higher in the diabetic group. However, hypertension duration was significantly higher in the nondiabetic group.

Table 3 shows the biochemical and clinical parameters of the two studied groups at presentation. Systolic and diastolic blood pressure, hypertension grade, and heart rate were significantly higher in the diabetic group. Also, lipid profile, markers of renal impairment, HbA1c, and random blood sugar were significantly higher in the diabetic group compared to the nondiabetic one.

Table 4 shows the clinical presentation of stroke in the diabetic and non-diabetic group. Diabetic patients had a significantly higher prevalence of motor deficit and dysarthria at presentation compared to non-diabetic.

According to the Glasgow Coma Scale (GCS), the diabetic group had GCS ranged from 3 to 15 with a mean of 13.27 ± 2.29, and the nondiabetic group GCS ranged from 3 to 15 with a mean of 12.42 ± 3.28. There was no significant difference between the two groups ($p = 0.127$).

Stroke severity was assessed by the National Institute of Health stroke scale, and we found in the diabetic group 16 patients had mild stroke severity, 60 patients had moderate stroke severity, 16 patients had moderate to severe stroke, and 8 had sever stroke; the mean was 11.07 ± 5.71 indicating moderate neurological impairment. While in the nondiabetic group there were 14 patients had mild stroke severity, 57 patients had moderate stroke severity, 17 patients had moderate to severe stroke, and 12 had severe stroke; the mean was 11.79 ± 6.11 which also indicates a moderate neurological impairment, and there was no statistical significance between both groups ($p = 0.465$).

Figure 1 shows the difference between the two groups in pathological stroke subtypes as the diabetic group had a significantly higher prevalence of ischemic stroke and lower hemorrhagic stroke.

Figure 2 shows the distribution of the clinical types of ischemic stroke in both groups according to the Oxfordshire Community Stroke Project classification by clinical assessment and radiological confirmation. Diabetic patients had more strokes in the posterior circulation and less total anterior circulation, but this difference was non-significant.

Discussion

Our findings in the present study confirm what had been reported previously about the association between hypertension and dyslipidemia with diabetes mellitus as hypertension in the present study was more frequent in the diabetic group (77% diabetic versus 63%

Table 2 Baseline characteristics for the studied cohort

Risk factors	Diabetic ($n = 100$)		Nondiabetic ($n = 100$)		Test of sig.	*p*
Smoking	44	44.0	48	48.0	$\chi^2 = 0.322$	0.570
AF	26	26.0	31	31.0	$\chi^2 = 0.613$	0.434
Dyslipidemia	62	62.0	45	45.0	$\chi^2 = 5.808$*	0.016*
Family history of cardiovascular event	40	40.0	35	35.0	$\chi^2 = 0.533$	0.465
HTN	**77**	**77.0**	**63**	**63.0**	$\chi^2 = 4.667$*	0.031*
Duration of HTN						
Min.–max.	1.0–40.0		3.0–30.0		$U = 1643.5$*	0.001*
Mean ± SD	9.56 ± 5.78		13.22 ± 7.09			
Median (IQR)	9.0 (5.0–12.0)		12.0 (8.5–16.0)			
Ages (years)	44.0–88.0		33.0–88.0		$t = 1.529$	$P = 0.128$
Min.–max.	62.05 ± 8.83		64.16 ± 10.61			
Mean ± SD	61.0 (56.0–68.0)		65.0 (56.0–68.0)			
Median (IQR)						

Table 3 Biochemical and clinical parameters at presentation

	Diabetic ($n = 100$)		Nondiabetic ($n = 100$)		Test of sig.	*p*
	No.	**%**	**No.**	**%**		
SBP						
Min.–max.	130.0–240.0		130.0–260.0		$t = 2.057$*	0.041*
Mean ± SD	177.5 ± 27.76		169.2 ± 29.30			
Median (IQR)	170.0 (155.0–195.0)		160.0 (150.0–180.0)			
DBP						
Min.–max.	80.0–140.0		70.0–150.0		$t = 2.742$*	0.007*
Mean ± SD	102.9 ± 15.26		96.95 ± 15.42			
Median (IQR)	100.0 (90.0–110.0)		90.0 (90.0–100.0)			
HTN grade						
I	20	20.0	30	30.0	$\chi^2 = 9.061$*	0.028*
II	23	23.0	32	32.0		
III	53	53.0	32	32.0		
High normal	4	4.0	6	6.0		
HR						
Min.–max.	60.0–140.0		56.0–160.0		$U = 3566.50$*	< 0.001*
Mean ± SD	82.47 ± 15.60		91.72 ± 21.0			
Median (IQR)	80.0 (72.50–89.0)		86.0 (77.0–108.0)			
TC						
Min.–max.	123.0–312.0		125.0–280.0		$t = 4.564$*	< 0.001*
Mean ± SD	214.1 ± 39.61		189.3 ± 37.02			
Median (IQR)	210.0 (187.0–235.0)		185.5 (160.0–215.0)			
TGs						
Min.–max.	90.0–289.0		89.0–215.0		$t = 3.781$*	< 0.001*
Mean ± SD	154.2 ± 35.69		136.0 ± 32.35			
Median (IQR)	153.0 (130.5–172.0)		129.0 (109.0–162.0)			
LDL-C						
Min.–max.	72.80–194.2		65.0–195.0		$t = 2.658$*	0.008*
Mean ± SD	116.2 ± 28.1		105.8 ± 27.25			
Median (IQR)	110.0 (95.3–136.5)		101.5 (85.0–119.7)			
HDL-C						
Min.–max.	31.70–85.0		36.0–80.0		$t = 2.453$*	0.015*
Mean ± SD.	49.77 ± 12.06		53.76 ± 10.86			
Median (IQR)	47.55 (40.0–56.5)		54.0 (45.0–60.4)			
Creatinine						
Min.–max.	0.40–3.73		0.20–3.40		$U = 3728.0$*	0.002*
Mean ± SD	1.36 ± 0.55		1.17 ± 0.63			
Median (IQR)	1.30 (1.0–1.5)		1.10 (0.77–1.5)			
Urea						
Min.–max.	13.0–124.0		17.0–148.0		$U = 4126.50$*	0.033*
Mean ± SD	45.87 ± 23.32		41.54 ± 23.97			
Median (IQR)	39.0 (32.0–54.0)		32.60 (26.0–48.0)			
HbA1c						
Min.–max.	6.80–11.0		4.50–6.0		$t = 29.298$*	< 0.001*
Mean ± SD	8.41 ± 1.04		5.16 ± 0.37			
Median (IQR)	8.10 (7.6–9.1)		5.10 (4.9–5.5)			

Table 3 (continued)

	Diabetic ($n = 100$)		Nondiabetic ($n = 100$)		Test of sig.	*p*
	No.	%	No.	%		
RBS						
Min.–max.	210.0–477.0		85.0–180.0		$U = 0.0$*	< 0.001*
Mean ± SD	292.52 ± 62.61		121.41 ± 24.39			
Median (IQR)	280.50 (243.5–322.5)		117.50 (99.5–137.5)			

Table 4 Comparison between the two studied groups according to presentation

Presentation	Diabetic ($n = 100$)		Nondiabetic ($n = 100$)		χ^2	*p*
	No.	%	No.	%		
DLC	42	42.0	45	45.0	0.183	0.669
Hemiparesis	87	87.0	76	76.0	4.013*	0.045*
Hemihypoesthesia	16	16.0	18	18.0	0.142	0.707
Aphasia	28	28.0	31	31.0	0.216	0.642
Dysarthria	58	58.0	44	44.0	3.922*	0.048*
Ataxia	7	7.0	4	4.0	0.866	0.352
Mouth deviation	34	34.0	31	31.0	0.205	0.651
Dysphagia	31	31.0	28	28.0	0.216	0.642
Headache	6	6.0	11	11.0	1.607	0.205
Vomiting	5	5.0	7	7.0	0.355	0.552

nondiabetic, $p = 0.031$). A large European prospective study by Megherbi et al. [4] showed that hypertension prevalence was significantly higher in diabetic patients with stroke in comparison with nondiabetic ($p < 0.001$). A similar result was also obtained from Karapanayiotides et al. [10] study in the Lausanne Stroke Registry ($p < 0.001$). In Laio et al. [11] nested cohort study among 221,254 patients with stroke, diabetic patients had a higher proportion of hypertension than nondiabetic ($p = < 0.0001$). Snarka et al. [12] study demonstrated that hypertension was found more frequently in diabetic patients with ischemic stroke compared to nondiabetic patients ($p = 0.041$), whereas in patients with hemorrhagic stroke, HTN was found in 100% of diabetic patients versus 84.6% nondiabetics ($p = 0.215$). Several studies assert hypertension is the single most important risk factor for hemorrhagic stroke [13, 14].

In fact, there are abundant evidence that diabetes and hypertension are strongly associated. In type 1 diabetes, diabetic nephropathy is the main factor in the pathogenesis that led to development of hypertension. While in type 2 diabetes and insulin resistance, hypertension is more frequent and usually occur as a part of the metabolic syndrome [15]. In our study, these factors were obviously present in the diabetic group, as the biomarkers of diabetic nephropathy and lipid profile were significantly higher compared to nondiabetic, which explain this higher prevalence of hypertension in the diabetic group.

Dyslipidemia was present in 62% of diabetic patients versus 45% of the nondiabetic patients ($p = 0.016$). This finding was consistent with several studies. Karapanayiotides et al. [10] demonstrated that hypercholesterolemia was significantly higher in diabetic patient compared to nondiabetic ($p < 0.0001$). Likewise, in Laio et al. [11] study, hyperlipidemia was more prevalent in stroke patients with diabetes, $p < 0.0001$. Diabetes and insulin resistance affect plasma lipoproteins production and clearance causing hyperlipidemia and thereby atherosclerotic lesions [15, 16].

Regarding other risk factors, our study revealed no significant difference between diabetic and nondiabetic in prevalence of current smoking (44% vs 48%, respectively), atrial fibrillation (26% vs 31%), and family history of cardiovascular events (40% vs 35%); these findings are almost similar to previous studies. In Chi and Lu [17] study, there was no significant difference between ischemic stroke patients with and without diabetes in atrial fibrillation, smoking, and family history of stroke. Megerbi et al. [4] reported no difference between diabetic and nondiabetic patients in prevalence of smoking, but atrial fibrillation was significantly less frequent in diabetic patients ($p =$

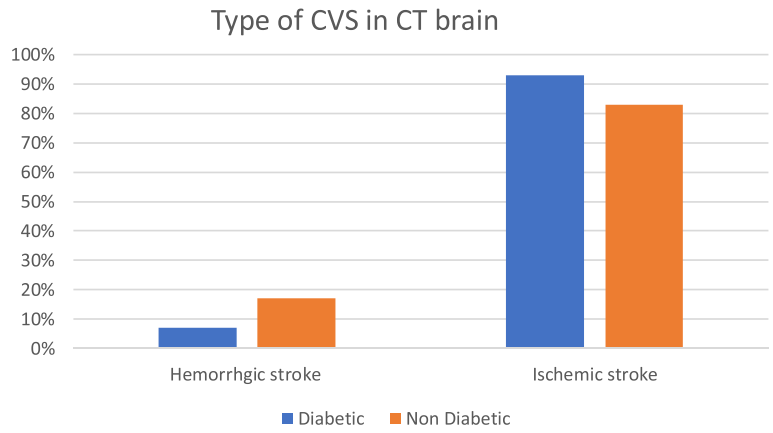

Fig. 1 Comparison between the two studied groups according to type of CVS in CT brain

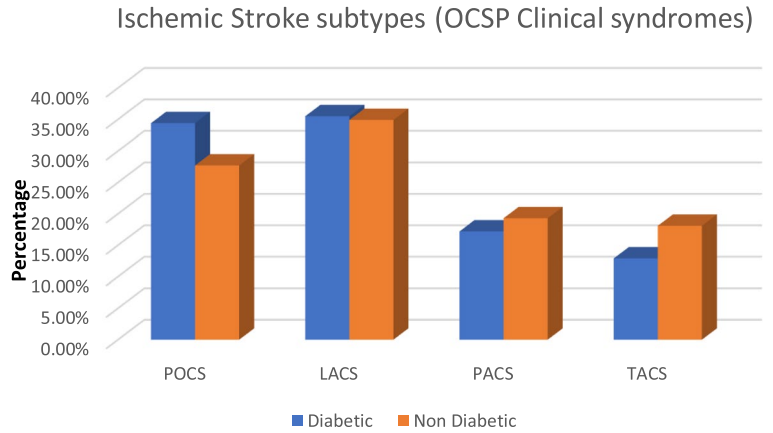

Fig. 2 Comparison between the two studied groups according to ischemic stroke subtypes (OCSP clinical syndromes). POCS, posterior circulation syndrome; LACS, lacunar syndrome; PACS, partial anterior circulation syndrome; TACS, total anterior circulation syndrome

0.012). However, another study considered diabetes as an independent risk factor for atrial fibrillation. But the causing mechanisms is not well known and supposed to be due to autonomic dysfunction [18]. The reason for this discrepancy may be explained by the suggestion of some studies that the higher association between diabetes and atrial fibrillation is related to longer diabetes duration and boor glycemic control [19].

In the present study, ischemic stroke prevalence was significantly higher in diabetic patients compared with nondiabetic (93% vs 83%), while hemorrhagic stroke was less frequent in diabetics (7% diabetic vs 17% nondiabetic) ($p = 0.030$). These results were consistent with Laio et al. [11] ($p < 0.0001$), Meghrebi et al. [4] ($p < 0.001$), and also Snarska et al. study [12] ($p = 0.001$).

The higher incidence of ischemic stroke in diabetic patients can not be considered due to a protective impact of diabetes against hemorrhagic stroke since several studies suggest diabetes mellitus is an independent risk factor for hemorrhagic stroke [20, 21]. Later studies demonstrated that dysfunctional angiogenesis and neovascularization occurring with diabetes may have a role in this increased incidence observed [22]. However, the atherogenic effect of diabetes, thickening of the basement membrane in addition to the hypercoagulability state [23, 24], may outweigh that effect increasing the risk for hemorrhage.

In the present study, there were some differences between diabetic and nondiabetic stroke subtypes with higher prevalence of POCS in diabetic patient, but this was non-significant. Unlike our study, Megherbi et al. found a difference in ischemic stroke subtypes ($p = 0.031$) with more LACS syndromes and POCS in diabetic patients. Other studies also reported the higher prevalence of posterior circulation infarctions in diabetics [25–27], and they suggest that diabetes may cause sever atherosclerosis in the posterior circulation more than the anterior circulation [26, 27]. The reason why

this difference was non-significant in our study may be explained by the small number of patients However, this difference is needed to be explained and to be further investigated on pathophysiological basis.

Regarding clinical presentation, the present study showed that diabetic patients were commonly presented with hemiparesis and dysarthria. Megherebi et al. [4] also reported similar findings as motor deficit and dysarthria were more common in the diabetic group. Moreover, diabetic patients were less frequently present with dysphagia and aphasia.

Good knowledge of stroke symptoms is important for patients and healthcare providers in order to make a rapid diagnosis and therapeutic intervention. Despite studies suggest diabetic patients may be more susceptible to particular types of strokes and may have different stroke pathogenesis, there is a paucity of studies investigating if this difference contributes to specific or nontraditional stroke symptoms in diabetic patients. How this difference will affect outcome and prognosis is needed to be examined.

In the present study, diabetic patients did not present with nontraditional symptoms, but particular symptoms were significantly higher than nondiabetic patients. Megherbi et al. [4] findings also were almost similar to ours which supports the hypothesis.

Conclusion

The present study showed a significant difference in stroke risk factors, pathological types, and presentation between diabetic and nondiabetic patients. Dyslipidemia and hypertension were significantly higher in the diabetic group. However, hypertension duration was significantly higher in the nondiabetic group. Moreover, diabetic patients had a significantly higher prevalence of motor deficit and dysarthria at presentation compared to nondiabetic. In addition, diabetic patients had a significantly higher prevalence of ischemic stroke and lower hemorrhagic stroke.

Abbreviations

RBS: Fasting blood sugar; HbA1c: Hemoglobin A1c; HTN: Hypertension; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; TC: Total cholesterol; TG: Triglycerides; DCL: Disturbed level of conciousness; AF: Atrial fibrillation.

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Authors' contributions

EY participated in formatting the design of the research, collected patients included in the study, data collection, statistical analysis of data, have drafted the work, wrote the manuscript, and final approval of the version to be published. KR has designed the research, substantively revised it, and approved the submitted version. SA conducted the laboratory work, participated in drafting the work, revised the manuscript, and approved the submitted version. SE was following the process of the study and interpretation of data, revised the manuscript, and approved the submitted version. The authors read and approved the final manuscript.

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Availability of data and materials

Data and material are available upon request.

Declarations

Ethics approval and consent to participate

This study was approved by the Research Ethics Committee, Faculty of Medicine, Alexandria University. Ethical approval serial number is 0105519 (date of approval 16 May 2018). Written and oral informed consent was obtained from all patients included in the study.

Consent for publication

Written informed consent for publication of their clinical details and/or clinical images was obtained from all participants included in study.

Competing interests

The authors declare that they have no competing interests.

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