

The Impact of Diabetes on Outcomes After Acute Ischemic Stroke: A Prospective Observational Study

Naveed Akhtar, MD,* Saadat Kamran, MD,* Rajvir Singh, PhD,†
Rayaz A. Malik, MRCP,‡ Dirk Deleu, FRCP,* Paula J. Bourke, PGD,*
Sujatha Joseph, MSc,* Mark D. Santos, MAN,* Deborah M. Morgan, BSc,*
Faisal M. Wadiwala, MD,* Reny Francis, MSc,* Blessy M. Babu, MBBS,*
Pooja George, MBBS,* Rumissa Ibrahim, MBBS,* Pablo Garcia-Bermejo, MD,* and
Ashfaq Shuaib, FRCPC*§

Background: Stroke in diabetics may delay recovery and increases the risk of early recurrence of stroke. We compared the outcomes of patients (with and without diabetes) admitted with an acute ischemic stroke (AIS) in the state of Qatar. *Patients and methods:* We prospectively compared the clinical presentation, complications, discharge outcome, and stroke recurrence at 90 days in patients with and without diabetes. *Results:* Five thousand two hundred twenty-eight stroke patients were admitted between January 2014 and December 2017. Two thousand nine hundred sixty-one had confirmed AIS, 1695 (57.2%) had diabetes, 429 (14.5%) had prediabetes and 873 (29.5%) had no diabetes. Comparing diabetic patients to prediabetic and nondiabetics, they were significantly older (58.5 ± 11.9 versus 54.0 ± 12.9 versus 49.5 ± 13.8 , $P = .0001$), had higher rates of hypertension (80.8% versus 67.4% versus 59.2%), previous stroke (18.0% versus 5.4% versus 6.2%), and coronary artery disease (12.9% versus 5.6% versus 5.0%; $P = .001$ for all). The percentage of patients with modified Rankin scale 3-6 at discharge (39.7% versus 32.6% versus 30.2%; $P = .0001$) and 90 days (26.7% versus 18.8% versus 21.4%, $P = .001$); 90-day mortality (6.2% versus 2.2% versus 5.2%; $P = .03$) and stroke recurrence (4.2% versus .7% versus 2.2%; $P = .005$) was significantly higher in diabetic patients. *Conclusions:* Patients with diabetes and AIS have more in-hospital complications, worse discharge outcomes, higher mortality and stroke recurrence at 90 days, compared to prediabetes and no diabetes.

Key Words: Diabetes—ischemic stroke—prognosis—recurrence—outcome
© 2018 National Stroke Association. Published by Elsevier Inc. All rights reserved.

INTRODUCTION

Diabetes mellitus (DM) and hyperglycemia are major risk factors for acute ischemic stroke (AIS).¹ Diabetes mediates its adverse effects on the vasculature through

diverse mechanisms, including greater endothelial injury, inflammation, and a heightened prothrombotic state.^{2,3}

Diabetes also alters the size and branching pattern of lenticulostriate arteries that may adversely affect the local circulation following acute stroke, leading to greater deficits

From the *The Stroke Program, The Neuroscience Institute, Hamad Medical Corporation, Doha, Qatar; †Department of Cardiology, Hamad Medical Corporation, Qatar; ‡Weill Cornell Medicine-Qatar, Education City, Qatar Foundation, Doha, Qatar; and §Department of Medicine (Neurology), University of Alberta Stroke Program, Edmonton, Alberta, Canada.

Received August 14, 2018; revision received September 24, 2018; accepted November 3, 2018.

Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Address correspondence to Ashfaq Shuaib MD FRCPC FAHA FAAN, University of Alberta Stroke Program, 7-112 CSB, 11350 - 83 Avenue, Edmonton, Alberta T6G 2R3, Canada. E-mails: ashfaq.shuaib@ualberta.ca, ashuaib@hamad.qa, kath.mckenzie@ualberta.ca.

1052-3057/\$ - see front matter

© 2018 National Stroke Association. Published by Elsevier Inc. All rights reserved.

<https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.11.003>

and delayed recovery.⁴ We have recently shown an increased prevalence of asymptomatic cerebrovascular small vessel disease (SVD) in Arabs compared to South Asians admitted with a stroke in Qatar.⁵ The prevalence of diabetes and metabolic syndrome are greatly increased in the Middle East and in South East Asia.⁶ There are no large prospective studies on the outcomes of AIS in relation to the status of glucose tolerance in the Middle East. Qatar has one of the highest rates of diagnosed⁷ and undiagnosed DM⁸ in the world and a diverse expatriate community, making it a unique population to study the effect of DM on stroke outcomes.⁹ We have undertaken a large prospective cohort study to assess the effect of DM on the type and severity of stroke, risk of immediate in-hospital complications, and 90-day recurrence of stroke and mortality in patients presenting with AIS.

Material and Methods

All patients admitted with a diagnosis of AIS to Hamad General Hospital (HGH), Qatar from January 1, 2014 through December 04, 2017, were included in the analysis from a hospital-based stroke-database. HGH is a Joint Commission International accredited 600-bed hospital, where 95% of all stroke patients in Qatar requiring hospital admissions are admitted. The stroke program, certified by the Joint Commission International, is equipped with all necessary laboratories, neuro-radiological and neuro-surgical facilities needed to manage patients with an acute stroke and has a 24-hour thrombolysis and thrombectomy service. Hyper-acute stroke patients are seen in the Emergency Department by the stroke team to ensure standardized management in relation to assessment and further management of stroke.

Patient Consent

This paper deals with anonymized data of subjects admitted to hospital stroke ward in the mentioned period of January 1, 2014 through December 04, 2017. This stroke database was set up to provide a base for various medical research and all data collected in this database are anonymized—and used only for statistical analysis and does not reveal any kind of personal information of patients. Therefore, this study did not require a consent form, as it is not a conventional clinical trial study.

Patient Characteristics

Patient characteristics including age, sex, nationality, medical comorbidities and prior medication, immediate Emergency Department care, door-to-needle time (for thrombolysis patients), National Institute of Health Stroke Scale (NIHSS) score, length of stay (LOS), neuroimaging, poststroke complications, in-hospital mortality, and recurrence were extracted from the HGH Stroke database. The modified Rankin scale (mRS) was assessed at discharge

and 90 days and patients were classified as having a good (mRS of $\leq 0-2$) or poor (mRS 3-6) outcome.

HbA1c was used according to the 2018 American Diabetes Association recommendations to categorize patients into those without diabetes ($<5.7\%$), prediabetes (5.7%-6.4%), and diabetes ($\geq 6.5\%$).¹⁰ Hypertension (HTN) on admission was defined as a systolic blood pressure greater than or equal to 140 mm Hg or a diastolic blood pressure greater than or equal to 90 mm Hg, or current treatment with antihypertensive drugs. Body mass index (in kg/m^2) was calculated; categorized as underweight ($<18.5 \text{ kg}/\text{m}^2$), normal weight (18.5-24.0 kg/m^2), or overweight/obese ($>24.0 \text{ kg}/\text{m}^2$).¹¹ Dyslipidemia was defined on the admission lipid profile or use of any lipid-lowering medication. Records of the common stroke-related complications, including aspiration pneumonia, urinary tract infection, bed-sores, and sepsis during hospitalization were collected from the HGH Stroke database.¹²

Patient Disposition

All patients admitted under the stroke service received acute care by a multidisciplinary stroke team following standardized stroke care protocols to minimize the risk of aspiration pneumonia, bladder infection, venous thrombosis, and pressure ulcers. The mechanism of stroke, severity at presentation, risk of complications, treatments received LOS in hospital, and the prognosis at discharge and 90 days were assessed. The stroke recurrence rate and mortality were determined by prearranged follow-up visits or phone interviews at day-90.

Data Collection and Analysis

All patients admitted with an acute stroke were enrolled and trained stroke coordinators prospectively entered data in the HGH Stroke database (Microsoft Office Access 2007 Database) after a confirmed diagnosis using the *International Classification of Disease, 10th Edition*, definitions (H34.1, I63.x, I64.x, I61.x, I60.x, G45.x).

Statistical Methods

Descriptive statistics in the form of mean \pm SD for interval variables and frequency with percentages for categorical variables are reported. The distribution of interval variables was assessed to use appropriate statistical tools. Student *t* tests between the 2 groups (recurrence/no recurrence) and One-Way ANOVA with post hoc (Bonferroni) for more than 2 groups were used to assess mean differences among groups. Chi-square tests were performed to assess for differences between categorical variables. Univariate and multivariate logistic regression analysis was done for recurrence of stroke at 90 days. Odds ratios, 95% CI with *P* values were presented with significant and important independent variables used for multivariate

analysis. Predictive probabilities were calculated using final multivariate model for area under the receiver operating characteristic (ROC) curve. Graphs are presented for important variables. A “*P*” value .05 (2-tailed) was considered significant. SPSS 21.0 statistical package was used for the analysis.

RESULTS

Patient Characteristics

A total of 5228 patients were admitted to HGH with a suspected stroke between January 2014 and December 2017. Of these, 2961 were included for analysis. Eighty-two percent were men, reflecting the high percentage of male expatriate workers in Qatar (<http://www.mdps.gov.qa/english/population>). The mean age of patients with ischemic stroke was 55.2 ± 13.3 years (range 19-105). Patients with DM were significantly older than those without diabetes (58.5 ± 11.9 versus 50.7 ± 13.4 years; $P = .001$). At admission, 47.4% (1404/2961) were already known to have diabetes, while 8.6% (255/2961) were diagnosed with diabetes and 14.5% (429/2961) with prediabetes on admission. Nearly 28.4% (471/1659) of diagnosed diabetic patients were on diabetic treatment at the time of stroke onset. Of these 10.9% (181/1659) were taking insulin and 21.9% (364/1659) were on oral anti-DM therapies. There was a significantly higher prevalence of HTN (80.8% versus 67.4 versus 59.2%; $P < .0001$), previous stroke (18.0% versus 5.4% versus 6.2%, $P < .0001$), and Coronary artery disease (CAD) (12.9% versus 5.6% versus 5.0%; $P < .0001$) in patients with diabetes compared to prediabetes and nondiabetes, respectively.

The risk factors, ethnicity, type and severity of stroke and treatment in patients with DM, prediabetes, and no diabetes are shown in [Table 1](#).

Complications Related to Acute Stroke During Admission

The rates of complications in the 3 groups are shown in [Table 1](#). A total of 272 medical complications occurred in 186 patients. The incidence of all complications (7.6% versus 4.9% versus 4.5%; $P = .004$), aspiration pneumonia ($P = .053$), urinary tract infection ($P = .02$), and sepsis ($P = .013$) were significantly greater in DM group compared to prediabetes and nondiabetes groups. Complications were seen at a higher frequency in patients with increasing age (62.2 ± 15.9 versus 54.8 ± 12.9 , $P < .0001$) and higher random blood sugar (RBS) (10.71 ± 5.5 versus 9.65 ± 5.2 , $P < .009$) and NIHSS (12.2 ± 7.3 versus 4.97 ± 4.8 , $P = .0001$) on admission. Even after exclusion of patients with complications ($n = 186$), the percentage of patients with greater disability (mRS of 3-6) at 90 days was significantly higher (35.6% versus 30.1% versus 27.3%, $P < .0001$) in diabetes group compared to prediabetes and nondiabetes groups.

Disability at Discharge and 90 Days

In 1339 (71.9%) patients, 90-day follow-up was done at follow-up visit in the stroke prevention clinic, while remaining (512/1860, 28.1%) patients through telephone calls. The percentage of patients with mRS of 3-6 at discharge (39.7% versus 32.6% versus 30.2%, $P < .0001$) and 90 days (26.7% versus 18.8% versus 21.4%, $P < .005$) was significantly greater in the DM group compared to prediabetes and nondiabetes groups ([Fig 1](#)). Disability was more severe with subcortical (lacunar) strokes at discharge ($n = 1466$; 30.7% versus 21.4% versus 19.4%, $P < .0001$) and 90 days (18.3% versus 9.7% versus 12.0%, $P < .006$). There was no difference in with cortical strokes when comparing diabetes group to prediabetes and nondiabetes groups at discharge and 90 days.

Mortality

There was no difference in the hospital mortality (2.6% versus 1.4% versus 2.2%, $P = .326$) within the 3 groups. However during the 90-day follow-up, there was a significant increase in mortality in the DM group compared to prediabetes and no diabetes (6.2% versus 2.2% versus 5.2%, $P = .033$, $n = 1860$; [Table 1](#)).

Risk of Recurrent Stroke

The overall rate of recurrent stroke during the study period was 3.1% (57/1860) 90 days after the index stroke. Of these, 4.2% had DM, .7% had prediabetes, and 2.2% no diabetes, $P < .005$ ([Fig 1](#), [Supplementary Table](#)). Recurrent strokes were more common in older patients (58.8 ± 13.0 versus 54.8 ± 13.1 , $P = .02$) and in those of Arab ethnicity (5.4% versus 1.2%, $P < .0001$). A history of DM ($P = .003$), HTN ($P = .034$), previous stroke ($P = .0001$), CAD ($P = .03$), and AF ($P = .032$) were all associated with a significantly higher risk of recurrent stroke. Body mass index ($P = .028$) and HbA1c ($P = .006$) were higher and total cholesterol ($P = .0001$) and low density lipoprotein ($P = .0001$) were significantly lower, attributed to the prior use of statins (47.4% versus 12.8%, $P < .0001$) in the group with recurrent stroke ([Supplementary Table](#)). Patients with recurrent stroke had greater disability (mRS 3-6) at discharge (54.4% versus 27.9%, $P < .0001$) ([Supplementary Table](#)).

Multivariate Analysis

Outcome at 90 Days

Significant variables at univariate analysis were used for multivariate logistic regression analysis to assess the adjusted risks for a poor outcome (mRS of 3-6) after the index event. Adjusted variables were calculated in the form of odds ratios (ORs) and 95% confidence interval (CI) with *P* values ([Table 2](#)).

Multivariate analysis showed that age (OR:1.029, 95% CI: 1.018-1.040, $P = .0001$), DM (OR: 1.374, 95% CI:

Table 1. Clinical characteristics, complications and outcomes comparing subjects with DM, pre-DM, and no DM (n = 2961)

Variables	Total (n = 2961)	Non-DM (n = 873)	Pre-DM (n = 429)	DM (n = 1659)	P value
Age	55.2±13.3	49.57±13.8	54.03±12.9	58.54±11.9	.0001
Age 50 or less	1042(35.2)	486(55.7)	178(41.5)	378(22.8)	.0001
Gender					
Male	2427(82.0)	732(83.8)	376(87.6)	1319(79.5)	.0001
Female	534(18.0)	141(16.2)	53(12.4)	340(20.5)	
Ethnicity					
Qatari	562(19.0)	99(17.6)	44(7.8)	419(74.6)	.0001
Non-Qatari Arab	448(15.1)	126(28.1)	47(10.5)	275(61.4)	
South Asian	1505(50.8)	434(28.8)	273(18.1)	798(53.0)	
Far Eastern	252(8.5)	128 (50.8)	41(16.3)	83(32.9)	
African	127(4.3)	44(34.6)	18(14.2)	65(51.2)	
Caucasian	67(2.3)	42(62.7)	6(9.0)	19(28.4)	
Hypertension	2147(72.5)	517(59.2)	289(67.4)	1341(80.8)	.0001
Dyslipidemia	1558(52.6)	407(46.6)	241(56.2)	910(54.9)	.0001
Previous stroke	375(12.7)	54(6.2)	23(5.4)	298(18.0)	.0001
Coronary artery disease	282(9.5)	44(5.0)	24(5.6)	214(12.9)	.0001
Atrial fibrillation	243(8.2)	79(9.0)	32(7.5)	132(8.0)	.528
Smoking	793(26.8)	221(25.3)	139(32.4)	433(26.1)	.016
Admission blood sugar (>=6.0 mmol/L; n = 2915)	1972(67.7)	383(44.7)	244(58.5)	1345(82.0)	.0001
Prior statin use	448(15.1)	68(7.8)	36(8.4)	344(20.7)	.0001
IV thrombolysis	398(13.4)	129(14.8)	75(17.5)	194(11.7)	.003
Thrombectomy	96(3.2)	41(4.7)	21(4.9)	34(2.0)	.0001
Prognosis at discharge					
Poor prognosis (mRS 3-6)	1062(35.9)	264(30.2)	140(32.6)	658(39.7)	.0001
Good prognosis (mRS 0-2)	1899(64.1)	609(69.8)	289(67.4)	1001(60.3)	
Prognosis at 90 d (n = 1860)					
Poor prognosis (mRS 3-6)	446(24.0)	119(21.4)	51(18.8)	276(26.7)	.005
Good prognosis (mRS 0-2)	1414(76.0)	437(78.6)	221(81.3)	756(73.3)	
Mortality at discharge	68(2.3)	19(2.2)	6(1.4)	43(2.6)	.33
Mortality at 90 d (n = 2860)	99(5.3)	29(5.2)	6(2.2)	64(6.2)	.033
TOAST classification (n = 2961)					
Large vessel disease	750(25.3)	210(24.1)	113(26.3)	427(25.7)	.021
Cardio embolic	248(8.4)	92(10.5)	24(5.6)	132(8.0)	
Small vessel disease	1466(49.5)	422(48.3)	206(48.0)	838(50.5)	
Stroke of determined origin	437(14.8)	125(14.3)	78(18.2)	234(14.1)	
Stroke of undetermined origin	60(2.0)	24(2.7)	8(1.9)	28(1.7)	
Recurrence 90 d (n = 1860)	57(3.1)	12/556(2.2)	2/272(0.7)	43/1032(4.2)	.005
Recurrence 30 d	32(1.1)	10(1.1)	1(2)	21(1.3)	.178
Any complication	186(6.3)	39(4.5)	21(4.9)	126(7.6)	.004
Pneumonia	110(3.7)	24(2.7)	12(2.8)	74(4.5)	.053
Urinary tract infection	98(3.3)	18(2.1)	12(2.8)	68(4.1)	.020
Deep venous thrombosis	1(.03)	1(1)	0	0	.302
Bed sores	30(1.0)	6(7)	5(1.2)	19(1.1)	.519
Sepsis	33(1.1)	7(8)	0	26(1.6)	.013
NIHSS at presentation	5.43 ± 5.3	5.56 ± 5.7	5.52 ± 4.9	5.33 ± 5.1	.545
SBP at presentation (n = 2935)	156.83 ± 30.5	155.91 ± 33.2	160.0 ± 32.4	156.51 ± 28.6	.064
DBP at presentation (n = 2927)	89.32 ± 19.2	93.19 ± 20.7	92.54 ± 19.6	86.46 ± 17.8	.0001
Body mass index (n = 2776)	27.51 ± 5.0	26.77 ± 4.6	27.32 ± 4.8	27.96 ± 5.3	.0001
RBS at presentation (n = 2915)	9.72 ± 5.2	6.31 ± 1.6	6.87 ± 1.9	12.22 ± 5.6	.0001
HbA1c	7.4 ± 2.4	5.29 ± .4	5.97 ± .3	8.88 ± 2.3	.0001
Cholesterol (n = 2864)	4.96 ± 1.3	4.97 ± 1.2	5.06 ± 1.2	4.93 ± 1.4	.169
Triglyceride (n = 2866)	1.71 ± 1.3	1.48 ± .9	1.59 ± .9	1.86 ± 1.4	.0001
HDL (n = 2866)	1.04 ± .5	1.01 ± .4	1.18 ± 6.4	1.11 ± 4.8	.697
LDL (n = 2866)	3.21 ± 1.3	3.34 ± 1.7	3.36 ± 1.1	3.11 ± 1.2	.0001
Length of stay (d) (n = 2957)	5.89 ± 8.6	5.45 ± 6.2	5.53 ± 9.9	6.23 ± 9.4	.064

Abbreviations: DBP, diastolic blood pressure; DM, diabetes mellitus; HDL, high density lipoprotein; LDL, Low density lipoprotein; mRS, modified Rankin Score; NIHSS, National Institute of Health Stroke Scale; RBS, random blood sugar; SBP, systolic blood pressure.

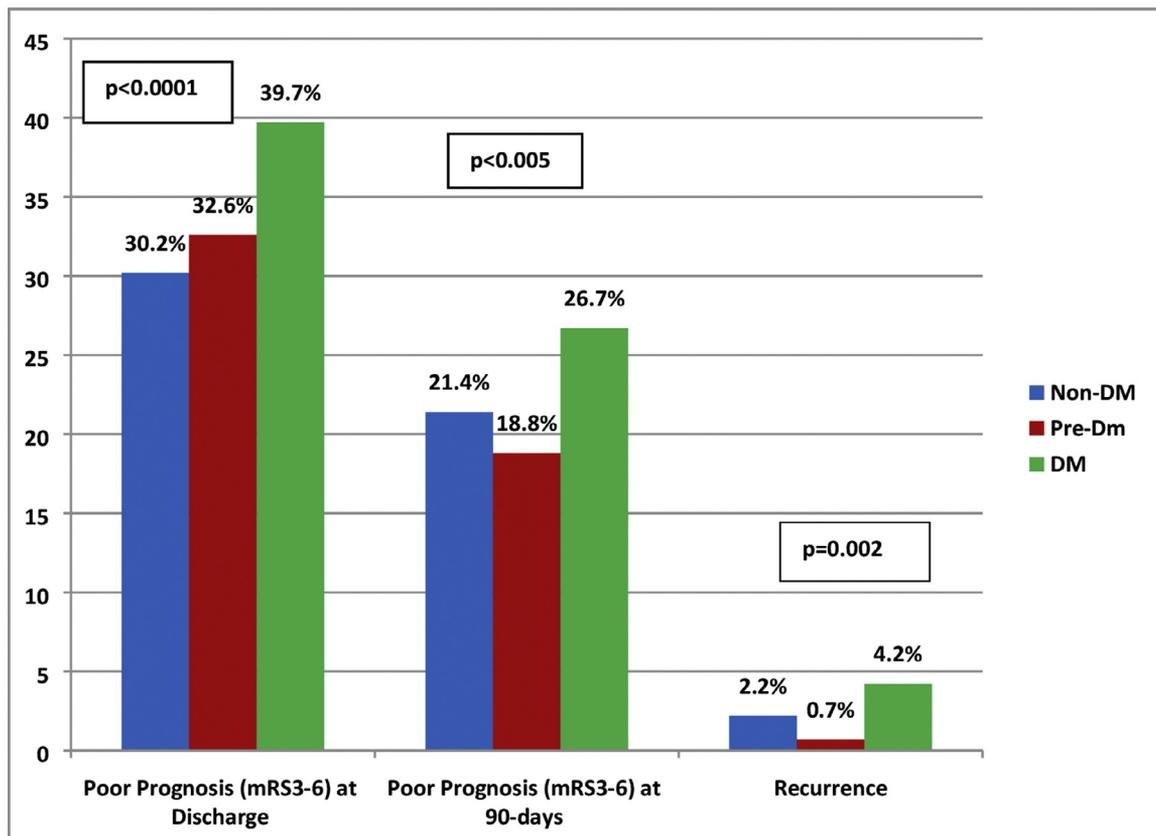


Figure 1. Greater disability (mRS 3-6) at discharge (n = 2961) and 90-day (n = 1860) and risk of recurrence at 90 days (n = 1860) in relation to diabetes status. Abbreviation: mRS, modified Rankin scale.

1.022-1.847, P = .035), NIHSS at admission (OR:1.203, 95% CI: 1.171-1.236, P = .0001), prior stroke (OR:1.765, 95% CI: 1.205-2.585, P = .004), complications (OR:2.90,

95% CI:1.552-5.42, P = .001), and LOS (OR:1.152, 95% CI: 1.116-1.19, P = .001) were associated with a poorer outcome. The area under the ROC curve was .88

Table 2. Multivariate logistic regression for poor outcome and recurrence of stroke at 90 d (n = 1860)

Poor outcome (mRS 3-6)	P value	Odds ratio	95% Confidence interval	
			Lower	Upper
Prior diabetes	.035	1.374	1.022	1.847
Age	.0001	1.029	1.018	1.040
NIHSS admission	.0001	1.203	1.171	1.236
Prior stroke	.004	1.765	1.205	2.585
Complications	.001	2.90	1.552	5.420
Length of stay	.0001	1.152	1.116	1.190
Risk of stroke recurrence				
Age	.009	.96	.94 - .99	.94 - .99
Arab	.03	2.07	1.07 - 4.00	1.07 - 4.00
DM	.866	1.08	.45 - 2.59	.45 - 2.59
HTN	.332	1.59	.62 - 4.04	.62 - 4.04
Prior stroke	.0001	16.23	8.29 - 31.76	8.29 - 31.76
HbA1c	.032	1.20	1.02 - 1.42	1.02 - 1.42
RBS on admission	.167	.95	.89 - 1.02	.89 - 1.02
Cholesterol	.001	.67	.52 - .86	.52 - .86
mRS (3-6)	.001	2.82	1.51 - 5.25	1.51 - 5.25

Abbreviations: DM, diabetes mellitus; HTN, hypertension; mRS, Modified Rankin Score; NIHSS, National Institute of Health Stroke Scale; RBS, random blood sugar.

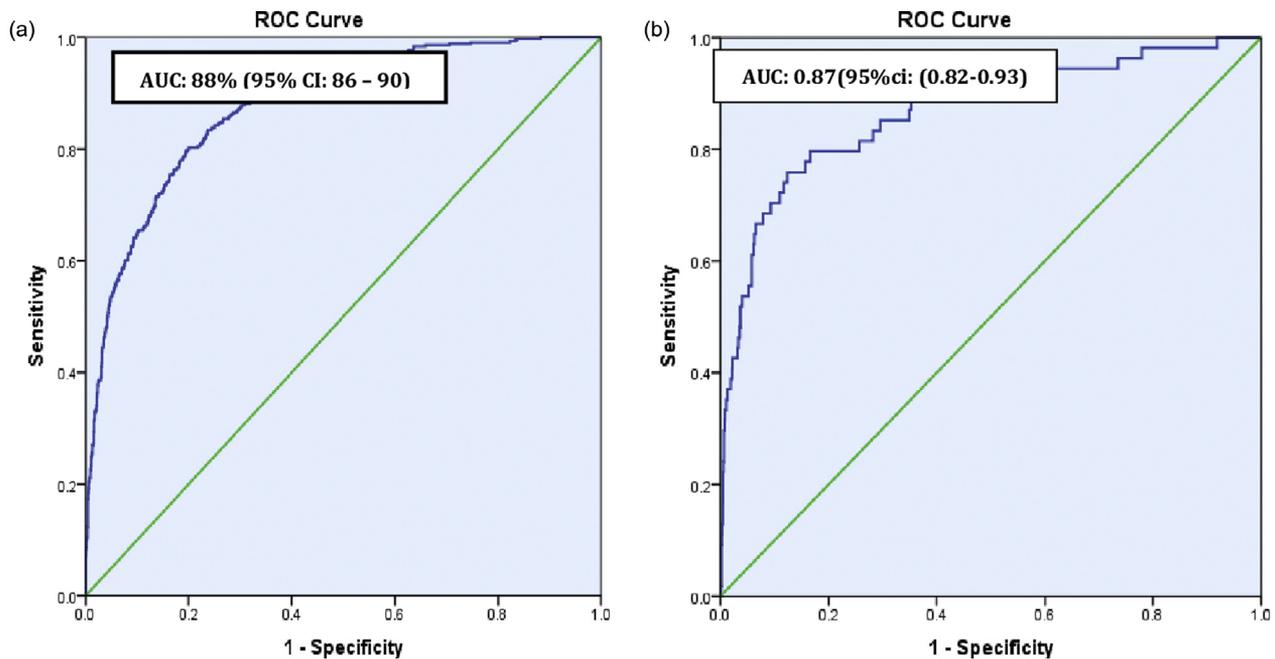


Figure 2. (a) ROC curve for the logistic regression model for predicting delayed improvement at 90 days. Variable(s) adjusted for age, DM, prior stroke, NIHSS on admission, complications, and length of stay. The area under the receiver operating characteristic curve was .87 (95% CI, .82-.93), showing 88% accuracy in predicting poor outcome of stroke using the model. (b) ROC curve for the logistic regression model predicting risk of recurrence. Variable(s) adjusted for age, ethnicity, DM, hypertension, prior stroke, HbA1c, random blood sugar, total cholesterol, and mRS (3-6) at discharge. The area under the receiver operating characteristic curve was .87 (95% CI, .82-.93), showing 87% accuracy in predicting a recurrence of stroke using the model. Abbreviations: CI, confidence interval; DM, diabetes mellitus; mRS, modified Rankin scale; ROC, receiver operating characteristic.

(95%CI, .86-.90) suggesting 89% accuracy in discriminating the outcome (Fig 2, a).

Multivariate logistic regression was also used to calculate the ORs for stroke recurrence adjusting for age, sex, ethnicity, DM, HTN, prior stroke, HbA1c, RBS, cholesterol on admission, and poor outcome (mRS 3-6) at discharge (Table 2). Age (OR: .96, 95% CI: .94-.99, $P < .009$), prior history of stroke (OR: 16.23, 95% CI: 8.29-31.76, $P < .0001$), HbA1c (OR: 1.20, 95% CI: 1.02-1.42, $P < .032$), total cholesterol (OR: .67, 95% CI: .52-.86, $P < .001$) and greater disability (mRS 3-6) at discharge (OR: 2.82, 95%CI: 1.51-5.25, $P < .001$) were associated with recurrent stroke. The area under the ROC curve was .87 (95% CI, .82-.93), showing 87% accuracy in discriminating between recurrence and no recurrence of stroke (Fig 2, b).

DISCUSSION

This is the largest prospective single-center study assessing the immediate and short-term adverse effects of diabetes and prediabetes on patients presenting with an AIS. Patients with DM and AIS were less likely to receive reperfusion therapy or undergo thrombectomy and had an increased incidence of in-hospital medical complications with a longer LOS. Disability at discharge and 90 days was greater; irrespective of the admission stroke diagnosis (TOAST classification) or stroke severity

(NIHSS score). Subjects with prediabetes had similar outcomes to nondiabetes stroke patients.

Very few studies have assessed the importance of DM as a risk factor or its relevance to outcome following AIS in the Middle East.¹³ A recent systematic review of 21,724 stroke patients showed that the incidence of diabetes (33.1%) and smoking (19.3%) was significantly higher, whilst the incidence of HTN (62.1%), dyslipidemia (36.8%), ischemic heart disease (24.6%), and atrial fibrillation (AF) (13.6%) were similar in stroke patients from the Middle East compared to North America.¹⁴ The significantly younger age for stroke in Qatar and other countries in the Middle East likely reflects the poor control of vascular risk factors in this population.¹⁵ A striking finding of our study was the very high prevalence of dysglycemia (RBS ≥ 6.0 mmol/L) in 83.5% patients, comprised of known diabetes, and newly diagnosed diabetes during admission for stroke. The prevalence of diabetes has increased by 40.3 % when we compare our results to a study on stroke in Qatari nationals published from the same institute 15 years ago.¹⁵

In the present study of patients admitted with ischemic stroke, the prevalence of diabetes was more than 3 times higher in Qatari patients and twice that in patients from Southeast Asia compared to Caucasians. An important observation was that patients with diabetes had a greater disability at discharge and at 90 days. Although significantly more patients with diabetes had medical

complications while in hospital, even after exclusion of these patients, the functional outcome at discharge and 90 days remained poorer. Previous studies have shown that hyperglycemia at admission can worsen outcome in patients with large strokes only,¹⁶ but not in patients with lacunar stroke or SVD.¹⁷ This may reflect the small number of patients with diabetes and SVD in previous studies. In the current study more than 50% of patients had SVD and greater disability and increased risk of recurrence was most evident in these patients. Structural abnormalities in perforator vessels and endothelial dysfunction together with an enhanced inflammatory/prothrombotic state^{2,4} in diabetes is likely to explain this increased risk.

In the current study the incidence of recurrent stroke was highest in patients with a history of previous stroke, diabetes, HTN, higher HbA1c, more severe deficits at discharge and lower total cholesterol, and low density lipoprotein, attributable to greater statin use. This is consistent with previous reports showing an increased risk of recurrent stroke in patients with DM.^{18,19} Comparing stroke patients with and without diabetes, the 30-day (4.9% versus 2.7%)²⁰ and 2-year (19.8% versus 12.3%)²¹ rate of recurrent stroke is almost doubled and has been attributed to higher rates of HTN, AF, and heart failure in patients with diabetes.²² In a recent analysis of the China National Stroke Registry, 9.8% of patients with a minor stroke suffered a recurrent stroke within 3 months and the multivariate model identified HTN, DM, AF, coronary heart disease, and previous stroke as independent predictors for recurrent stroke.²³ Similarly, in the present study we show that older age, Arab ethnicity, diabetes, history of HTN, prior stroke, and CAD and AF increase the risk of recurrent stroke. We have further created a logistical regression model which can predict with very high accuracy (AUC 87%), the risk of recurrent stroke in this population (Fig 2,b).

This is the largest prospective study to date which has assessed outcomes in patients with diabetes and prediabetes admitted with AIS in the Middle East. This is particularly relevant given the rapidly increasing prevalence of diabetes in the Middle East. Moreover, we have the unique opportunity to assess the impact of diabetes on stroke outcomes in a diverse population from the Middle East, South East Asia, and the Far East. We have identified multiple, potentially treatable risk factors that may contribute to the worse outcomes following AIS in patients with diabetes.

We acknowledge several limitations of this study. We have not assessed patients with type 1 and type 2 diabetes separately. There were no differences in the severity of stroke based on the NIHSS at admission, however, we did not assess the volume of acute infarction or account for the presence and severity of preexisting SVD. We do not have details regarding the exact therapies used in the management of DM, HTN, and dyslipidemia in this population.

In conclusion, we report a very high prevalence of previously diagnosed and newly diagnosed DM and prediabetes in patients admitted with AIS in Qatar. Patients with DM had a higher risk of in-hospital complications, greater disability at discharge and 90 days, and a higher incidence of recurrent stroke and increased mortality within 90 days of an AIS.

Conflicting Interests

The authors declare that there is no conflict of interest.

Acknowledgments: We acknowledge the assistance of all the physicians, nurses, and staff of the stroke team in Hamad Medical Corporation.

Supplementary material

Supplementary data to this article can be found online at doi:[10.1016/j.jstrokecerebrovasdis.2018.11.003](https://doi.org/10.1016/j.jstrokecerebrovasdis.2018.11.003).

References

1. Luitse MJ, Biessels GJ, Rutten GE, et al. Diabetes, hyperglycaemia, and acute ischaemic stroke. *Lancet Neurolog* 2012;11:261-271.
2. Pechlivani N, Ajjan R. Thrombosis and vascular inflammation in diabetes: mechanisms and potential therapeutic targets. *Front Cardiovasc Med* 2018;5:1.
3. Huang D, Refaat M, Mohammedi K, et al. Macrovascular complications in patients with diabetes and prediabetes. *BioMed Res Int* 2017.
4. Yashiro S, Kameda H, Chida A, et al. Evaluation of lenticulostriate arteries changes by 7 T magnetic resonance angiography in type 2 diabetes. *J Atheroscl Thromb* 2018. <https://doi.org/10.5551/jat.43869>.
5. Akhtar N, Salam A, Kamran S, et al. Pre-existing small vessel disease in patients with acute stroke from the Middle East, Southeast Asia, and Philippines. *Transl Stroke Res* 2018;9(3):1-9.
6. Ansarimoghaddam A, Ali AH, Iraj Z, et al. Prevalence of metabolic syndrome in middle-east countries: meta-analysis of cross-sectional studies. *Diabetes Metab Syndr: Clin Res Rev* 2018;12:195-201.
7. Bener A, Kim EJ, Mutlu F, et al. Burden of diabetes mellitus attributable to demographic levels in Qatar: an emerging public health problem. *Diabetes Metab Syndr: Clin Res Rev* 2014;8:216-220.
8. Mook-Kanamori MJ, El-Din Selim MM, Takiddin AH, et al. Elevated HbA1c levels in individuals not diagnosed with type 2 diabetes in Qatar: a pilot study. *Qatar Med J* 2015;2014.
9. Ibrahim F, Deleu D, Akhtar N, et al. Burden of stroke in Qatar. *J Stroke Cerebrovasc Dis* 2015;24:2875-2879.
10. American Diabetes Association. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes—2018. *Diabetes Care* 2018;41:S13-S27.
11. Zhou BF. Cooperative Meta-Analysis Group of the Working Group on Obesity in C. Predictive values of body mass index and waist circumference for risk factors of certain related diseases in Chinese adults—study on optimal cut-off points of body mass index and waist circumference in Chinese adults. *Biomed Environ Sci* 2002;15: 83-96.

12. Akhtar N, Kamran S, Singh R, et al. Beneficial effects of implementing stroke protocols require establishment of a geographically distinct unit. *Stroke* 2015;46:3494-3501.
13. Ntaios G, Abatzi C, Alexandrou M, et al. Persistent hyperglycemia at 24-48 h in acute hyperglycemic stroke patients is not associated with a worse functional outcome. *Cerebrovasc Dis* 2011;32:561-566.
14. Behrouz R, Powers CJ. Epidemiology of classical risk factors in stroke patients in the Middle East. *Eur J Neurol* 2016;23:262-269.
15. Khan FY. Risk factors of young ischemic stroke in Qatar. *Clin Neurol Neurosurg* 2007;109:770-773.
16. Kruyt ND, Nys GM, Van der Worp HB, et al. Hyperglycemia and cognitive outcome after ischemic stroke. *J Neurol Sci* 2008;270:141-147.
17. Uyttenboogaart M, Koch M.W., Stewart R.E., et al: Moderate hyperglycaemia is associated with favourable outcome in acute lacunar stroke *Brain* 2007;130:1626-1630.
18. Wu S, Shi Y, Wang C, et al. Investigators for the Survey on Abnormal Glucose Regulation in Patients With Acute Stroke Across China (ACROSS-China). Glycated hemoglobin independently predicts stroke recurrence within one year after acute first-ever non-cardioembolic strokes onset in a Chinese cohort study. *PLoS One* 2013;8:e80690.
19. Hankey GJ, Jamrozik K, Broadhurst RJ, et al. Long-term risk of first recurrent stroke in the Perth Community Stroke Study. *Stroke* 1998;29:2491-2500.
20. Sacco RL, Foulkes MA, Mohr JP, et al. Determinants of early recurrence of cerebral infarction. The Stroke Data Bank. *Stroke* 1989;20:983-989.
21. Hier DB, Foulkes MA, Swiontoniowski M, et al. Stroke recurrence within 2 years after ischemic infarction. *Stroke* 1991;22:155-161.
22. Olsson T, Viitanen M, Asplund K, et al. Prognosis after stroke in diabetic patients. A controlled prospective study. *Diabetologia* 1990;33:244-249.
23. Wu L, Wang A, Wang X, et al. Factors for short-term outcomes in patients with a minor stroke: results from China National Stroke Registry. *BMC Neurol* 2015;15:253.