Clinical profile of stroke patients and the association of carotid intima-media thickness at Al-Madinah, Saudi Arabia

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Abstract: Background: Stroke, a common neurological disorder which can be ischemic or hemorrhagic, is a leading cause of morbidity and mortality worldwide. Carotid intima-media thickness (CIMT) is a sensitive subclinical atherosclerosis marker and a strong predictor of subsequent cerebrovascular morbidity. **Aim of the work:** This study sought to detect the risk factors associated with cerebral stroke and to investigate the relationship between these risk factors and (CIMT) in both ischemic stroke (IS) and hemorrhagic stroke (HS). **Patients and methods:** This age and sex-matched case control study was carried out on 50 cerebral stroke patients with a mean age of 51 ± 7.05 years and 50 nonstroke patients with a mean age of 50.70 ± 7.18 years. Careful history taking and clinical examination was conducted, including age; gender; smoking habits; associated comorbidity, preexisting stroke, and preexisting coronary heart disease. CIMT was measured with high resolution ultrasonography by experienced radiologists. **Results**: The study revealed high statistical significance with body mass index (BMI), moderate and heavy smoking, CIMT, hyperlipidemia, diabetes mellitus (DM), and preexisting ischemic heart disease (IHD) in patients who had had a stroke compared to nonstroke patients. There was a highly significant statistical increase in moderate and heavy smokers who suffered IS compared to those with HS. IHD and hypertension was significantly present in HS patients compared to IS patients. The presence of DM was statistically more common among patients with IS than those with HS. **Conclusion**: The risk for cerebral stroke was higher among patients with elevated BMI, who are moderate to heavy smokers, have elevated CIMT, hyperlipidemia, DM, and IHD. The risk for IS was higher among patients who are moderate to heavy smokers, and have DM; whereas the risk for HS was higher among patients with hypertension and IHD. CIMT caused no significant difference between IS and HS patients.

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Keywords: Cerebral stroke, ischemic stroke, hemorrhagic stroke, carotid intima-media thickness (CIMT).

Introduction:

Stroke is one of the leading causes of morbidity and mortality worldwide (1,2). Both ischemic and hemorrhagic, stroke is a common and devastating disorder (3). Stroke is clinically diagnosed as sudden onset of focal and global disturbances of cerebral function lasting 24 hours or longer and likely to result in death with no apparent cause other than that of vascular origin (4). CIMT is a marker of subclinical atherosclerosis, a strong predictor of subsequent cardiovascular and cerebrovascular morbidity (5,6). Increases in the thickness of the intima and media of the carotid artery have been associated with an increased risk of myocardial infarction (MI) and stroke in subjects without a history of cardiovascular disease (7). An increase in the CIMT by 0.1 mm increases the risk of MI by 10% to 15% and of stroke by 13% to 18% (8). The risk factors for stroke are modifiable and non-modifiable. The modifiable risk factors are mostly related to atherosclerotic burden and include diabetes, hypertension, smoking and hyperlipidemia (3).

The purpose of this study is to detect the risk factors associated with cerebral stroke and to investigate the relationship between these risk factors and CIMT in both IS and HS.

Patients and methods: This case-control study was carried out on 50 cerebral stroke patients (27 males and 23 females, with a mean age of 51 ± 7.05 years) and 50 nonstroke patients (27 males and 23 females, with a mean age of 50.70 ± 7.18 years) who were admitted to King Fahd Hospital, Al-Madinah Al-Munawara, Saudi Arabia. The control group was age and gender matched with the cases. Controls were selected from inpatients and outpatients at the neurology outpatient clinic of the hospital. The diagnosis of stroke was made by referring neurologists from the admitting hospital, proven by brain CT/MRI.

Adherence to federal and state regulations concerning the welfare of human subjects was maintained throughout the study. Participants' rights, privacy, health, and well-being were safeguarded through informed consent forms they were asked to read and sign if they agreed to participate in the study.

All cerebral stroke and nonstroke patients were subjected to:

- A thorough history taking and careful clinical examination that included noting age, gender, smoking habits, associated co morbidities (DM, hypertension and dyslipidemia), preexisting stroke, and preexisting coronary heart disease.
- BMI) was computed as weight (kilograms) divided by height (meters squared); blood samples were taken for routine laboratory investigations.
- CIMT measurements were performed with high-resolution ultrasonography by trained physicians using a high-resolution B-mode tomographic ultrasound system (Esaote Biomedica SpA, Italy) with a linear 7.5 MHz transducer. Measurements were conducted on the far wall of the right and left common carotid arteries, 1.5 cm proximal to the bifurcation. The transducer was manipulated so the lumen diameter was maximized in the longitudinal plane. CIMT was measured online at the end of diastole as the distance from the leading edge of the first echogenic line to that of the second echogenic line. The first and second lines represent the lumen-intimal interface and the collage-contained upper layer of tunica adventitia, respectively. The greater value of the right and left common CIMT was used for analysis (9). In healthy middle-age adults, the distance from the CCA lumen-intima interface and the media-adventitia interface measures 0.6-0.7 mm (10).

Statistical analysis: Data on the main study aim was analyzed using SPSS version 16. Descriptive characteristics for participants are expressed as mean and standard deviation for continuous variables, number and percent for categorical variables. The independent sample t-test was utilized to show the significant difference between the continuous variable and Chi square test for the categorical variables. The level of significance was accepted at $p \leq 0.05$. Odds ratio (OR) and confidence intervals (CI) were used to test the risk of studied variables in association with cerebrovascular stroke.

Results

The mean age of patients in this study who had experienced a stroke was 51 ± 7.05 years, while nonstroke patients were 50.70 ± 7.18 years. Males constituted 54% of the cases and controls; females, 46%. Characteristics of the stroke and nonstroke patients are presented in **Table 1** according to the studied variables. Highly statistically significant increases were noted in BMI, CIMT, hyperlipidemia, DM, and IHD in patients with stroke compared to nonstroke patients. Also, there was a highly statistically significant increase of moderate to heavy smokers in patients who had experienced a stroke compared to nonstroke patients; and a highly statistically significant increase of non smokers in nonstroke patients compared to stroke patients. There were no statistically significant differences between stroke and nonstroke patients regarding hypertension. The main clinical features in stroke patients in this study were weakness (60%) followed by confusion (24%); 84% of nonstroke patients complained of headaches.

In this study the association between studied variables and stroke showed the highest risk of stroke in heavy smokers as presented in **Table 2**, with the OR and their 95% CI (OR= 6.61; 95% CI= 3.13¬ – 8.21); moderate smokers (OR= 5.22; 95% CI= 2.13 – 7.51); and IHD (OR= 4.63; 95% CI= 1.55 – 13.84). Confusion is 31 times more likely to be associated with stroke patients (OR= 31.50; 95% CI= 20.23 – 42.41) than nonstroke patients; weakness is 26 times more likely to be associated with stroke (OR= 26.25; 95% CI= 15.86 – 41.34) than nonstroke patients. No significant associated risks of hypertension or gender on occurrence of stroke were noted.

There was a highly statistically significant increase of moderate and heavy smokers in those who suffered IS compared to HS patients as shown in **Table 3** and a highly statistically significant increase of nonsmokers among those who suffered HS compared to IS. IHD increased significantly in HS patients compared to those with IS. There was a statistically significant increase in those with hypertension in HS (73.3%) patients compared to IS (20%) patients. DM was significantly present statistically more frequently among patients with IS (48.6%) than those with HS (13.3%). There were no significant differences between IS and HS patients regarding age, gender, BMI, CIMT, hyperlipidemia and the main clinical manifestation.

As shown in **Table 4** the highest risk of HS was associated with hypertension (OR= 11.0; 95% CI= 2.67 – 45.17), and IHD (OR= 5.06; 95% CI= 1.38 – 18.57), while the lowest risk of HS was associated with DM (OR= 0.16; 95% CI= 0.03 – 0.83). Other variables (gender, hyperlipidemia and the main clinical manifestation) showed no significant associated risk.

Discussion: Stroke, both ischemic and hemorrhagic, is a common and devastating disorder. Currently, ischemic heart disease and stroke are the leading causes of mortality worldwide, with more than 80% of deaths occurring in low and middle income countries (11). The purpose of this study is to detect the risk factors associated with cerebral stroke and to investigate the relationship between these risk factors and CIMT in both ischemic and hemorrhagic cerebral stroke. Our study showed highly statistically significant increases in BMI in stroke patients

compared to nonstroke patients and no significant differences between IS and HS patients regarding age, gender, and BMI. Song et al. 2004 (12), reported a positive association across the whole range of BMI and ischemic stroke, with a confounder-adjusted hazard of 11% (95% CI, 1.09 to 1.12) for a 1 kg/m2 higher BMI. A J-shaped association was observed between BMI and HS; groups with a higher BMI than the reference category (22 to 23 kg/m2) had significantly increased risks. On the other hand, Susan et al. 1996 (13), demonstrated that BMI was not significantly associated with the risk of stroke.

This study revealed highly statistically significant increases in moderate to heavy smokers, and those with hyperlipidemia, DM, and IHD in stroke compared to nonstroke patients and highly statistically significant increases in moderate to heavy smokers in ischemic stroke compared to HS patients. IHD and hypertension is statistically significantly increased in HS patients compared to IS patients. DM was statistically significantly increased among patients with IS than those with HS. Liu et al. 2005 (14), reported that patients in their study (n_3,901) who smoked and had hypercholesterolemia, migraine, previous transient ischemic attack, atrial fibrillation, and heart disease, more frequently had IS; whereas hypertension was the only significant factor related to HS. In their study, Hajat et al. 2001 (15), showed those of increasing age, who suffered a previous stroke, and/or diabetes more often experienced IS, whereas ischemic heart disease, atrial fibrillation, hypertension, alcohol intake, and smoking was not significantly present in either of the stroke subtypes. Based on 39,484 patients, Klaus et al. 2009 (16), reported well-established risk factors and markers of atherosclerotic and occlusive arterial disease, such as diabetes, atrial fibrillation, previous myocardial infarction, previous stroke, and intermittent arterial claudication, were associated with IS rather than HS. Smoking and high alcohol intake favored HS, whereas age, gender, and hypertension did not herald stroke type.

Table 1: Characteristics of patients studied

	Stroke No= 50		**Nonstroke No= 50**		P value
	No.	**%**	**No.**	**%**	
Age (Years) M±SD	51.46±7.05		50.70±7.18		0.59
Body mass index (K gm/height^2) M±SD	28.48±3.67		26.30±3.6		0.00*
CIMT M±SD	2.06±0.54		0.82±0.40		0.00*
Gender					
Male	27	54.0	27	54.0	
Female	23	46.0	23	46.0	1.00
Smoking					
Non smoker	10	20.0	22	44.0	
Mild smoker	9	18.0	16	32.0	
Moderate smoker	19	38.0	8	16.0	
Heavy smoker	12	24.0	4	8.0	0.00*
Hyperlipidemia					
No	29	58.0	42	84.0	
Yes	21	42.0	8	16.0	0.01*
IHD					
No	33	66.0	45	90.0	
Yes	17	34.0	5	10.0	0.01*
Hypertension					
No	32	64.0	39	78.0	
Yes	18	36.0	11	22.0	0.12
DM					
No	31	62.0	45	90.0	
Yes	19	38.0	5	10.0	0.00*
Main clinical feature					
Headache	8	16.0	42	84.0	
Weakness	30	60.0	6	12.0	
Confusion	12	24.0	2	4.0	0.00*

*Significant difference

Table 2: Odds ratios (OR) and their 95% confidence intervals (CIs) for the association between the studied variables with stroke

	Stroke No=50	**Nonstroke No=50**	OR	
Gender				
Female	23	23	**1.00**	**Reference**
Male	27	27	1.00	0.45 – 2.11
Smoking				
Non smoker	10	22	**1.00**	**Reference**
Mild smoker	9	16	1.23	1.09 – 2.50
Moderate smoker	19	8	5.22	2.13 –7.51
Heavy smoker	12	4	6.61	3.13–8.21
Hyperlipidemia				
No	29	42	**1.00**	**Reference**
Yes	21	8	3.80	1.48 – 9.75
IHD				
No	33	45	**1.00**	**Reference**
Yes	17	5	4.63	1.55 – 13.84
Hypertension				
No	32	39	**1.00**	**Reference**
Yes	18	11	1.99	0.82 – 4.82
DM				
No	31	45	**1.00**	**Reference**
Yes	19	5	5.51	1.86 – 16.34
Main clinical feature				
Headache	8	42	**1.00**	**Reference**
Weakness	30	6	26.25	15.86 – 41.34
Confusion	12	2	31.50	20.23 – 42.41

Table 3: Relationship between studied variables and type of stroke

	Ischemic stroke No=35		**Hemorrhagic stroke No=15**		P value
	No.	**%**	**No.**	**%**	
Age (in years)	50 ±7.10		52.86 ± 6.97		0.36
Body mass index	28.42 ± 3.47		28.60± 4.23		0.88
CIMT	2.08 ± 0.53		2.00 ±0.59		0.61
Gender					
Male	21	60.0	6	40.0	
Female	14	40.0	9	60.0	0.19
Smoking Non smoker	7	20.0	3	20.0	
Mild smoker	5	14.3	4	26.7	
Moderate smoker	13	37.1	6	40.0	
Heavy smoker	10	28.6	2	13.3	0.00*
Hyperlipidemia					
No	22	62.9	7	46.7	
Yes	13	37.1	8	53.3	0.28
IHD					
No	27	77.1	6	40.0	
Yes	8	22.9	9	60.0	0.01*
Hypertension					
No	28	80.0	4	26.7	
Yes	7	20.0	11	73.3	0.00*
DM					
No	18	51.4	13	86.7	
Yes	17	48.6	2	13.3	0.01*
Main clinical feature					
Headache	5	14.3	3	20	
Weakness	23	65.7	7	46.7	
Confusion	7	20.0	5	33.3	0.44

*Significant difference

Table 4: Odds ratios (OR) and their 95% confidence intervals (CIs) for the association between the studied variables with the type of stroke

Factor	Type of stroke		OR	95% CI
	Ischemic stroke No=35	Hemorrhagic stroke No=15		
Gender				
Female	14	9	**1.00**	**Reference**
Male	21	6	0.44	0.12 – 2.11
Smoking				
Non smoker	7	3	**1.00**	**Reference**
Mild smoker	5	4	1.86	0.82 – 3.25
Moderate smoker	13	6	1.07	0.54 – 2.43
Heavy smoker	10	2	0.46	0.23 – 0.76
Hyperlipidemia				
No	22	7	**1.00**	**Reference**
Yes	13	8	1.93	0.56 – 6.58
IHD				
No	27	6	**1.00**	**Reference**
Yes	8	9	5.06	1.38 – 18.57
Hypertension				
No	28	4	**1.00**	**Reference**
Yes	7	11	11.00	2.67 – 45.17
DM				
No	18	13	**1.00**	**Reference**
Yes	17	2	0.16	0.03 – 0.83
Main clinical feature				
Headache	5	3	**1.00**	**Reference**
Weakness	23	7	0.50	0.03 – 1.03
Confusion	7	5	1.19	0.92 – 1.82

This study revealed highly statistically significant increases in CIMT in stroke compared to nonstroke patients, but no significant differences between IS and HS patients regarding CIMT. This is in accordance with Jain et al. 2012 (17), who reported a statistically significant increase in the intima-media thickness of the common carotid artery in patients with CT-proven IS. Also, Chien et al. 2008 (18), found similar results in a community-based cohort study and reported a significant association between CIMT and incidence of stroke in Chinese adults. Touboul et al. 2000 (19), reported that mean measurements for common carotid intimal-medial thickness (CCA IMT) of 470 stroke patients and 463 control patients were 0.797 and 0.735 mm, respectively. They also reported meaningful relationships between stroke and increased IMT. A study by Freitas et al. 2012 (20), among three groups of patients (those with IS, HS and no event) showed the risk of IS increased with the increase of CCA IMT. Therefore they introduced increased CCA IMT as an independent predictor of the risk for IS, but not for HS. Ohira et al. 2011 (21), also reported a close relationship between CCA IMT and HS and IS.

Conclusion:

This study agreed with previously published studies regarding IS and HS. The risk for cerebral stroke was higher among patients with elevated BMI, who were moderate to heavy smokers, had elevated CIMT, hyperlipidemia, DM, and IHD. The risk for IS was higher among patients who were moderate to heavy smokers, and had DM. The risk for HS was higher among patients with hypertension and IHD. There were no significant differences between IS and HS patients regarding CIMT. Further study may be needed with different radiological techniques to compare specificity and sensitivity of elevated CIMT and even prognostication for stroke patients.

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