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Frequency and risk factors of carotid artery disease among ischemic stroke patients in the south Egypt: hospital-based study

Eman Khedr¹, Abeer A. Tony², Mohamed Habel² and Ahmed Nasr^{1*} 

Abstract

Background: Limited data are available on the frequency of carotid artery disease among cerebrovascular ischemic stroke (CVS) patients in south Egypt. The aim of the present study is to determine the prevalence and risk factors of extracranial atherosclerosis among stroke patients using extracranial duplex ultrasound.

Results: 142 patients (76.8%) were males and 43 (23.2%) were females. Their mean age was 63.3 ± 9.79 years with no significant difference between the mean age of the male and female groups. NIHSS score ranged from 3 to 25 (mean \pm S.D; 11.89 ± 4.91). 66 patients (35.7%) had no atherosclerotic changes, 75 patient (40.5%) had stenosis $< 70\%$ and 44 patients (23.8%) had stenosis $\geq 70\%$. The most prevalent modifiable risk factors for atherosclerosis were hypertension (74.8%), hyperlipidemia (70.6%), smoking (59.7%) and DM (45.4%).

Conclusion: Atherosclerosis among people in the south Egypt is relatively high in comparison to other regions in Egypt and Middle East. This is a call for performing further population-based epidemiological studies, to address the exact magnitude of the problem and invest into prevention.

Keywords: Extracranial, Atherosclerosis, Cerebrovascular, Ischemic, Stroke, South Egypt

Background

Cerebrovascular stroke (CVS) is one of the most common causes of death and disability in the World. It accounts for almost 5% of all disability-adjusted life-years and 10% of all deaths worldwide [1, 2]. The mean and median crude prevalence rates in south Egypt were 721.6/100,000 and 655/100,000, while the mean and median crude incidence rates were 187/100,000 and 180.5/100,000, respectively [3]. Atherosclerosis is one of the major causes of ischemic stroke, it can lead to CVS through progressive stenosis, occlusion of the extra or intracranial vessels and or arterio-arterial embolization from an athermanous plaque [4]. Extracranial atherosclerosis is common among Caucasian stroke patients [5], for example in the

United States and Western communities, extracranial carotid artery disease was estimated to be responsible for 20–30% of strokes [6], while less common in Asian and African populations [5]. Little is known about the prevalence of extracranial atherosclerosis among Egyptian patients who had an ischemic stroke. One study investigated the prevalence of atherosclerosis among CVS patients in Cairo and found that the prevalence of significant extracranial carotid lesions was 16% and non-significant extracranial carotid lesions was 38%. However, up to our knowledge, no studies were done in the south of Egypt.

Duplex Ultrasound plays an important role in establishing the presence, and severity of extracranial arterial atherosclerosis, stenosis and or occlusion in acute stroke. It is relatively cheap, easily available, and can be performed at the bedside. It has been suggested as an essential component of a comprehensive stroke center. Many studies have assessed the accuracy and reliability

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of duplex ultrasound by comparing it to digital subtraction angiography as a reference method, with an excellent accuracy to identify high-grade stenosis (70%) with sensitivity up to 98% [7]. The aim of our work is to study the frequency and risk factors of carotid artery disease among patients with acute ischemic stroke in the south Egypt using duplex Ultrasound.

Methods

Our hospital based cross-sectional study was performed in the period from August 2017 to August 2018. One hundred and eighty-five patients with acute cerebrovascular stroke (CVS) were recruited according to the definition of Stroke [8] from the department of Neurology at one of the University Hospitals, at the south Egypt.

We prospectively studied patients with the following inclusion criteria: acute CVS (duration < 1 month) and Transient ischemic attack (TIA) in patients > 18 years. The following were the exclusion criteria: Patients with hemorrhagic stroke and refusal to participate. All patients were subjected to the following: complete history taking including the demographic data, and risk factors, such as smoking, hypertension, diabetes, dyslipidemia, any history of cardiac disease. The hypertensive patient was defined as a patient with systolic blood pressure 140 mmHg or above and/or diastolic blood pressure 90 mmHg or above, measured in at least two different occasions or if a patient was previously known to have taken antihypertensive drugs [9]. Diabetes mellitus (DM) was defined as fasting plasma glucose of ≥ 126 mg/dl, and/or 2-h plasma glucose in the 75 g oral glucose tolerance test ≥ 200 mg/dL, random plasma glucose ≥ 200 mg/dl and HbA1c $\geq 6.5\%$ (a criterion which is recommended by the World Health Organization) [10]. History of cigarette smoking which considered positive if the patient had smoked 10 cigarettes daily for at least 1 year. Ischemic heart disease (IHD) was considered if the patient had a recent or history of myocardial infarction, were on anti-angina drugs, or had typical ECG findings of recent / previous ischemic events. The patients with nonspecific ST segment and/or T wave changes were not considered as IHD. The assessment of stroke severity with the National Institutes of Health Stroke Scale (NIHSS) was performed to each patient as well as full Laboratory screening and neuroimaging including CT brain and MRI, MRA brain to confirm our findings.

Patients or their family members gave signed an informed consent after explanation of the study methods was provided. Local ethical committee proved the study.

Duplex ultrasonography was performed for each patient using a Philips HD5 (Philips Medical Systems, Nederland B.V.) with L 3–12 MHz linear transducer probe. The examination of extracranial arteries including

Intimal medial thickness (IMT) of the common carotid artery (CCA). Quantification of the IMT at the distal wall of the CCA was done for both sides for every patient and the highest value of the 2 sides was used. The peak systolic velocities (PSVs) and end diastolic velocities (EDVs) were measured in the common, internal, and external carotid arteries (CCA, ICA, ECA) with L 3–12 MHz linear transducer probe and when stenosis was detected the velocities were measured at the maximally stenotic area. The examination was performed by two experienced sonographers to confirm the descriptive findings and measurements among screened patients. The criteria of atherosclerotic changes were interpreted according to the criteria published by the Society of Radiologists in Ultrasound as CCA IMT > 0.1 cm was considered abnormal and A significant ICA stenosis or $\geq 70\%$ ICA stenosis is diagnosed when the ICA PSV is greater than 230 cm/s and visible plaque and luminal narrowing are seen at grayscale and color Doppler US. Additional criteria include ICA/CCA PSV ratio > 4 and ICA EDV > 100 cm/s. The higher the Doppler parameter lies above the threshold of 230 cm/s, the greater the likelihood of severe disease [11]. Peak systolic velocities (PSVs) and end diastolic velocities (EDVs) were measured in the common, external, and internal carotid arteries and when stenosis was detected the velocities were measured at the maximally stenotic area.

Data were analyzed using IBM SPSS Statistics for Windows, Version 24.0. Released 2016. Armonk, NY: IBM Corp. Descriptive statistics: means, standard deviations, medians and percentages were calculated. Test of significances: Chi-square test was used to compare the difference in distribution of frequencies among different groups. For continuous variables, independent *t* test analysis was carried out to compare the means of normally distributed data, while Mann–Whitney *U* test was calculated to test the median differences of the data that do not follow normal distribution. For continuous variables with more than two categories; ANOVA test was calculated to test the mean differences of the data that follow normal distribution. Agreement between MRA and Duplex in diagnosis of extracranial stenosis was examined using weighted Cohen's kappa coefficient (κ); values < 0 indicating no agreement and 0–0.20 slight, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 substantial, and 0.81–1 almost perfect agreement. A *p* value equals or less than 0.05 was considered significant.

Results

185 patients with CVS were included in this study, 142 patients (76.8%) were males and 43 (23.2%) were females. Their ages ranged from 43 to 87 years with mean age 63.3 ± 9.79 years and without significant

difference between the mean age of the male and female groups. NIHSS score ranged from 3 to 25 (mean ± S.D; 11.89 ± 4.91). (The baseline characteristics of both groups shown in Table 1).

119 patients (64.3%) showed extracranial atherosclerotic changes, while 66 patients (35.7%) showed no atherosclerotic changes. The mean age of the atherosclerotic group (64.99 ± 9.11) was significantly higher than the mean age of the non-atherosclerotic group (60.2 ± 10.3). Males were significantly higher in the atherosclerotic group (76.3%) than non-atherosclerotic group (45.8%). The prevalence of DM, hypertension, hyperlipidemia, and smoking were significantly higher among atherosclerotic group than non-atherosclerotic group (Table 2).

The significant extracranial atherosclerosis was observed in 44 patients (23.8%), most of them were males 43 (97.7%) and older than 60 years (95.5%). The most prevalent risk factors among this group were Hypertension (97.7%), hyperlipidemia (88.6%), smoking (75%), DM (65.9%) and IHD (54.5%). The non-significant extracranial atherosclerosis (stenosis < 70%) was observed in 75 patients (40.5% of our patients).

65.3% of them are older than 60 years and 81.3% of them are males (Table 3). The prevalence of the previously mentioned risk factors was significantly higher among group of significant extracranial atherosclerosis.

Our ultrasonographic results were confirmed with Magnetic resonance Angiography on Brain. The MRA protocol screened extracranial carotid starting from its origin at the arch of the Aorta. The overall agreement between MRA and duplex was in 95.4% of cases and discordant results were 4.6% of cases, weighted kappa agreement 0.906, *p* value < 0.001.

Multivariate logistic regression analysis showed that hypertension (OR 18.866, *p* value 0.007), age (odds ratio,

Table 1 Baseline characteristics of the study population

Variable	Number (%)
Age (mean ± S.D.)	63.3 ± 9.79
≤ 60 years	73 (39.5%)
> 60 years	112 (60.5%)
Gender	
Male	142 (76.8%)
Female	43 (23.2%)
DM	71 (38.4%)
Hypertension	116 (62.7%)
Ischemic heart disease	61 (33%)
Dyslipidemia	96 (51.9%)
Smoking	91 (49.2%)
NIHSS (mean ± S.D.)	11.89 ± 4.91

S.D. standard deviation

Table 2 Distribution of risk factors among atherosclerotic and non-atherosclerotic groups

	Non-atherosclerotic patients (n = 66) Number (%)	Atherosclerotic patients (n = 119) Number (%)	<i>p</i> -value
Age	60.2 ± 10.3	64.99 ± 9.11	0.001**
< 60 years	45 (68.2%)	28 (23.5%)	< 0.001**
> 60 years	21 (31.8%)	91 (76.5%)	
Gender			
Male	38 (57.6%)	104 (87.4%)	< 0.001**
Female	28 (42.4%)	15 (12.6%)	
DM	17 (25.8%)	54 (45.4%)	0.009**
Hypertension	27 (40.9%)	89 (74.8%)	0.001**
Ischemic heart disease	20 (30.3%)	41 (34.5%)	0.565
Dyslipidemia	19 (28.7%)	84 (70.6%)	< 0.001**
Smoking	20 (30.3%)	71 (59.7%)	< 0.001**
NIHSS	11.74 ± 4.91	11.97 ± 4.99	0.769

OR 8.638, *p* value 0.012), hyperlipidemia (OR 5.783, *p* value 0.007), and smoking (OR 4.858, *p* value 0.003) were independent predictors of the severity of carotid-atherosclerotic disease (Table 4).

Discussion

The sonographic results of our study clearly outlined the carotid atherosclerotic changes among CVS patients in the south Egypt and identified the risk factors associated with these changes.

Table 3 Frequency of different degrees of carotid atherosclerosis among the study population

	Extracranial stenosis < 70% (n = 75)	Extracranial stenosis ≥ 70% (n = 44)	<i>p</i> -value
Age group			
< 60 years	26 (34.7%)	2 (4.5%)	< 0.001
≥ 60 years	49 (65.3%)	42 (95.5%)	
Sex			
Male	61 (81.3%)	43 (97.7%)	0.009
Female	14 (18.7%)	1 (2.3%)	
DM	25 (33.3%)	29 (65.9%)	0.001
Hypertension	46 (61.3%)	43 (97.7%)	< 0.001
Ischemic heart disease	17 (22.7%)	24 (54.5%)	< 0.001
Dyslipidemia	45(60%)	39 (88.6%)	0.001
Smoking	38 (50.7%)	33 (75%)	0.009
NIHSS (mean ± SD)	12.12 ± 2.6	11.80 ± 1.7	0.533

Table 4 Independent predictors of significant extra cranial atherosclerosis $\geq 70\%$

Factor	Odds ratio	95% CI*	p-value
Age (≥ 60 years)	8.638	1.607–16.424	0.012
Sex (male)	1.167	0.454–1.822	0.142
DM	1.457	0.512–4.145	0.481
Hypertension	18.866	2.256–37.157	0.007
Ischemic heart disease	1.682	0.564–5.016	0.351
Dyslipidemia	5.783	1.620–19.651	0.007
Smoking	4.858	1.713–13.781	0.003

CI confidence interval

Bolding the numbers was used to draw the attention of the readers to the positive results, bold values are the independent predictors of the atherosclerosis

119 patients (64.3%) out of 185 patients showed extracranial carotid atherosclerotic changes.

The frequency was higher than population in the Cairo region as atherosclerotic carotid artery disease was present in 41% of the study population [12]. Our frequency was higher than population in the Iran (49%) [13], Pakistan (56%) of stroke patients [14]. Another study in China showed that the prevalence of carotid atherosclerosis among patients with first-ever cerebral infarction (59.38%) [15] and 30.4% among Indian stroke patients [16]. Our frequency was near to its frequency among population in United States. Examination of 1189 members of the Framingham cohort (asymptomatic), aged 66–93 years, revealed atherosclerotic changes in 70% of patients [17]. These findings mean that population in the south of Egypt have high frequency of carotid atherosclerosis near to Caucasian population and higher than population in north Egypt, another population in the middle east and Asian population.

44 patients (23.8%) showed significant carotid stenosis 70–99%, while 75 patients (40.5%) showed stenosis $< 70\%$. This percentage of significant carotid stenosis was much higher than the population in the Cairo region (0.8%), while frequency of carotid stenosis $< 70\%$ was similar to our which was 41% [12]. Another study performed in the Cairo region also showed that their prevalence of significant extracranial carotid lesions was 16% and non-significant extracranial carotid lesions was recorded in 38% [18]. The marked discrepancy between the previous two studies could be attributed to the variation in the sample size which was 4733 patients in the first study and 50 in the second one. Moreover, the first study included stroke and ischemic heart disease patients while the second study included only stroke patients. Although this discrepancy, our prevalence of significant carotid atherosclerosis was considered higher than Cairo region.

In the present study the significant extracranial atherosclerosis found to be higher also than population in the Middle East, such as Iran population (18%) [13] and Saudi population (9%) [19]. Our significant stenosis were higher than Asian population, such as Pakistani populations (12%) [20] and Taiwan population (9%) [21] and (6%) [22]. Our frequency of significant stenosis was as high as Caucasian population (20–30%) [23–25]. This high percentage of significant carotid stenosis could be explained by the high percent of vascular risk factors associated with this group, which play an important role for developing atheroma.

The hypertension, diabetes mellitus, dyslipidemia and smoking were the most important modifiable vascular risk factors associated with carotid atherosclerosis and the multivariate stepwise logistic regression analysis of our data showed that Age, hypertension, hyperlipidemia and smoking are independent predictors of severe carotid atherosclerosis ($\geq 70\%$).

Comparing the prevalence of vascular risk factors in our study with other studies showed that the prevalence of hypertension among the atherosclerotic group was 74.8% which is higher than its prevalence in Assiut and Qena governorates in the north of southern Egypt (66% and 62.2%, respectively) [26, 27], much higher than north of Egypt (38%) [12]. The current study prevalence was near to Caucasians (72%), Hispanics (70%) and Asians (75%) and lower than its prevalence among African Americans (97%) [25].

The high prevalence rate among people in the south of Egypt in comparison to north of Egypt could be explained by Hasan and colleagues [28], Mosley and colleagues [29] whom studied blood pressure differences among Egyptian population and found high prevalence of hypertension among people in Aswan Governorate, they hypothesized that hypertension is higher among dark skin people which is common among people in Aswan Governorate. The high prevalence rate of hypertension among population in Aswan in comparison to other population in the south of Egypt could be explained by their selection criteria of the study sample as they did not exclude patients with cardioembolic, hypercoagulable states and vasculitis syndromes, such as the current study.

We had high prevalence of DM (75.4%) than people in the Cairo region (38%) [18], Assiut region 38.6% [26], people in Pakistan (37%) [20] and Asians (37%), Hispanics (50%), Caucasians (28%) and African Americans (31%) [25]. We had slightly higher prevalence rate of Dyslipidemia (68.4%) than people at the Cairo region (62%) [18], much higher than Caucasians (19%), African Americans (16%), Hispanics (15%) and Asians (9%) [25]. The high rates of DM and Dyslipidemia could be explained by

Table 5 Distribution of atherosclerotic ischemic stroke risk factors among people in the south of Egypt in comparison to different regions

	DM	Hypertension	Dyslipidemia	Smoking
Our study	75.4%	83%	68.4	71.9%
Cairo [18]	38%	76%	62%	50%
Assiut [3, 26]	38.6%	66%		
North of Egypt (%) [12]	27.6%	38%		
Pakistan [20]	37%	59%		24%
Caucasians [25]	28%	72%	19%	56%
Hispanics [25]	50%	70%	15%	
Asians [25]	37%	75%	9%	
African Americans [25]	31%	97%	16%	59%

unhealthy feeding habits among population in the south of Egypt and lack of physical exercise [30]. People in the south of Egypt had higher rate of smoking (71.9%) than people in the Cairo region (50%) [18], Caucasians (56%) and African Americans (59%) and people in Pakistan (25%) [20] (Table 5).

Conclusion

The high prevalence rates of the vascular risk factors among population in the south Egypt could explain the higher frequency of carotid atherosclerosis in the south Egypt, as 23.8% showed significant carotid stenosis (70–99%), while 40.5% showed insignificant stenosis (<70%).

Limitations of our study

The present study had some limitations such as its hospital-based study and not population-based study which considered more reliable indicator of true disease patterns. Female patients in the south Egypt prefer to continue their treatment at home which was reflected on the sex distribution in our sample. Moreover, Doppler studies are operator-dependent, with a sensitivity and specificity of 90% and 88% [7]. We did not analyze inter-observer variability for evaluation of degree of atherosclerosis, which may be a source of potential bias.

Acknowledgements

Not applicable.

Authors' contributions

All authors have read and approved the manuscript. EK: developed the theory and supervised the findings of this work. AT: Investigated the patients and supervised the findings of the work. MH: investigated the patients. AN: Participated in the research idea development, wrote the manuscript with input from all authors. All authors read and approved the final manuscript.

Funding

Not applicable.

Availability of data and materials

The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Patients or their family members gave signed an informed consent after explanation of the study methods was provided. Local ethical committee of the faculty of medicine, Aswan University proved the study in September 2017 (IRB no: ASWU/171/9/17).

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Received: 15 June 2021 Accepted: 4 September 2021

Published online: 20 September 2021

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