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Original Research

Retrospective cohort study on risk factors for developing ischemic stroke

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Abstract

Background: There is a paucity of studies describing the risk factors for developing ischemic stroke in our region. **Objective:** The objective of the current study was to delineate the potential risk factors for the development of ischemic stroke. **Methods:** We have conducted a retrospective cohort hospital-based study that has enrolled 231 subjects. The subjects have had presented to the emergency department in a tertiary hospital in the United Arab Emirates. Subjects were diagnosed with ischemic stroke within 24 hours of presentation. **Outcome measure:** The main outcome measure was the development of ischemic stroke during an indexed hospital visit. **Results:** The mean age was 47.5 ±3.2 with a higher preponderance of males over females (60.9%) and 48.1% were ≥ 65 years. The final logistic regression model for the development of ischemic stroke contains seven variables. In descending order, the seven predictive risk factors for the development of ischemic stroke were: hypertension (OR 6.1, CI 2.4-9.5; P = 0.029), coronary artery disease (OR 4.2, 3.7-9.1; P = 0.038), low physical activity (OR 4.2, CI 2.1-9.1; P = 0.035), history of previous stroke (OR 4.1, 1.4-3.4; P = 0.033), atrial fibrillation (OR 3.2, CI 2.6-8.2; P = 0.017), family history of stroke (OR 3.1, 1.3-6.9; P = 0.042) and diabetes mellitus (OR 2.7, CI 1.25-6.1; P = 0.035). The specificity of the model was 58.1%; the sensitivity was 86.1%, and the overall accuracy was 75.7%. **Conclusion:** It is prudent to control modifiable risk factors for the development of strokes such as hypertension, diabetes, atrial fibrillation, coronary artery disease, and low physical activity.

Keywords: Ischemic stroke; Model; Modifiable and non-modifiable; Predictors; Risk factors

INTRODUCTION

Stroke ranks as the second major cause of death and disability worldwide.[1] Globally, over the past four decades, stroke incidence rates have fallen by 42.0% in high-income countries and increased by more than 100.0% in low and middle-income countries.[2] Ischemic stroke is the most common type of stroke caused by a blockage or clot in a blood vessel in the brain, while hemorrhagic stroke is due to rupture of a blood vessel or an abnormal vascular structure. The severity of ischemic stroke depends on factors such as the type of stroke (ischemic or hemorrhagic), the side of the brain where the stroke occurred (right or left hemisphere), the affected brain lobes, the damaged size, the body functions controlled by the affected area, the duration of blood interruption and the time to get to the hospital.[3] The global of the burden of disease has estimated that about 26 million survivors of stroke, the majority with ischemic stroke (71.0%) and an annual mortality rate of about 6.5 million from them about 51.0% died from ischemic stroke.[2] Males are at higher risk of ischemic stroke than women (133 vs. 99 per 100,000).[4] Stroke is high bothersome life-changing event, which influences not only stroke patients but also their families.[5] For elderly patients, 6 months after stroke, 26.0% are dependent in their daily activities, and 46.0% have cognitive deficits.[6] Although stroke conventionally described as a disease of elderly people, incidence in middle aged is increasingly manifesting as a public health problem.[7] The average age at stroke onset among individuals is decreasing, and stroke incidence and hospitalization rates are rising among middle aged in low or middle-income countries.[8,9] Stroke is considered as disease which can be attributed to the long-lasting exposure to risk factors of different comorbidities or due to behavior that increases the chances of stroke incidence. There are non-modifiable risk factors that triggers stroke such as positive family history, stroke history, age, gender, geographical, hereditary factors and family history.[10,11] The possible role of a positive family history on increasing the risk of stroke has been identified as genetic heritability, inheritance of susceptibility to the effects of such risk factors, familial sharing of cultural/environmental and interaction between genetic and environmental factors.[12] Epidemiological studies support modifiable behavioral lifestyle changes of individual contributing factors of sedentary lifestyle, obesity control, smoking and alcohol. Modification of these factors should greatly affect the incidence of stroke and even mortality rates.[9,11,13]

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A contribution of the modifiable risk factors has essential negative impact and include comorbidities such as hypertension, diabetes mellitus, high blood cholesterol, coronary artery diseases (CAD), valvular disease, atrial fibrillation (AF) and target international normalized ratio (INR) in cardio-embolic strokes. It is assumed that about 90% of strokes can be explained by high blood pressure, AF, diabetes mellitus, smoking and obesity.[14]

A better understanding of contributions of modifiable risk factors to the burden of stroke is important for effective preventive strategies. Primary prevention of stoke among individuals who have not previously experienced a stroke or transient ischemic attack (TIA) is particularly substantial because 77.0% of strokes incidence are first events. The risk of developing a first stroke can be lowered by 80.0% in people, who practice a healthy lifestyle compared with those who do not have this lifestyle change.[15]

OBJECTIVE

The objective of the current study was to delineate the potential risk factors for the development of ischemic stroke.

METHODS

The current study was retrospective cohort study conducted to determine the risk factors for development of ischemic stroke in a sample of 231 subjects. Subjects have had presented within 24 hours from onset of ischemic stroke, to the emergency department in a tertiary hospital, at Al Ain City, United Arab Emirates, during the period from March 2019 to February 2020. The sample size was calculated based on the annual admission to the stroke unit at the hospital. Subjects with hemorrhagic stroke and/or with cerebral venous infarction were excluded from the study. All data collected were directly entered into SPSS to enable the development of a risk factor model for development of ischemic stroke. The procedures used to identify the risk factors (modifiable and nonmodifiable) for the development of ischemic stroke and to build a model were based on the validated procedure published by Hosmer and Lemeshow.[16,17]

STATISTICAL ANALYSIS

We have used univariate and multivariate logistic regression analyses as per Hosmer and Lemshow.[16,17] Logistic regression analysis was performed with model entry set at P = 0.05 to delineate the risk factors for development of ischemic stroke. The application of univariate statistical analysis (chi-squared) has revealed that demographics, medical history, comorbidities and social factors were significantly related (P < 0.1) to the development of ischemic stroke. The multivariate analysis was conducted using stepwise backward logistic regression analysis. The variables with significant univariate test (P < 0.1) were included in the multivariate model. The total number of variables with P value less than 0.1 from the chi-squared tests (likelihood ratio tests statistic) was 20 variables. With reference to the total number of subjects in the study population (N = 231) and as per the recommendations of Hosmer and Lemshow[16] the rule of 10 was followed, which suggests a final predictive model with 10 variables (i.e., one-tenth the smaller group of subjects).

We have entered the significant variables into stepwise backward elimination logistic regression analyses with model entry set at P = 0.2, and model removal set at P = 0.2.17 Repeating this procedure for further elimination with entry and removal values of P = 0.15, P = 0.01, and P = 0.05 yielded final model predictive risk factors for the development of ischemic stroke. Further regression was performed and removal set this time at P = 0.02. A final predictive model with 7 variables was produced. When the cutoff point for risk assessment was set at 0.5, that is, above this point, a risk factor was considered significantly predictive for ischemic stroke.

RESULTS

The mean age (years) was 47.5 ±2.3 (males 48.6 ±0.8 and females 46.5 ±1.9). Slightly more than half of our sample was males (120, 51.9%), and (111, 48.1%) were elderly (≥ 65 years). Slightly less than half of subjects were overweight (112, 48.5%). More than two-third were classified as having sedentary lifestyle of low physical activity (169, 73.1%). Slightly more than half were cigarette smokers, (118, 55.4%). The most documented comorbidities were: hypertension (148, 64.1%), dyslipidemia (109, 47.2%), diabetes mellitus (73, 31.6%), left ventricular hypertrophy (52, 22.1%) and severe renal dysfunction (29, 12.8%) (Table 1).

The severity of ischemic stroke for subjects presented within 24 hours from onset of ischemic stroke, at the emergency department was based on the National Institutes of Health Stroke Scale (NIHSS) score. The cases were classified as mild (28, 12.1%), moderate (160, 69.3%), moderate to severe (30, 13%) and severe (13, 5.6%). The majority of the subjects (160, 69.3%) were having moderate 5 - 15 NIHSS score (Table 2).

The significant non-modifiable predictors of ischemic stroke were: ≥ 65 years 48.1% (OR =1.3; CI = 0.9 - 1.6; P = 0.041, family history 15.6% (OR = 1.7, CI = 1.3 - 1.9; P = 0.039), history of TIA 7.4%, (OR =1.6, CI = 1.4 - 2.0; P = 0.043) and history of previous stroke 6.9% (OR = 2.4, CI = 1.8 - 2.8; P = 0.032) (Table 3).

The significant modifiable predictors of ischemic stroke were: hypertension 64.1% (OR = 2.5, CI =2.2-2.8; P = 0.021), AF 12.8%, (OR = 2.2, CI =1.7- 2.4; P = 0.039), CAD 4.3%, (OR = 2.1, CI =1.7-2.3; P = 0.033), valvular heart disease 10.4%, (OR = 1.2, CI =0.9-1.6; P = 0.046), dyslipidemia 47.2%, (OR =1.3, CI =1.0-1.6; P = 0.032), diabetes mellitus 31.6% (OR = 2.3, CI = 1.8 - 2.4; P = 0.036). Furthermore, overweight [BMI 25 - < 30 Kg/m2] 53.2%, (OR = 1.1, CI = 0.8 to 1.3; P = 0.048), obesity class one [BMI ≥ 30 kg/m2] 22.1% (OR = 1.4, CI = 0.8 – 1.7; P = 0.041) sedentary life of low physical activity 73.1% (OR = 1.8, CI = 1.4 to 2.2; P = 0.043); and being smoker 55.4% (OR = 1.7, CI = 1.4 - 2.3; P = 0.038) (Table 4).

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Table 1. Socio-demographic, anthropometric and comorbidities in the sample (231 subjects)

The parameters	Male Frequency (%)	Female Frequency (%)	Total
Gender	141(61.1)	90 (38.9)	231
Median age (years)	48.6 ± 0.8	46.5 ±1.9	47.5 ±2.3
Age strata (years)*			
18 - 34	15 (53.6)	13 (46.6)	28 (12.1)
35 - 64	48 (52.2)	44 (47.8)	92 (39.8)
≥ 65	57 (51.4)	54 (48.6)	111 (48.1)
Comorbidities			
History of TIA	9 (52.9)	8 (47.1)	17 (7.4)
History of previous stroke	9 (56.2)	7 (43.8)	16 (6.9)
Family history	25 (69.4)	11 (30.6)	36 (15.6)
BMI			
18.5 - 24.9 Kg/m^2 (normal)	25 (43.9)	32 (56.1)	57 (24.7)
25 - 29.9 Kg/m^2 (over weight)	51 (41.5)	72 (58.5)	123 (53.2)
30 - 34.9 kg/m^2 (obesity class 1)	19 (37.3)	32 (62.7)	51 (22.1)
Life style			
Low physical activity)	93 (55.1)	76 (44.9)	169 (73.1)
Cigarette smoking	103 (87.3)	15 (12.7)	118 (55.4)
Comorbidities			
Hypertension	77 (52.1)	71 (47.9)	148 (64.1)
Dyslipidemia	63 (57.8)	46 (42.2)	109 (47.2)
Diabetes Mellitus	38 (52.1)	35 (47.9)	73 (31.6)
Left ventricular hypertrophy	18 (34.6)	34 (65.4)	52 (22.1)
AF	15 (51.7)	14 (48.3)	29 (12.8)
Severe renal dysfunction	15 (51.7)	14 (48.3)	29(12.8)
Thyroid disorders	10 (34.5)	19 (65.4)	29 (12.6)
Valvular heart disease	14 (58.3)	10 (41.7)	24 (10.4)
Liver dysfunction	7 (43.8)	9 (56.2)	16 (6.6)
CAD	4 (40.0)	6 (60.0)	10 (4.3)
Rheumatic heart disease	3 (42.9)	4 (57.1)	7 (3.1)

AF: atrial fibrillation; BMI: Body Mass Index; CAD: coronary artery disease; TIA: transient ischemic stroke

Table 2. The severity of stroke at presentation to the emergency department of the 231 subjects with ischemic stroke based on of NIHSS scale (Appendix 1)

NIHSS Scale	Frequency	Percent (%)
No stroke symptoms	0	0
Mild (1-4)	28	12.1
Moderate (5-15)	160*	69.3*
Moderate to severe (16-20)	30	13.0
Severe (21-42)	13	5.6
Total	231	100.0

NIHSS: National Institutes of Health Stroke Scale; **(%)**: Per cent; *The highest percent in the rows

Table 3. The non-modifiable risk factors as predictors of ischemic stroke

Non-modifiable risk factors	OR (95% CI)	P-value
≥ 65 years	1.3 (0.9 - 1.6)	0.041*
History of TIA	1.6 (1.4 – 2.0)	0.043*
Family history of stroke	1.7 (1.3 - 1.9)	0.039*
History of previous stroke	2.4 (1.8 - 2.8)	0.032*

OR: Odds ratio; CI: confidence interval; *: P < 0.05; TIA: transient ischemic stroke

Table 4. The modifiable risk factors as predictors of ischemic stroke

Risk Factor	OR (95% CI)	P-value
Body Mass Index (BMI)		
25 - 29.9 Kg/m^2 (over weight)	1.1 (0.8 - 1.3)	0.048*
30 - 34.9 kg/m^2 (obesity class 1)	1.4 (0.8 - 1.7)	0.041*
Low physical activity	1.8 (1.4 - 2.2)	0.043*
Cigarette smoking	1.7 (1.4 - 2.3)	0.038*
Comorbidities		
Hypertension	2.5 (2.2 - 2.8)	0.021*
Diabetes Mellitus	2.3 (1.8 - 2.4)	0.036*
AF	2.2 (1.7 - 2.4)	0.039*
CAD	2.1 (1.7 - 2.3)	0.033*
Dyslipidemia	1.3 (1.0 - 1.6)	0.032*
Valvular heart disease	1.2 (0.9 - 1.6)	0.046*

AF: atrial fibrillation; CI: confidence interval; CAD: Coronary artery diseases; OR: Odds ratio; * P <0.05

The final logistic regression model for the development of ischemic stroke contains seven variables. In descending order, the seven predictive risk factors for the development of ischemic stroke were: hypertension (OR 6.1, CI 2.4-9.5; P = 0.029), CAD (OR 4.2, 3.7-9.1; P = 0.038), low physical activity (OR 4.2, CI 2.1-9.1; P =0.035), history of previous stroke (OR 4.1, 1.4-3.4; P =0.033), AF (OR 3.2, CI 2.6-8.2; P = 0.017), Family history of stroke (OR 3.1, 1.3-6.9; P = 0.042) and Diabetes Mellitus (OR 2.7, CI 1.25-6.1, P = 0.035) (Table 5).

The final predictive model for development of ischemic stroke has included seven significantly statistical variables (P < 0.05).

Table 5. The final logistic regression model for the development of ischemic stroke

Risk Factor	Variable coefficient (B)	OR (95% CI)	P-value*
Sedentary lifestyle (low physical activity)	1.6	4.2 (2.1-9.1)	0.035*
Family history of stroke	1.1	3.1 (1.3-6.9)	0.042*
History of previous stroke	1.4	4.1 (1.4-3.4)	0.033*
Hypertension	1.8	6.1 (2.4-9.5)	0.029*
Diabetes Mellitus	1.4	2.7 (1.25-6.1)	0.035*
AF	1.6	3.2 (2.6-8.2)	0.017*
CAD	1.7	4.2 (3.7-9.1)	0.038*

AF: atrial fibrillation; CI: confidence interval; CAD: Coronary artery diseases; OR: Odds ratio; * P <0.05 (*P* value was calculated from the likelihood ratio test)

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The specificity of the model was 58.1%; the sensitivity was 86.1%, and the overall accuracy was 75.7% (Table 6).

Table 6. Observed and predicted totals from the logistic regression model for the development of ischemic stroke

Observed	Predicted		Row totals
	Yes	No	
Yes	61	37	98
No	30	103	133
Column totals	91	140	231

The cut-off point for risk assessment was set at 0.5 i.e., above this point a patient is considered to be at high risk of developing ischemic stroke.

- The specificity of the model was 58.1%, the sensitivity was 86.1%, and the overall accuracy was 75.7%.

DISCUSSIONS

The main finding of the current study was the identification of the significant modifiable and non-modifiable risk factors that contributes to the development of ischemic stroke in our population. The non-modifiable risk factors were: age ≥ 65 years, family history of stroke, history of TIA and history of previous stroke. While the modifiable risk factors were: hypertension, AF, CAD, valvular heart disease, dyslipidemia, diabetes mellitus, overweight, obesity class one, sedentary life of low physical activity and being cigarette smokers.

In our study 61.1% were males which were similar to one study carried out in Egypt,[18] in addition to another study in high income country which stated that males were at higher risk of ischemic stroke than females (133 versus 99 per 100,000).[14] The other finding of the current study indicated that the majority of subjects with ischemic stroke presented to the hospital experienced moderate stroke subtype (69.5%) based on NIHSS baseline. This was higher than that reported in one study in 2014, where 30.3% of ischemic stroke had moderate subtype based on NIHSS score.[19]

Nonmodifiable risk factors

The statistically significant non-modifiable risk factors reported were: ≥ 65 years, family history of stroke; history of transient ischemic stroke and history of previous stroke. The significant negative impact of elderly in ischemic stroke in the current study showed similar finding of one study by Fabris and associates who have reported the affirmed independent association of elderly age explained with carotid atherosclerosis where mean age of patients with significant carotid artery stenosis was more than 65 years.[20] Furthermore, advancing age has a major negative impact on stroke morbidity.[21]

The current study has shown that a family history of stroke was an independent risk factor for developing ischemic stroke and the association between the family history and the risk for developing stroke have been found in the current study in agreement with the study,[22] which has shown the influence of family history on stroke and stroke recovery among Asian populations. Various mechanisms can elucidate the contributing role of a family history on developing the risk of stroke, including genetic heritability of stroke, heritage of susceptibility to the effects of such risk factors, familial sharing of life style factors, and interaction between genetic and environmental factors.[23]

History of previous stroke was recorded in 17.1% of ischemic stroke subjects in the current study which is lower than result from previous research done by Altafi and co-workers who found that history of previous stroke was associated with 26% of ischemic stroke cases.[24]

Modifiable risk factors

In our population and based on the developed risk factor model, the statistically significant modifiable risk factors were: hypertension, diabetes mellitus, AF, CAD and low physical activity.

In the present study, hypertension was the most common risk factor for ischemic stroke, which was detected in 64.1%. This is in agreement with one study[25] conducted by Soliman and co-workers indicating that hypertension accounting for 62.3% of subjects with ischemic stroke. The explanation to the contribution of hypertension as a most significant attributed factor for stroke is grasped with atherosclerosis theory of hypertension due to thickening of the artery walls, resulting in narrowing and eventual blockage of the vessel (ischemic stroke). Also, the circulating debris from damaged atherosclerotic artery walls can cause a stroke by lodging in and blocking a blood vessel in the brain. This is also matching with elderly age as a risk factor for ischemic stroke and the high prevalence of hypertension in older subjects.

In our study, diabetes mellitus had affirmed contributed factors of stroke and this in agreement with study carried out by Patlolla and El Tallawy.[19,26] The diabetes risk factor in this study was accounting for 31.9% of subjects which was slightly lower than in the study conducted by El Tallawy which has recorded 36.5% and lower than another study carried in low-income country (Alexandria-Egypt)[27] which has recorded 66.8% of subjects. The co-morbidity of diabetes represents an independent predictor of reduced survival and further highlights the excess risk of thromboembolism in subjects with AF.[28] In the current study AF (cardio-embolic stroke) which is a highly prevalent arrhythmia accounting for 12.8% of acute ischemic stroke. This outcome was matching with the previous report published in United States Cardiology Review[29] and estimated AF contributing fivefold increase in the risk of stroke. However, this risk is not homogeneous and varies based on the presence of several demographic and comorbidity factors.[30] In the present study CAD and vulvular diseases are affirmed contributing factors to developing stroke with odds ratio 2.1 and 1.2, respectively. This was similar to the findings reported by Bokma study.[31]

Experiencing regular exercise reduces the risk of diabetes, high blood pressure, high cholesterol, and other conditions that increase the risk of ischemic stroke. Deborath Lucia de Oliveira Diniz has reported that sedentary lifestyle was more common in patient with stroke and this finding convenient with our study that predicted low physical activity was recorded in 78.1% (OR=1.7) of subjects developing acute ischemic stroke.[32]

There is strong evidence for the impact of effective interventions delivered by the pharmacist in the management of risk-factor for the development of ischemic stroke. The proved interventions have included the risk-factor reduction and risk-factor target achievement, as reported in a recent Cochrane library systematic review[33] and in a small randomized clinical trial in China.[34] More clinical pharmacists' interventions directed towards drug-related problems have shown to optimize drug therapy in subjects with ischemic stroke.[35]

LIMITATIONS

Our small sample size may hinder generalizability of the risk factor model for the development of ischemic stroke. However, the generalization of the developed model deserves greater attention in similar setting with similar population characteristics. The other limitations of the current study could be the lack of complete data on the nutritional status, lack of data on medication adherence and recurrent cardiovascular events.

CONCLUSIONS

The final predictive model for developing ischemic stroke comprised of modifiable and non-modifiable risk factors. The non-modifiable risk factors were: age ≥ 65 years, family histories of stroke, histories of TIA and histories of previous stroke. While the modifiable risk factors were: hypertension, AF, coronary artery disease, valvular heart disease, dyslipidemia, diabetes mellitus, overweight, obesity class one, sedentary life of low physical activity and cigarette smokers. The final predictive model for risk factors that contribute to the development of ischemic stroke has specificity of 58.1%, sensitivity of 86.1%, and the overall accuracy was 75.7%.

The developed risk model can be emulated by health professionals of similar population characteristics to prevent early ischemic stroke or minimizes the chances for recurrent stroke.

Future research should be directed towards modifiable risk factors for the development of ischemic stroke such as lipid profile, glycosylated hemoglobin and blood pressure control. Interventions directed towards the global burden of ischemic stroke that encompasses behavioral, clinical and economical aspects (at organizational and system levels.) would be of paramount importance.

ABBREVIATIONS

AF	Atrial fibrillation
CAD	Coronary artery disease
INR	International normalized ratio
TIA	Transient ischemic attack

ETHICS APPROVAL

The study was approved by the local ethical committee at the hospital.

DECLARATIONS

Conflicts of interest

We declare no conflicts of interest.

Funding

We have no funding to declare.

Availability of data and material (data transparency)

No data available.

Code availability (software application or custom code)

Not applicable.

Consent to participate

Participants consented.

Consent for publication (include appropriate statements)

All authors consented for publication of this manuscript.

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