

Undiagnosed major risk factors in acute ischaemic stroke patients in Qatar: analysis from the Qatar stroke registry

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ABSTRACT

Objective We examined the presentation to hospital, subtypes of ischaemic stroke for patients admitted to stroke services in Qatar and their 90-day prognosis based on the modified Rankin Scale (mRS) for those with diagnosed and undiagnosed diabetes, hypertension and dyslipidaemia.

Methods We conducted a retrospective analysis of patients admitted with acute ischaemic stroke from January 2014 to April 2024. The mRS was dichotomised with favourable outcome (0–2) and unfavourable outcome (3–6).

Results A total of 9479 patients were included in the study. Patients with a prior history of hypertension and dyslipidaemia and untreated/undiagnosed for these risk factors on admission were more likely to present with a lower National Institute of Health Stroke Scale (NIHSS) score at admission ($p < 0.001$). These patients were also more likely to present with small vessel disease (SVD) or subcortical stroke ($p < 0.001$). Multivariate analysis revealed that age (adjusted OR 1.05, 95% CI 1.04 to 1.06) and hypertension (adjusted OR 1.44, 95% CI 1.07 to 1.96) were more likely to have an mRS score of 3–6 at 90 days while males (adjusted OR 0.56, 95% CI 0.46 to 0.69), prior antidiabetic therapy (adjusted OR 0.52, 95% CI 0.34 to 0.79) and undiagnosed diabetes (adjusted OR 0.46, 95% CI 0.22 to 0.99) were protective against an mRS score of 3–6 at 90 days after adjusting for covariates.

Conclusion Patients with a prior history of hypertension and dyslipidaemia and undiagnosed on admission are more likely to present with a lower NIHSS score but have a worse outcome at 90 days. The lower NIHSS may be explained by a higher frequency of SVD.

INTRODUCTION

Stroke is a major cause of disability and death worldwide, with approximately 12–15 million cases reported annually.^{1 2} Compared with developed/higher-income countries, lower-income and middle-income countries have a higher incidence of stroke due to limited access to education, resources and preventative measures.³ There are several risk factors associated with stroke, that is, hypertension, dyslipidaemia, smoking, diabetes and heart conditions. For some patients, these risk

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ There are several risk factors associated with stroke, with variable incidence rates reported. For some patients, these risk factors are only diagnosed after an acute ischaemic stroke episode. Late recognition or undermanagement of these risk factors predisposes them to higher risks of ischaemic stroke and intracranial haemorrhage.

WHAT THIS STUDY ADDS

⇒ Patients with a prior history of hypertension, dyslipidaemia and those who present as untreated/undiagnosed for these risk factors on admission are more likely to present with a lower National Institute of Health Stroke Scale (NIHSS) score at admission. The lower NIHSS may be explained by a higher frequency of small vessel disease. Males, prior antidiabetic therapy and undiagnosed diabetes were protective against a modified Rankin Scale (mRS) score of 3–6 at 90 days.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our study demonstrated that patients with undiagnosed diabetes, hypertension and dyslipidaemia on admission were not likely to have a high mRS (3–6) at 90 days. Conversely, undiagnosed diabetes was found to have a protective effect against a high mRS score at 90 days.

factors are only diagnosed after an acute ischaemic stroke episode, with variable incidence rates reported. For instance, atrial fibrillation was newly diagnosed in 10.5%–11.2% of patients after stroke,^{4 5} dyslipidaemia in 20.4%,⁶ type 2 diabetes mellitus in 9.4%–16.4%^{5 7} and structural cardiac disease in 3%.⁵ In a cohort study of 1727 patients in Qatar, 39.4%–74.5% and 72.9%–82.4% of patients were discovered to have untreated diabetes mellitus and hypertension at baseline, respectively.⁸ Boehme *et al*⁹ also reported that 79.5%–95.1% of patients with at least 1 risk condition for stroke were inappropriately treated, with the largest discrepancy observed for the management of hypertension,

hypercholesterolaemia and atrial fibrillation. Undermanagement or late recognition of these risk factors increases the risks of ischaemic stroke and intracranial haemorrhage.

In the Middle East and North African (MENA) region, there are approximately 7.3 million cases of stroke reported annually, with 300 000 deaths reported in 2019.¹⁰ Hypertension and diabetes are also the most common modifiable risk factors for stroke in the MENA region.¹ In some countries (eg, Qatar), the number of expatriates outnumbers the local population by a ratio of almost 10:1. Most of the expatriates are temporary workers from South Asia and Middle Eastern regions.⁸ The majority of this cohort is also from lower socioeconomic backgrounds, where vascular risk factors may be poorly controlled due to their socioeconomic circumstances.⁸ Previous studies have reported that for some patients, vascular risk factors such as hypertension and dyslipidaemia are only discovered after an acute ischaemic stroke episode.¹¹ To our knowledge, there are no follow-up data on these patients' functional outcomes after these index events.

In this study, we examined the presentation to hospital, subtypes of ischaemic stroke as defined by the TOAST classification and 90-day prognosis for patients admitted to stroke services in Qatar for those with diagnosed and undiagnosed diabetes, hypertension and dyslipidaemia.

METHODS

Data from patients admitted with a stroke to Hamad General Hospital (HGH), Doha, Qatar from January 2014 through April 2024 were analysed from a hospital-based prospective stroke registry. HGH is a Joint Commission International accredited 600-bed hospital and it is the only tertiary care medical facility in Qatar where the stroke service is located. 95% of all strokes in Qatar requiring admission to hospital are admitted to HGH. HGH is equipped with all the necessary laboratory, neuroradiological and neurosurgical facilities and infrastructure required to manage acute stroke patients.

Patient characteristics

Patient characteristics including age, sex, nationality, medical comorbidities and prior medication were collected in the Stroke Registry. Data from the National Institute of Health Stroke Scale (NIHSS) score, neuroimaging data, postdischarge disposition were entered into the registry. Ischaemic stroke was diagnosed according to the WHO criteria¹² and stroke subtypes by the TOAST criteria.¹³ The modified Rankin scale (MRS) measurements were done at discharge and at 90 days following onset of symptoms. The patients were classified as favourable (mRS $\leq 0-2$) or unfavourable (mRS 3-6) outcome. We used the dichotomised mRS scale as it is the most common method in use to evaluate recovery at 90 days.¹⁴

Diabetes was diagnosed according to the American diabetes Association (ADA) and WHO recommendation¹⁵ and included patients with a previous diagnosis of

diabetes, on medication for diabetes or an HbA1c of more than 6.5%, and the diagnosis of pre-diabetes was based on an HbA1c of 5.7%–6.4% as per the 2015 ADA clinical practice recommendations. Hypertension was defined as systolic blood pressure (BP) ≥ 140 mm Hg or a diastolic pressure ≥ 90 mm Hg, or on current treatment with antihypertensive drugs. We kept track of the number of patients with hypertension or diabetes who were unaware of these conditions at the time of presentation to the hospital. Dyslipidaemia was defined as low-density lipoprotein (LDL)-cholesterol level ≥ 3.62 mmol/L, high-density lipoprotein (HDL) cholesterol level ≤ 1.03 mmol/L, triglycerides ≥ 1.69 mmol/L or current treatment with a cholesterol-lowering drug.

Data collection

On identification and confirmation of diagnosis using the International Classification of Disease, 10th edition, definitions (H34.1, 163.x, 164.x, 161.x, 160.x and G45.x), patients' data were collected by trained stroke coordinators. The ethnicities of the patients were recorded at admission.

Data analysis and statistics

Descriptive results for all continuous variables were reported as mean \pm SD for normally distributed data or median with range for data with non-normal distributions. The distribution of continuous variables was assessed before using statistical tools. Age, sex, admission NIHSS scores, modified Rankin score (mRS) at 90 days all had a non-normal distribution, as a result, the Kruskal-Wallis test was performed. Dunn's test was subsequently performed for post hoc analysis. Pearson χ^2 test or Fisher's exact test was performed whenever appropriate to compare the proportion of all categorical variables between the groups. Multiple logistic regression analysis was performed to assess for risk factors associated with mRS at 90 days after selecting important and significant variables at univariate analysis. OR and the 95% CI for the OR were reported. A $p \leq 0.05$ (two tailed) was considered significant. SPSS statistical package was used for the analysis (SPSS Version 29.0.0.0).

RESULTS

Patient characteristics

A total of 9479 patients with a diagnosis of acute ischaemic stroke were admitted to HGH between January 2014 and April 2024. The age and sex of the patients are shown in online supplemental appendix table 1. The majority of the patients were men 7589 (80.1%). This is reflective of Qatar's demographics where a large majority of the population is composed of male expatriate community. The median age (IQR) of all patients presenting with stroke was 54 (46–64).

The risk factors associated with ischaemic stroke examined in this study were as follows: diabetes, hypertension and dyslipidaemia. For each of these risk factors,

participants were categorised as 'no history of the risk factor on admission', 'previously diagnosed with the risk factor on admission' and 'undiagnosed/untreated for the risk factor on admission'. In total, there were 5553 patients with diabetes on admission: 24.9% had no history of diabetes, 48.8% had a history of diabetes and 9.8% did not know they had diabetes on admission. 16.5% of the patients were also categorised as 'prediabetic'. Kruskal-Wallis H test and Dunn's post hoc test were performed and there was no significant difference in admission NIHSS and mRS scores at 90 days between undiagnosed diabetic and patients with pre-diabetes ($p=0.34$ and $p=0.24$, respectively). Therefore, patients with pre-diabetes were combined with undiagnosed diabetes patients into one category for analysis.

Hypertension was present in 6912 patients at admission: 27.1% had no history of hypertension, 61.1% had a history of hypertension and 11.8% were unaware of their hypertension at time of admission. Lastly, 5015 dyslipidaemia patients were admitted: 53.9% had no history of dyslipidaemia, 19.9% had a history of dyslipidaemia and 26.3% did not know they had dyslipidaemia on admission. For all three cohorts, patients with risk factors had the highest median age compared with their counterparts. 28.6% (2714/6765) participants had a smoking history.

Diagnosis

Stroke diagnosis is shown in online supplemental appendix table 2. Admission TOAST classification was significantly different between 'no diabetes', 'diabetes' and 'undiagnosed diabetes' patients on admission, $p<0.001$. Similar observations were seen for the hypertensive ($p<0.001$) and dyslipidaemia subgroups ($p<0.001$). Small vessel disease was the most common ischaemic stroke subtype for all cohorts ($p<0.001$).

Admission NIHSS score

NIHSS score was analysed as both a categorical and continuous variable. Pearson χ^2 test revealed that there was a significant association between risk factor status and admission NIHSS scores: hypertension: χ^2 (4, $N=9433$)=53.24, $p<0.001$; diabetes: χ^2 (4, $N=9433$)=29.64, $p<0.001$ and dyslipidaemia: χ^2 (4, $N=9433$)=72.22, $p<0.001$ (table 1). Diabetes was initially associated with a lower NIHSS score at admission ($p=0.01$) (table 2), however, after applying Bonferroni correction, significance was lost ($p=0.053$). In contrast, hypertension and dyslipidaemia remained significantly associated with lower NIHSS admission scores. A summary of mean admission NIHSS score between the three risk factors cohorts can be seen in figure 1A–C.

Prognosis at discharge and 90-day outcome

Prognosis at 90 days was analysed as both a categorical and continuous variable. Pearson χ^2 test revealed that there was a significant association between risk factor status and mRS score at 90 days: hypertension: χ^2 (2, $N=7104$)=74.46, $p<0.001$; diabetes: χ^2 (2, $N=7104$)=75.23,

$p<0.001$ and dyslipidaemia: χ^2 (2, $N=7104$)=108.56, $p<0.001$ (table 2).

When mRS was analysed as a continuous variable using the Kruskal-Wallis and Dunn's post hoc test, the mRS score at 90 days remained significantly different between diabetic and non-diabetic patients ($p<0.001$) and diabetic and undiagnosed diabetes patients ($p<0.001$) (table 1). There was also a higher proportion of patients with diabetes with an mRS score of 3–6 (38.5%) compared with non-diabetic patients (30.0%) and undiagnosed diabetes patients (30.2%) (table 2).

For the hypertension cohort, the mRS score at 90 days was significantly different between all subgroups: normotensive versus hypertensive ($p<0.001$); normotensive versus undiagnosed hypertension ($p=0.045$) and hypertensive versus undiagnosed hypertension ($p<0.001$) (table 1). Further analysis revealed that hypertensive patients had the highest proportion of mRS scores of 3–6 (37.4%) compared with normotensive (28.4%) and undiagnosed hypertension (25.8%) (table 2).

Lastly, for the dyslipidaemia cohort, the mRS score at 90 days was significantly different between all subgroups: no dyslipidaemia versus dyslipidaemia ($p<0.001$); no dyslipidaemia versus undiagnosed dyslipidaemia ($p<0.001$) and dyslipidaemia versus undiagnosed dyslipidaemia ($p<0.001$) (table 1). Dyslipidaemia patients had the highest proportion of mRS scores of 3–6 (41.7%) compared with non-dyslipidaemia patients (34.7%) and undiagnosed dyslipidaemia patients (24.9%).

Lipid profiles

Serum cholesterol, serum triglycerides, serum HDL and serum LDL were all significantly different between the dyslipidaemia subgroups ($p<0.001$) (online supplemental appendix table 3).

Risk factors associated with ischaemic stroke

Table 3 details a multiple binary logistic regression model to identify significant independent factors associated with mRS scores of 3–6 at 90 days adjusting for age, sex, concomitant risk factors and prior treatment. Age and hypertension were identified as significant predictors of an mRS score of 3–6 at 90 days (adjusted OR 1.05, 95% CI 1.04 to 1.06 and adjusted OR 1.44, 95% CI 1.07 to 1.96, respectively). Conversely, the male sex, prior usage of antidiabetic therapy and undiagnosed diabetes were protective against an mRS score of 3–6 at 90 days (adjusted OR 0.56, 95% CI 0.46 to 0.69; adjusted OR 0.52, 95% CI 0.34 to 0.79; adjusted OR of 0.46, 95% CI 0.22 to 0.99, respectively). The presence of dyslipidaemia and undiagnosed dyslipidaemia were not significantly associated with an mRS score of 3–6 at 90 days (adjusted ORs (95% CIs) 1.00 (0.80 to 1.26) and 0.93 (0.71 to 1.24)), respectively. Similarly, the presence of undiagnosed hypertension was not significantly associated with an mRS score of 3–6 at 90 days (adjusted OR 1.49, 95% CI 0.95 to 2.33).

Table 1 Summary of group differences for admission NIHSS score and prognosis at discharge (mRS at 90 days) using Kruskal-Wallis H test and Dunn's post hoc test

Admission NIHSS Score	No Diabetes (n=2349)	Diabetes (n=4599)	Undiagnosed diabetes (n=2485)	Overall significance*	No diabetes vs diabetes*	No diabetes vs undiagnosed diabetes*	Diabetes vs undiagnosed diabetes*
	4831.52	4651.86	4729.31	0.053	0.16	1.00	0.13
	No hypertension (n=2553)	Hypertension (n=5761)	Undiagnosed hypertension (n=1119)	–	No hypertension vs hypertension*	No hypertension vs undiagnosed hypertension*	Hypertension vs undiagnosed hypertension*
	4937.89	4621.44	4704.99	<0.001†	<0.001†	0.049†	1.00
	No dyslipidaemia (n=5079)	Dyslipidaemia (n=1866)	Undiagnosed dyslipidaemia (n=2488)	–	No dyslipidaemia vs dyslipidaemia*	No dyslipidaemia vs undiagnosed dyslipidaemia*	Dyslipidaemia vs undiagnosed dyslipidaemia*
	4835.31	4468.24	4662.06	<0.001†	.00†	.03†	0.06
mRS at 90 days	No Diabetes (n=1807)	Diabetes (n=3500)	Undiagnosed diabetes (n=1797)	Overall significance ¹	No diabetes vs diabetes*	No diabetes vs undiagnosed diabetes*	Diabetes vs undiagnosed diabetes*
	3422.90	3129.44	3345.81	<0.001†	<0.001†	0.74	<0.001†
	No hypertension (n=1904)	Hypertension (n=4369)	Undiagnosed hypertension (n=831)	–	No hypertension vs hypertension*	No hypertension vs undiagnosed hypertension*	Hypertension vs undiagnosed hypertension*
	3371.71	3703.32	3173.82	<0.001†	<0.001†	0.05†	<0.001†
	No dyslipidaemia (n=3745)	Dyslipidaemia (n=1499)	Undiagnosed dyslipidaemia (n=1860)	–	No dyslipidaemia vs dyslipidaemia*	No dyslipidaemia vs undiagnosed dyslipidaemia*	Dyslipidaemia vs undiagnosed dyslipidaemia*
	3589.29	3888.52	3207.62	<0.001†	<0.001†	<0.001†	<0.001†

*Bonferroni correction for multiple tests has been applied for the p values reported.
†p≤0.05
mRS, modified Rankin Score; NIHSS, National Institute of Health Stroke Scale/Score.

DISCUSSION

Our study shows that patients with a prior history of hypertension and dyslipidaemia as well as those who appear as untreated/undiagnosed for these risk factors on admission are more likely to present with a lower NIHSS score at admission. These patients were also more likely to present with small vessel disease or subcortical stroke. This may in part explain the lower NIHSS at presentation. However, for patients with prior histories of hypertension and dyslipidaemia, their prognosis at 90 days was worse compared with patients without these risk factors and those who were undiagnosed for these risk factors at the time of admission. Further analysis revealed that age and hypertension were strongly associated with a high mRS score (3–6) at 90 days, adjusting for covariates. Conversely, the male sex, prior antidiabetic therapy and undiagnosed diabetes were protective against a high mRS score at 90 days.

Similar to other studies that have reported the adverse effects of diabetes on ischaemic stroke outcomes,^{16 17} we

observed a better prognosis at 90 days (lower mRS scores) for patients with undiagnosed diabetes compared with patients with diabetes. Similarly, multivariate regression analysis revealed that patients with undiagnosed diabetes were 0.46 times less likely to develop a higher mRS score at 90 days. This may be because the 'undiagnosed' diabetics had milder disease. The undiagnosed diabetes had a median (IQR) HbA1c of 6.2 (5.9–7.2) compared to patients with diabetes 8.5 (7.0–10.4). High levels of HbA1c, that is, ≥6.5, have been demonstrated to be significantly associated with poorer neurological outcomes (adjusted OR of 2.387, 95% CI 1.201 to 4.745).¹⁸ Similarly, Lei *et al*¹⁹ reported that patients with a HbA1C >8.3 had significantly higher rates of mortality at 3 months (p=0.012) and 1 year (p=0.034). Interestingly, the use of antidiabetic therapy seemed to be protective against poor ischaemic stroke outcomes. Mima *et al*²⁰ have previously reported that administration of metformin in diabetes mellitus patients prior to stroke onset may be associated with reduced neurological severity (OR 11.3, p=0.046).

Table 2 Summary of admission NIHSS scores and prognosis at discharge between diabetic, hypertensive and dyslipidaemia patients

Admission NIHSS score	No diabetes (n=2349)	Diabetes (n=4599)	Undiagnosed diabetes (n=2485)	Overall significance*
Total				<0.001†
Mild stroke (NIHSS 0–4)	1413 (60.2%)	2888 (62.8%)	1510 (60.8%)	
Moderate stroke (NIHSS 5–10)	511 (21.8%)	1066 (23.2%)	632 (25.4%)	
Severe stroke (NIHSS 11 or more)	425 (18.1%)	645 (14.0%)	343 (13.8%)	
	No Hypertension (n=2553)	Hypertension (n=5761)	Undiagnosed Hypertension (n=1119)	
Total				<0.001†
Mild stroke (NIHSS 0–4)	1462 (57.3%)	3639 (63.2%)	710 (63.4%)	
Moderate stroke (NIHSS 5–10)	602 (23.6%)	1335 (13.2%)	272 (24.3%)	
Severe stroke (NIHSS 11 or more)	489 (19.2%)	787 (13.7%)	137 (12.2%)	
	No dyslipidaemia (n=5079)	Dyslipidaemia (n=1866)	Undiagnosed dyslipidaemia (n=2488)	
Total				<0.001†
Mild stroke (NIHSS 0–4)	2996 (59.0%)	1239 (66.4%)	1576 (63.3%)	
Moderate stroke (NIHSS 5–10)	1216 (23.9%)	359 (19.2%)	634 (25.5%)	
Severe stroke (NIHSS 11 or more)	867 (17.1%)	268 (14.4%)	278 (11.2%)	
Prognosis at 90 days	No diabetes (n=1807)	Diabetes (n=3500)	Undiagnosed diabetes (n=1797)	
Total				<0.001†
Favourable prognosis (mRS 0–2)	1265 (70.0%)	2152 (61.5%)	1297 (72.2%)	
Unfavourable prognosis (mRS 3–6)	542 (30.0%)	1348 (38.5%)	500 (27.8%)	
	No hypertension (n=1904)	Hypertension (n=4369)	Undiagnosed hypertension (n=831)	
Total				<0.001†
Favourable prognosis (mRS 0–2)	1363 (71.6%)	2734 (62.6%)	617 (74.2%)	
Unfavourable prognosis (mRS 3–6)	541 (28.4%)	1635 (37.4%)	214 (25.8%)	
	No dyslipidaemia (n=3745)	Dyslipidaemia (n=1499)	Undiagnosed dyslipidaemia (n=1860)	
Total				<0.001†
Favourable prognosis (mRS 0–2)	2444 (65.3%)	874 (58.3%)	1396 (75.1%)	
Unfavourable Prognosis (mRS 3–6)	1301 (34.7%)	625 (41.7%)	464 (24.9%)	

*P value has been measured using Pearson χ^2 test.
 †p<0.05.
 mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale.

Similarly, we have shown that prestroke treatment with metformin improved the mRS at 90 days outcome by a factor of 0.14 (incidence risk ratio of 0.86, $p=0.006$).²¹ In our current study, the use of antidiabetic therapy prior to admission was protective against a higher mRS score at 90 days (adjusted OR 0.52, 95% CI 0.34 to 0.79).

Previous reports suggest that patients with dyslipidaemia may have better outcomes following an acute stroke.^{22 23} In the SPARCL trial,²⁴ a 13.7 mg/dL increase in HDL was associated with a 13% reduction in ischaemic stroke risk as well as major adverse cardiac events. Similarly, Ali *et al*²⁵ reported a 2.27-fold higher mortality rate in the low-normal HDL group compared with the high HDL group

($p=0.049$) as well as a higher 1-year stroke recurrence rate for the low-normal HDL group ($p=0.034$). Similarly, in our study, known dyslipidaemia and undiagnosed dyslipidaemia were not strongly associated with a higher mRS score at 90 days after adjusting for covariates (adjusted OR 1.00, 95% CI 0.80 to 1.26 and adjusted OR 0.93, 95% CI 0.71 to 1.24).

Our study also showed that males were 0.56 times less likely to have an mRS score of 3–6 at 90 days compared with females ($p<0.001$). This is likely secondary to the younger age of the predominantly younger expatriate male population in Qatar (the median age of males in our study was 53 compared with 63 for females). There

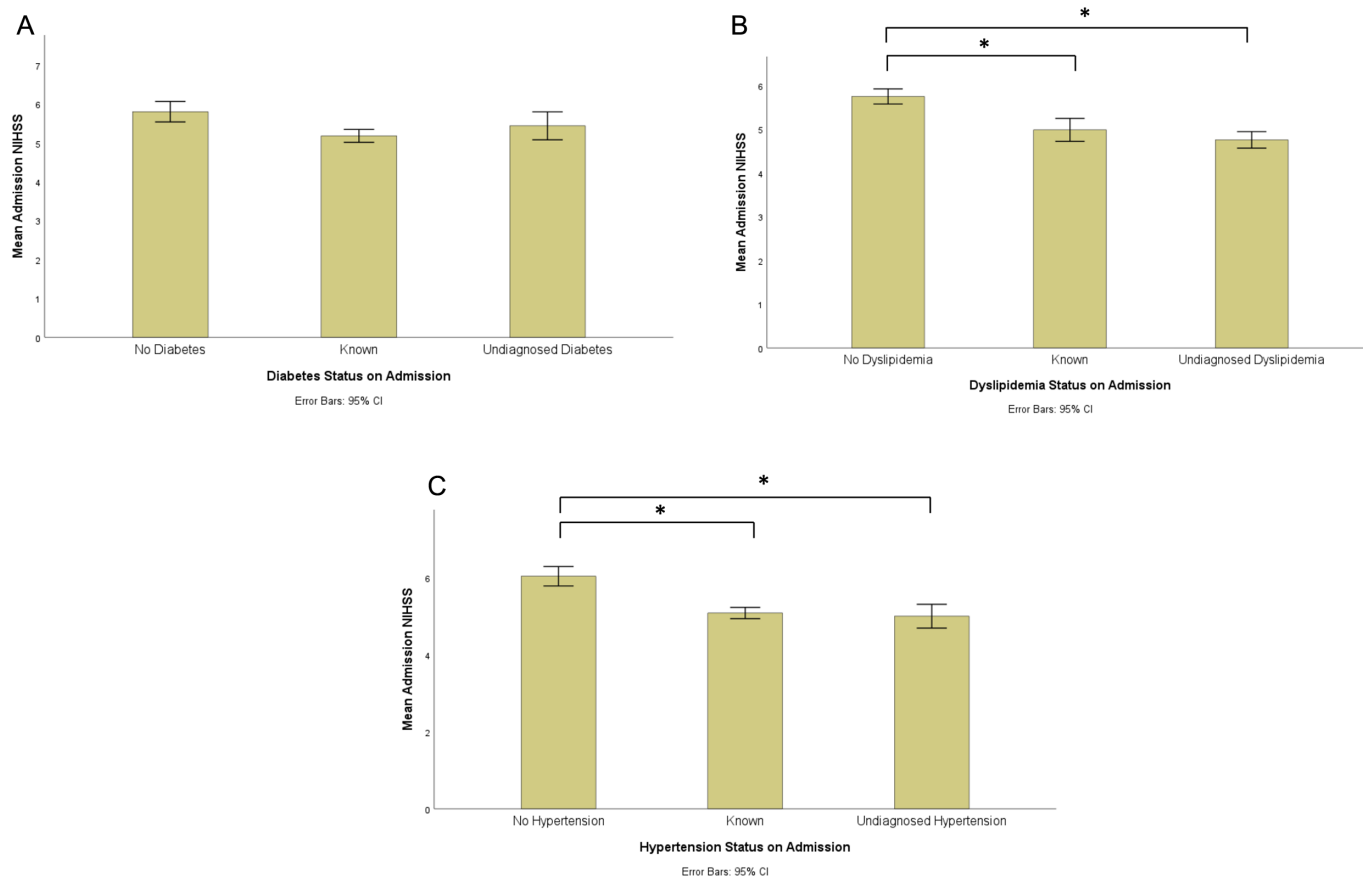


Figure 1 A. Mean admission NIHSS score and diabetes status on admission mean admission. Figure 1B. NIHSS score and dyslipidaemia status on admission. * $p \leq 0.05$. Figure 1 C. Mean admission NIHSS score and hypertension status on admission * $p \leq 0.05$. Abbreviations: NIHSS, National Institute of Health Stroke Scale.

are additional biological differences that may explain this effect. It has been reported that women and men differ in their baseline functional status during their first stroke onset, with the former exhibiting a poorer functional baseline.²⁶ This is attributed to females' older age during their first stroke episode²⁷ and living arrangements whereby females tend to live alone.²⁸ Females are also more predisposed to obesity²⁹ and hypertension.³⁰ In addition, the male patients were younger, were more likely to have small vessel disease and had lower NIHSS at admission. These factors may contribute to the better outcome at 90 days.

In our study, we also observed that patients with undiagnosed risk factors for diabetes, hypertension and dyslipidaemia, all had lower mRS scores at 90 days compared with patients with known risk factors. One reason for this is that a higher proportion of patients from these undiagnosed risk factor categories presented with small vessel disease compared with the known risk factors group. Several studies have reported that patients who present with small vessel disease have a better outcome than patients diagnosed with strokes or other aetiologies. In a study composed of 1816 patients, Arsava *et al*³¹ reported that regardless of the etiologic stroke classification system used (CCS vs TOAST vs ASCO), patients with small artery occlusion all had the lowest 90 day cumulative mortality

risk ($p < 0.001$) compared with large artery atherosclerosis, cardiac embolism, strokes of uncommon causes and undetermined causes. Markaki *et al*³² also reported that the 1-year and 4-year mortality rates were lowest for patients with small artery occlusion compared with patients with large artery atherosclerosis, cardioembolic stroke and patients with strokes of unknown aetiology. However, in a retrospective analysis of 538 patients, Wei *et al*³³ observed the 90-day mortality rate to be highest among patients with small artery occlusion (28.57%) compared with 12.5% for patients with stroke of other determined causes and 10.21% for large artery atherosclerosis ($p < 0.001$). A potential explanation for this discrepancy is that none of the patients enrolled in this study had a minor stroke, therefore, they may be more prone to poorer outcomes. Another rationale is that for patients with known risk factors, their conditions might be more severe than patients with no risk factors and undiagnosed risk factors, which might predispose them to higher mRS scores.

Although some studies have reported hypertension to be protective against mortality after stroke, we found a strong association between hypertension (adjusted OR 1.44, 95% CI 1.07 to 1.96) and a higher mRS score at 90 days but not undiagnosed hypertension (adjusted OR 1.49, 95% CI 0.95 to 2.33). In several observational studies, both extremes of high and low BP values are

Table 3 Bivariate and multivariate logistic regression analysis to identify the risk factors associated with mRS of 3–6 at 90 days

Determinants	mRS score of 0–2 at 90 days			mRS score of 3–6 at 90 days			Bivariate logistic regression analysis			Multivariate logistic regression analysis		
	n	(%)		n	(%)		Standardised beta	OR (95% CI)	P value	Standardised beta	OR (95% CI)	P value
Age	53	(45–61)	60	(49–72)	0.045	1.05 (1.04 to 1.05)	<0.001	1.05 (1.04 to 1.06)	<0.001	0.050	1.05 (1.04 to 1.06)	<0.001
Sex												
Female	796	(52.3%)	725	(47.7%)	–	1	–	1	–	–	1	–
Male	3918	(70.2%)	1665	(29.8%)	–0.762	0.47 (0.42 to 0.52)	<0.001	0.56 (0.46 to 0.69)	<0.001	–0.578	0.56 (0.46 to 0.69)	<0.001
Diabetes status												
No diabetes	1265	(70.0%)	542	(30.0%)	–	1	–	1	–	–	1	–
Diabetes	2152	(61.5%)	1348	(38.5%)	–0.106	1.46 (1.30 to 1.65)	<0.001	0.55 (0.29 to 1.02)	0.06	–0.604	0.55 (0.29 to 1.02)	0.06
Undiagnosed	1297	(72.2%)	500	(27.8%)	–0.848	0.90 (0.78 to 1.04)	0.15	0.46 (0.22 to 0.99)	0.048	–0.772	0.46 (0.22 to 0.99)	0.048
Prior antidiabetic therapy												
No	86	(57.3%)	64	(42.7%)	–	1	–	1	–	–	1	–
Yes	1264	(59.2%)	871	(40.8%)	0.077	1.08 (0.77 to 1.51)	0.65	0.52 (0.34 to 0.79)	0.002	–0.663	0.52 (0.34 to 0.79)	0.002
Hypertension status												
No hypertension	1363	(71.6%)	541	(28.4%)	–	1	–	1	–	–	1	–
Hypertension	2734	(62.6%)	1635	(37.4%)	–0.545	0.58 (0.49 to 0.69)	<0.001	1.44 (1.07 to 1.96)	0.02	0.368	1.44 (1.07 to 1.96)	0.02
Undiagnosed	617	(74.2%)	214	(25.8%)	–0.410	0.66 (0.59 to 0.75)	<0.001	1.49 (0.95 to 2.33)	0.08	0.399	1.49 (0.95 to 2.33)	0.08
Prior antihypertensive therapy												
No	3199	(70.8%)	1319	(29.2%)	–	1	–	1	–	–	1	–
Yes	1515	(58.6%)	1071	(41.4%)	–0.539	0.58 (0.53 to 0.65)	<0.001	1.15 (0.89 to 1.49)	0.29	0.140	1.15 (0.89 to 1.49)	0.29
Dyslipidaemia status												
No dyslipidaemia	2444	(65.3%)	1301	(34.7%)	–	1	–	1	–	–	1	–
Dyslipidaemia	874	(58.3%)	625	(41.7%)	–0.766	0.47 (0.40 to 0.54)	<0.001	1.00 (0.80 to 1.26)	0.99	0.001	1.00 (0.80 to 1.26)	0.99
Undiagnosed	1396	(75.1%)	464	(24.9%)	–0.295	0.74 (0.66 to 0.84)	<0.001	0.93 (0.71 to 1.24)	0.64	–0.068	0.93 (0.71 to 1.24)	0.64
Prior statin therapy												
No	3645	(69.4%)	1605	(30.6%)	–	1	–	1	–	–	1	–
Yes	1047	(57.5%)	773	(42.5%)	–0.517	0.60 (0.53 to 0.67)	<0.001	1.07 (0.84 to 1.36)	0.59	0.065	1.07 (0.84 to 1.36)	0.59
Smoking												
No	3206	(62.9%)	1894	(37.1%)	–	1	–	1	–	–	1	–
Yes	1508	(75.2%)	496	(24.8%)	–0.586	0.56 (0.50 to 0.63)	<0.001	0.92 (0.73 to 1.15)	0.45	–0.086	0.92 (0.73 to 1.15)	0.45

Values are reported as median (IQR) unless indicated otherwise. mRS, modified Rankin Scale.

associated with poor outcomes following stroke.^{34 35} After an ischaemic episode, a penumbra of viable brain tissues exists around the infarcted area and an acute hypertensive response can be beneficial in this instance as it preserves the cerebral blood flow to the hypoperfused area.³⁶ Conversely, high BP can increase the risk of oedema formation, haematoma enlargement and haemorrhagic transformation in ischaemic stroke.³⁷ Perhaps there is an optimal range of BP and depending on patient characteristics, having a history of hypertension can be beneficial for some but adverse for others. In our study, we did not collect data on the duration of our patients' hypertension, therefore, depending on how long they had this condition for, this can be associated with a low or high mRS score at 90 days. Future studies should examine how the duration of hypertension can affect patients' outcomes following ischaemic stroke. We also did not observe a significant association between smoking history and higher mRS score at 90 days (adjusted OR 0.92, 95% CI 0.73 to 1.15). A potential explanation for this is that smokers are more likely to be younger and are more likely to experience small vessel disease compared with other stroke subtypes.³⁸ Indeed, in our study, smokers were significantly younger than non-smokers ($p < 0.001$).

There are several limitations to our study. First, we do not know the duration of the diabetes, hypertension and dyslipidaemia prior to the acute stroke or how well these conditions were treated prior to the stroke, although such data are often difficult to collect and have inherent inaccuracies, that is, recall biases. There were other risk factors that we did not assess in our study such as history of atrial fibrillation, ischaemic heart disease, congestive heart failure, valvular heart disease and usage of prior antithrombotic prior to stroke onset. We also had missing data for the mRS score at 90 days on 2249 patients (out of 9479). Since Qatar's population is composed of mainly of expatriate workers, it is impossible to collect data for everyone as they may have moved back to their home country once their work contract ended. Our patient sample is also composed of largely Middle Eastern ethnicity (Qatari, Arabs), South Asian and Far Eastern (Asians), therefore, our results might have differed if we recruited patients of other ethnicities. However, given the large sample size of our study and the prospective design, we believe our results provide valuable information on ischaemic stroke outcomes between patients with known risk factors and those with undiagnosed and/or no known risk factors. Lastly, we did not collect patient's level of education, household income, geographical location and occupation, which could inform us of patients' awareness of stroke risk factors as well as capacity to access care/services to manage these conditions.

CONCLUSION

Patients with a prior history of hypertension and dyslipidaemia as well as those who were untreated/undiagnosed for these risk factors on admission are more likely to

present with a low NIHSS admission score. These patients were also more likely to present with small vessel disease or subcortical stroke. In contrast, patients with these risk factors had a higher proportion of poor outcomes (higher mRS scores) at 90 days. A similar trend was not observed for patients with undiagnosed risk factors. Multivariate analysis revealed that age and hypertension were independent predictors of a higher mRS score (3–6) at 90 days while the male sex, undiagnosed diabetes and prior antidiabetic therapy were protective against a higher mRS score at 90 days.

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REFERENCES

- 1 Rukn SA, Mazya MV, Hentati F, *et al*. Stroke in the Middle-East and North Africa: A 2-year prospective observational study of stroke characteristics in the region—Results from the Safe Implementation of Treatments in Stroke (SITS)—Middle-East and North African (MENA). *Int J Stroke* 2019;14:715–22.
- 2 Go AS, Mozaffarian D, Roger VL, *et al*. Heart disease and stroke statistics—2014 update: a report from the American Heart Association. *Circulation* 2014;129:e28–292.

- 3 Owolabi M, Johnson W, Khan T, *et al.* Effectively Combating Stroke in Low- and Middle-Income Countries: Placing Proof in Pragmatism—The Lancet Neurology Commission. *J Stroke Med* 2018;1:65–7.
- 4 Giralt-Steinhauer E, Cuadrado-Godia E, Soriano-Tárraga C, *et al.* New-Onset Paroxysmal Atrial Fibrillation Diagnosis in Ischemic Stroke Patients. *Eur Neurol* 2015;74:211–7.
- 5 Bugnicourt J-M, Flament M, Guillaumont M-P, *et al.* Predictors of newly diagnosed atrial fibrillation in cryptogenic stroke: a cohort study. *Eur J Neurol* 2013;20:1352–9.
- 6 Horváth E, Vadasdi K, Vastagh I, *et al.* Role of diagnosis of dyslipidemia in primary and secondary vascular prevention in a neurology department. *Ideggyogy Sz* 2010;63:121–4.
- 7 Matz K, Keresztes K, Tatschl C, *et al.* Disorders of glucose metabolism in acute stroke patients: an underrecognized problem. *Diabetes Care* 2006;29:792–7.
- 8 Akhtar N, Salam A, Kamran S, *et al.* Ethnic variation in acute cerebrovascular disease: Analysis from the Qatar stroke registry. *Eur Stroke J* 2016;1:231–41.
- 9 Boehme C, Toell T, Mayer-Suess L, *et al.* The dimension of preventable stroke in a large representative patient cohort. *Neurology (E-Cronicon)* 2019;93:e2121–32.
- 10 Jaberinezhad M, Farhoudi M, Nejadghaderi SA, *et al.* The burden of stroke and its attributable risk factors in the Middle East and North Africa region, 1990–2019. *Sci Rep* 2022;12:2700.
- 11 Rêgo A, Nannoni S, Scherz A, *et al.* Undiagnosed major risk factors in acute ischaemic stroke patients: frequency, profile, stroke mechanisms and outcome. *Eur J Neurol* 2024;31:e16011.
- 12 Hatano S. Experience from a multicentre stroke register: a preliminary report. *Bull World Health Organ* 1976;54:541–53.
- 13 Adams HP, Bendixen BH, Kappelle LJ, *et al.* Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. *TOAST Trial of Org 10172 in Acute Stroke Treatment Stroke* 1993;24:35–41.
- 14 Touma L, Fillion KB, Sterling LH, *et al.* Stent Retrievers for the Treatment of Acute Ischemic Stroke: A Systematic Review and Meta-analysis of Randomized Clinical Trials. *JAMA Neurol* 2016;73:275–81.
- 15 MC, Shaw JE, Jones GR, *et al.* Guidance concerning the use of glycated haemoglobin (HbA1c) for the diagnosis of diabetes mellitus. *Med J Aust* 2015;203:89–90.
- 16 MacIntosh BJ, Cohen E, Colby-Milley J, *et al.* Diabetes Mellitus Is Associated With Poor In-Hospital and Long-Term Outcomes in Young and Midlife Stroke Survivors. *J Am Heart Assoc* 2021;10:e019991.
- 17 Liao C-C, Shih C-C, Yeh C-C, *et al.* Impact of Diabetes on Stroke Risk and Outcomes: Two Nationwide Retrospective Cohort Studies. *Medicine (Baltimore)* 2015;94:e2282.
- 18 Wang H, Cheng Y, Chen S, *et al.* Impact of Elevated Hemoglobin A1c Levels on Functional Outcome in Patients with Acute Ischemic Stroke. *J Stroke Cerebrovasc Dis* 2019;28:470–6.
- 19 Lei C, Wu B, Liu M, *et al.* Association between hemoglobin A_{1c} levels and clinical outcome in ischemic stroke patients with or without diabetes. *J Clin Neurosci* 2015;22:498–503.
- 20 Mima Y, Kuwashiro T, Yasaka M, *et al.* Impact of Metformin on the Severity and Outcomes of Acute Ischemic Stroke in Patients with Type 2 Diabetes Mellitus. *J Stroke Cerebrovasc Dis* 2016;25:436–46.
- 21 Akhtar N, Singh R, Kamran S, *et al.* Diabetes: Chronic Metformin Treatment and Outcome Following Acute Stroke. *Front Neurol* 2022;13:849607.
- 22 Wannamethee SG, Shaper AG, Ebrahim S. HDL-Cholesterol, total cholesterol, and the risk of stroke in middle-aged British men. *Stroke* 2000;31:1882–8.
- 23 Glasser SP, Mosher A, Howard G, *et al.* What is the association of lipid levels and incident stroke? *Int J Cardiol* 2016;220:890–4.
- 24 Amarenco P, Goldstein LB, Callahan A 3rd, *et al.* Baseline blood pressure, low- and high-density lipoproteins, and triglycerides and the risk of vascular events in the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial. *Atherosclerosis* 2009;204:515–20.
- 25 Ali A, Obaid O, Akhtar N, *et al.* Association between HDL levels and stroke outcomes in the Arab population. *Sci Rep* 2024;14:3071.
- 26 Ospel JM, Goyal M. A review of endovascular treatment for medium vessel occlusion stroke. *J Neurointerv Surg* 2021;13:623–30.
- 27 Appellos P, Stegmayr B, Terént A. Sex differences in stroke epidemiology: a systematic review. *Stroke* 2009;40:1082–90.
- 28 Mainz J, Andersen G, Valentin JB, *et al.* Disentangling Sex Differences in Use of Reperfusion Therapy in Patients With Acute Ischemic Stroke. *Stroke* 2020;51:2332–8.
- 29 Peters SAE, Carcel C, Millett ERC, *et al.* Sex differences in the association between major risk factors and the risk of stroke in the UK Biobank cohort study. *Neurology (E-Cronicon)* 2020;95:e2715–26.
- 30 Peters SAE, Huxley RR, Woodward M. Comparison of the sex-specific associations between systolic blood pressure and the risk of cardiovascular disease: a systematic review and meta-analysis of 124 cohort studies, including 1.2 million individuals. *Stroke* 2013;44:2394–401.
- 31 Arsava EM, Helenius J, Avery R, *et al.* Assessment of the Predictive Validity of Etiologic Stroke Classification. *JAMA Neurol* 2017;74:419–26.
- 32 Markaki I, Franzén I, Talani C, *et al.* Long-term survival of ischemic cerebrovascular disease in the acute inflammatory stroke study, a hospital-based cohort described by TOAST and ASCO. *Cerebrovasc Dis* 2013;35:213–9.
- 33 Wei W, Li S, San F, *et al.* Retrospective analysis of prognosis and risk factors of patients with stroke by TOAST. *Medicine (Baltimore)* 2018;97:e0412.
- 34 Carlberg B, Asplund K, Hägg E. The prognostic value of admission blood pressure in patients with acute stroke. *Stroke* 1993;24:1372–5.
- 35 Castillo J, Leira R, García MM, *et al.* Blood pressure decrease during the acute phase of ischemic stroke is associated with brain injury and poor stroke outcome. *Stroke* 2004;35:520–6.
- 36 Owens WB. Blood pressure control in acute cerebrovascular disease. *J Clin Hypertens (Greenwich)* 2011;13:205–11.
- 37 Lattanzi S, Silvestrini M. Blood pressure in acute intra-cerebral hemorrhage. *Ann Transl Med* 2016;4:320.
- 38 Ihle-Hansen H, Thommessen B, Wyller TB, *et al.* Risk factors for and incidence of subtypes of ischemic stroke. *Funct Neurol* 2012;27:35–40.