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Demographic and risk factors profile of intracranial atherosclerotic stenosis in the Kingdom of Bahrain

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Abstract

Background: Intracranial atherosclerotic stenosis (ICAS) is one of the most common causes of stroke worldwide. This study aimed to analyze the demographic and risk factor profiles of ICAS in the Kingdom of Bahrain. The study population included 477 patients who were hospitalized in the Neurology Department from March 1, 2018, to September 1, 2020 because of acute ischemic stroke and underwent arterial brain imaging (CTA or MRA) examination during their hospitalization.

Results: Of 477 patients, 123 (25.7%) had ICAS. A history of stroke/transient ischemic attack was significantly higher in patients with intracranial stenosis ($P=0.012$). Patients with ICAS had significant concurrent extracranial arterial stenosis (ECAS) ($P=0.00$). In Bahraini patients, dyslipidemia was associated with a higher percentage of developing ICAS, but this was statistically nonsignificant ($p=0.06$).

Conclusions: An independent and significant correlation was found between ICAS and stroke recurrence. In addition, a concurrent existence of ECAS and ICAS was noted.

Keywords: Ischemic stroke, Intracranial atherosclerotic stenosis, Kingdom of Bahrain, ICAS risk factors, Stroke recurrence

Background

Intracranial atherosclerotic stenosis (ICAS) is a leading cause of stroke worldwide; however, the prevalence of ICAS varies across different populations, with Asians, Hispanics, and African Americans appearing to be the most affected [1–5]. In the United States of America, it has been reported that up to 10% of the estimated 900,000 strokes or transient ischemic attacks (TIAs) are affected annually by ICAS, and the recurrence risk in these patients is 15% per year [6]. ICAS is projected to account for 33–50% of stroke cases and more than 50% of TIAs in Chinese communities [5].

Bahrain is an archipelago kingdom situated off the eastern coast of Saudi Arabia in the Arab Gulf. It is the smallest country in the Gulf Cooperation Council (GCC), with an area of 778 km^2 [7]. Bahrain's population has nearly doubled since 2001, mainly due to globalization, and is now approximately 1.5 million people, with 52.6% of them being expatriates [7]. Most of these non-nationals are South and Southeast Asian foreign workers, mainly in India, Bangladesh, Pakistan, and the Philippines [8]. According to previous studies, the incidence of stroke has doubled in Bahrain's population [9, 10]. However, no studies have addressed the relationship between ICAS and stroke in Bahrain and other GCC countries.

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This study aimed to investigate ICAS as a potential risk factor for ischemic stroke in the The Kingdom of Bahrain and to highlight the associated risk factors.

Methods

Electronic files of all patients admitted under Neurology care with a diagnosis of stroke during the period from 1st March 2018 to 1st Sept 2020 were reviewed. Fifty-four patients with the diagnosis of patient intracranial hemorrhage were excluded. The remaining 477 Patients were classified into two groups according to the presence or absence of ICAS. The demographic and risk factor profiles for both groups were studied, and risk factor stratification was performed based on nationality (Bahraini and non-Bahraini).

Using the method provided in the Warfarin-Aspirin for Symptomatic Intracranial Disease study, ICAS was defined as a reduction in luminal diameter of at least 50% [6]. The North American Symptomatic Carotid Endarterectomy Trial method was used to assess extracranial atherosclerosis in the carotid artery at the bifurcation level. Extracranial atherosclerosis was diagnosed if the luminal diameter was reduced by at least 50%.

Patients were diagnosed with hypertension if they were taking antihypertensive medication or had systolic blood pressure greater than 140 mmHg or diastolic blood pressure greater than 90 mmHg on two separate occasions. Diabetes mellitus was diagnosed if the patient was currently receiving insulin or oral hypoglycemic medications or if their fasting blood glucose level was > 200 mg/dl. Hyperlipidemia was defined as the use of lipid-lowering medications, fasting serum total cholesterol concentration of 200 mg/dL, low-density lipoprotein cholesterol concentration of 140 mg/dL, high-density lipoprotein cholesterol concentration of 40 mg/dL, triglyceride concentration of 150 mg/dL, or a previous diagnosis of hyperlipidemia. A clinician identified atrial fibrillation by reviewing patient electrocardiograms, reviewing medical records, or based on a previous medical diagnosis. A history of myocardial infarction, angina pectoris, evidence of ischemia on electrocardiography, or medical records was used to define ischemic heart disease. A history of intermittent claudication, peripheral vascular surgery, angioplasty, or a previous diagnosis was used to characterize the peripheral vascular disease.

Statistical analyses were performed using SPSS version 25.0. Descriptive statistics were used to compute the frequencies, percentages, means, and standard deviations. The chi-square test was used to compare significant differences between the two groups with categorical data. Logistic regression methods were used to compute the odds ratio (OR) for all independent risk factors for ICAS. All statistical analyses were two-tailed, and a p value of less than 0.05 was considered significant.

Results

The average age of the 477 individuals analysed was 60.64 ± 14.95 years. There were 315 male patients (66%) and 161 non-Bahraini patients (33.7%). Arterial brain imaging, which included CTA (377 (79%)) and MRA, revealed that 123 (25.7%) patients had potentially symptomatic ICAS. Table 1 shows the patients' demographic characteristics and the distribution of risk factors.

Logistic regression analysis revealed that only ECAS (OR = 3.53, 95% CI = 1.95–6.26, $p = 0.000$) and stroke recurrence (OR = 1.76, 95% CI = 1.13–2.74, $p = 0.012$) were independent and significant predictors for the presence of ICAS. There was no effect of nationality,

Table 1 Distribution of demographic and vascular risk factors and vascular diseases in the whole group of patients

	Non ICAS ($n = 354$)	ICAS ($n = 123$)	p value
Gender			
Male	231 (65.3%)	84 (68.3%)	0.58
Female	123 (34.7%)	39 (31.7%)	
Age (mean ± SD)	60.57 ± 15.44	60.54 ± 13.48	0.93
Nationality			
Bahraini	232 (65.5%)	89 (72.4%)	0.18
Non-Bahraini	122 (34.5%)	34 (27.6%)	
HTN			
Yes	266 (75.1%)	89 (72.4%)	0.55
No	88 (24.9%)	34 (27.6%)	
DM			
Yes	202 (57.2%)	81 (65.9%)	0.11
No	151 (42.8%)	42 (34.1%)	
Previous stroke/TIA			
Yes	85 (24.0%)	44 (35.8%)	**0.013**
No	269 (76. %)	79 (64.2%)	
IHD			
Yes	77 (21.8%)	24 (19.5%)	0.70
No	277 (78.2%)	99 (80.5%)	
PAD			
Yes	13 (3.7%)	3 (2.4%)	0.77
No	341 (96.3%)	120 (97.6%)	
Dyslipidemia			
Yes	115 (32.6%)	34 (27.9%)	0.36
No	238 (67.4%)	88 (72.1%)	
ECAS			
Yes	26 (7.8%)	28 (22.8%)	**0.00**
No	309 (92.2%)	95 (77.2%)	

ICAS intracranial atherosclerotic stenosis, *HTN* hypertension, *DM* diabetes mellitus, *TIA* transient ischemic attack, *CAD* coronary arterial disease, *PAD* peripheral arterial disease, *ECAS* extracranial atherosclerotic stenosis

hypertension, diabetes, dyslipidemia, ischemic heart disease, or peripheral heart disease before or after the logistic regression analysis (Table 2).

The analysis of ICAS risk factors in Bahraini versus non-Bahraini patients found that dyslipidaemia was more prevalent in Bahraini patients (marginally significant $P=0.06$). Table 3 shows the distribution of risk variables among patients with ICAS by nationality.

Discussion

We assessed the possible predictors of symptomatic ICAS in a cohort of patients with ischemic stroke admitted to the Kingdom of Bahrain's only comprehensive stroke center during the study period. To diagnose ICAS, we used CTA/MRA, considered a reliable method for detecting intracranial stenosis [11, 12].

The percentage of strokes attributable to ICAS is higher in the Asian population (33–50%) [6] compared to the United States and western nations (10–15%) [5]. In this study, the prevalence of strokes attributed to ICAS in the Bahraini population was similar to that observed in studies conducted in other Middle Eastern countries [13–15].

Many studies show that advancing age is associated with a rise in the prevalence and severity of ICAS [16–19]. The current study could not find a significant correlation between the age of stroke onset and ICAS, similar to previous studies conducted in other Middle Eastern countries [13, 15].

The relationship between ICAS and gender remains contentious. Several studies have demonstrated a female preponderance in ICAS [20, 21], whereas others have shown a male preponderance [22]. Similar to other studies done in the Middle East [13, 15], we did not find any correlation between gender and ICAS in stroke patients of the Bahraini population. We observed that patients with potentially symptomatic ICAS had a higher prevalence of ECAS. This coexistence can be explained by the fact that, as a systematic disease, atherosclerotic disease commonly affects multiple vascular beds [23, 24].

Another notable result in this study was the higher prevalence of previous stroke and TIA in the ICAS group. This association has been proven in many studies [25, 26]. These studies have proven a correlation between the presence or severity of ICAS and the risk of recurrent stroke and mortality [25, 26].

Numerous clinical studies have confirmed the correlation between hypertension and ICAS [16, 22]. In addition, hypertension has been linked to the severity of ICAS [13, 16, 18]. The current study failed to prove this correlation, similar to the result of one Middle Eastern study [15]. Furthermore, because of the study method, we could not study the relationship between hypertension and the severity of ICAS.

Clinical studies revealed diabetes as a significant risk factor for ICAS in symptomatic and asymptomatic patients [17, 18]. In the Korean population, diabetes has been recognized as a risk factor for ICAS only beyond the age of 50 and in cases of atherosclerosis of the posterior circulation [19]. In our study, there was no significant relationship between diabetes and ICAS. This is similar to other regional studies [15]. This could be because the current study did not look at the relationship between diabetes and ICAS based on DM age distribution or ICAS location.

There is a consistent relationship between dyslipidemia and ECAS, but this relationship remains uncertain for ICAS [20, 22, 27, 28]. Dyslipidemia was slightly associated with intracranial stenosis in Bahraini patients, but it was not statistically significant. In the Middle East, a previous study [13] found a link between ICAS and dyslipidemia, but another study [15] did not.

This was a retrospective study; hence, the findings cannot prove a temporal association between the examined risk variables and ICAS, nor can they be extrapolated to the complete the population of Bahrain. Several risk variables considered in the study were based on self-reports or previous medical records, which could lead to under-reporting. As the investigated cohort only included patients admitted during the first 24 h after stroke onset, the prevalence of ICAS may be under-reported. There was also a discrepancy in the number of Bahraini and non-Bahraini patients included in the study, which may have affected the role of ethnicity in ICAS. Due to the overall study design, we were unable to investigate additional conventional risk factors, such as smoking and metabolic syndrome.

Table 2 Logistic regression analysis of possible predictors of intracranial stenosis in patients with acute ischemic stroke

Risk factors	Odds ratio (95% CI)	*P* value
Age	0.99 (0.98–1.01)	0.93
Gender	1.14 (0.74–1.77)	0.54
Nationality	1.37 (0.87–2.16)	0.16
HTN	0.88 (0.54–1.36)	0.54
DM	1.44 (0.93–2.22)	0.09
Previous stroke	1.76 (1.13–2.74)	**0.012**
IHD	0.87 (0.52–1.45)	0.60
PAD	0.65 (0.18–2.34)	0.51
Dyslipidemia	0.79 (0.50–1.25)	0.33
ECAS	3.53 (1.95–6.26)	**0.000**

ICAS intracranial atherosclerotic stenosis, *HTN* hypertension, *DM* diabetes mellitus, *TIA* transient ischemic attack, *IHD* ischemic heart disease, *PAD* peripheral arterial disease, *ECAS* extracranial atherosclerotic stenosis

Table 3 Distribution of risk factors across nationalities

	No HTN		**HTN**	
	NICAS	**ICAS**	**NICAS**	**ICAS**
Bahraini	47	24	185	65
Non-Bahraini	41	10	81	24
	Chi square p= 0.10		Chi square p= 0.50	
	No DM		**DM**	
	ICAS	**ICAS**	**NICAS**	**ICAS**
Bahraini	82	27	149	62
Non-Bahraini	69	15	53	19
	Chi square p= 0.29		Chi square p= 0.65	
	No dyslipidemia		**Dyslipidemia**	
	NICAS	**ICAS**	**NICAS**	**ICAS**
Bahraini	149	58	82	30
Non-Bahraini	89	30	33	4
	Chi square p= 0.60		Chi square p= 0.06	
	No previous stroke/TIA		**Previous stroke/TIA**	
	NICAS	**ICAS**	**NICAS**	**ICAS**
Bahraini	164	51	68	38
Non-Bahraini	105	28	17	6
	Chi square p= 0.60		Chi square p= 0.470	
	No IHD		**IHD**	
	NICAS	**ICAS**	**NICAS**	**ICAS**
Bahraini	173	68	59	21
Non-Bahraini	104	31	18	3
	Chi-square p= 0. 27		Chi square p= 0.388	
	No PAD		**PAD**	
	NICAS	**ICAS**	**NICAS**	**ICAS**
Bahraini	222	86	10	3
Non-Bahraini	119	34	3	0
	Chi square p= 0.21		Chi square p= 1.0	
	No ECAS		**ECAS**	
	NICAS	**ICAS**	**NICAS**	**ICAS**
Bahraini	173	68	59	21
Non-Bahraini	104	31	18	3
	Chi square p= 0.27		Chi square p= 0.388	

ICAS intracranial atherosclerotic stenosis, *NICAS* non intracranial atherosclerotic stenosis, *HTN* hypertension, *DM* diabetes mellitus, *TIA* transient ischemic attack, *IHD* ischemic heart disease, *PAD* peripheral arterial disease, *ECAS* extracranial atherosclerosis

The current study strengths include the use of CTA and MRA to diagnose intracranial stenosis, both of which are not operator-dependent. Another point of strength was the inclusion of neck arteries in arterial brain imaging for all analyzed group populations.

Conclusions

This study focused on the determinants of potentially symptomatic intracranial stenosis and demonstrated that extracranial stenosis in general and dyslipidemia in the Bahraini population were independent predictors

of ICAS. Intracranial atherosclerosis (ICAS) is a major cause of ischemic stroke in Bahrain and is associated with a higher rate of stroke recurrence. Further long-term studies on the risk factors of symptomatic and asymptomatic ICAS are needed.

Abbreviations

ICAS: Intracranial atherosclerotic stenosis; ECAS: Extracranial arterial stenosis; TIA: Transient ischemic attacks; GCC: Gulf Cooperation Council; CTA: Computed tomographic angiography; MRA: Magnetic resonant angiography; DM: Diabetes mellitus.

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Author contributions

F. A, M. W. M., and A. H. contributed to the conception, design, drafting, and revising of the manuscript. N. A., R. A., A. A., and A. Q. contributed to data acquisition. P. D., M.W.M., and A. H. contributed to data analysis and interpretation. All authors read and approved the final manuscript.

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Availability of data and materials

All data generated or analysed during this study are included in this article. Further inquiries can be directed to the corresponding author.

Declarations

Ethics approval and consent to participate

The study protocol was reviewed and approved by the IRB Board of King Hamad University Hospital (approval number (20-340). Consent to participate was not required as we used the available electronic data after approval from the IRB research department at King Hamad University Hospital (approval number (20-340).

Consent of publication

Not applicable.

Competing interests

The authors declare that they have no conflict of interest.

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