Ischaemic stroke in Jordan: a 2-year hospital-based study of subtypes and risk factors

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السكتة الدماغية الإقفارية في الأردن: دراسة مرتكزة على المستشفيات لمدة سنتين حول الأنماط الفرعية وعوامل الاختطار

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الخلاصة: أجريت دراسة استعادية شملت 200 مريض متعاقب عانوا من سكتة دماغية لأول مرة في حياتهم، وأدخلوا في مستشفى الجامعة الأردنية خلال فترة سنتين. وقد كان العمر الوسطي 61.2 عاماً (متراوحاً بين 29 – 95 عاماً)، وكان أكثر الأنماط الفرعية شيوعاً هو الاحتشاء الجوبي (51.5٪) إلا أن تكرار السكتات الدماغية الناجمة عن صمّات قلبية المنشأ كان منخفضاً (8.0٪)، وكان أكثر عوامل الاختطار شيوعاً ارتفاع ضغط الدم والسكري والتدخين في السكتات الدماغية الناجمة عن التصلب العصيدي وليس عن صمات قلبية المنشأ. وكان الرجفان الأذيني المزمن أكثر عوامل الاختطار شيوعاً في السكتات الدماغية الناجمة عن صمات قلبية المنشأ. ولم يكن لدى أي من المرضى تضيق شديد في الشريان السباتي خارج القحف أو في الشريان الفقري (تضيق يزيد على 50٪). وتظهر السكتات الدماغية الجوبية بشكل رئيسي على شكل سكتة دماغية حركية صرفة (لدى 67 مريضاً من بين 103 مرضى) وقد تركزت بشكل رئيسي في المحفظة الداخلية (لدى 34 مريضاً من بين 103 مرضى). أما النتائج الحميدة المآل (85٪ من الحالات خرجت من المستشفى إلى المنزل، ومعظمها بعجز عصبي طفيف) فكانت ناجمة عن الاحتشاءات الجوبية التي تغلب حدوثها في أعمار صغيرة نسبياً.

ABSTRACT A retrospective study was made of 200 consecutive patients with first-ever ischaemic stroke, admitted to Jordan University Hospital over a 2-year period. The mean age was 61.2 years (range 29–95). The most common stroke subtype was lacunar infarct (51.5%), but frequency of cardioembolic stroke was low (8.0%). Hypertension, diabetes mellitus and smoking were the most common risk factors for atherosclerotic non-cardioembolic stroke. Chronic atrial fibrillation was the most common risk factor for cardioembolic stroke. No patient had severe extracranial carotid or vertebral artery stenosis (> 50% narrowing). Lacunar strokes presented predominantly as pure motor stroke (67/103) and were mainly in the internal capsule (34/103). The favourable outcome (85% discharged home) may be due to the relatively young age and the predominance of lacunar infarcts.

L'accident ischémique cérébral en Jordanie : étude hospitalière sur deux ans des sous-types et des facteurs de risque

RESUME Une étude rétrospective a été réalisée sur une période de deux ans chez 200 patients consécutivement admis à l'Hôpital universitaire de Jordanie pour un premier infarctus cérébral. L'âge moyen était de 61,2 ans (fourchette : 29-95 ans). Le sous-type d'accident cérébral le plus courant était l'infarctus lacunaire (51,5 %), mais la fréquence des embolies cérébrales d'origine cardiaque était faible (8,0 %). L'hypertension, le diabète sucré et le tabagisme étaient les facteurs de risque les plus courants pour les infarctus cérébraux non cardio-emboliques d'origine athéroscléreotique. La fibrillation auriculaire chronique était le facteur de risque le plus courant pour les embolies cérébrales d'origine cardiaque. Aucun patient n'avait de sténose sévère de l'artère vertébrale ou de la carotide extracrânienne (> 50 % de rétrécissement). Les infarctus lacunaires se présentaient principalement comme une hémiplégie motrice pure (67/103) et étaient localisés surtout dans la capsule interne (34/103). L'issue favorable (85 % des patients sont rentrés à leur domicile à la sortie de l'hôpital) peut être due à l'âge relativement jeune et à la prédominance des infarctus lacunaires.

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Introduction

Stroke is the third leading cause of death and among the leading causes of disability in the United States, Europe and many developing countries [1]. More recent studies demonstrate that different ethnic/racial populations may have different incidence rates and may be predisposed to different stroke subtypes. For instance, African Americans have a significantly higher incidence and mortality rate compared with white people [2]. Elderly Hispanic patients have a lower mortality rate secondary to stroke compared with white people. African-Americans and Native Americans also present more frequently with lacunar infarcts and intracranial haemorrhage [3]. Meanwhile, the difference in cardioembolic stroke rates between African-Americans and whites is not statistically significant. However, these rates are lower in Hispanic Americans [3].

Few studies have explored the risk factors and prevalence of stroke in the Arab population and no study could be found regarding stroke in Jordan [4–8]. A hospital-based study in Sudan demonstrated an earlier incidence of stroke but a similar risk factor profile to other populations [7]. In a hospital-based study in Qatar, patients also had earlier peak stroke rates as well as higher rates of hypertension and diabetes [8]. The largest Arab registry is in Saudi Arabia, which also demonstrated an earlier onset of stroke [4]. In Saudi Arabia, large infarcts (56%–67% of all strokes) were the most common stroke type; there was also a large proportion of lacunar infarcts (33%–46%) [4].

This case review of 200 Jordanian patients with ischaemic stroke was conducted to explore the age and sex distribution, stroke subtypes, risk factors, clinical and imaging findings, treatment and outcome.

Methods

The Jordan University Hospital is a 530-bed tertiary care teaching hospital providing health care to a large section of the middle-class Jordanian population. As the major university hospital in Jordan, it serves as a principal referral centre for the entire Jordanian population. The case notes of 200 consecutive patients with first-ever ischaemic stroke admitted to the hospital through the emergency department between January 2000 and December 2001 were reviewed.

We applied the definition of stroke given by the World Health Organization [9]: rapidly developing clinical signs of focal or global disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than vascular origin.

All patients had an initial computed tomography (CT) brain scan to exclude intracerebral haemorrhage followed after a few days by a second CT and/or magnetic resonance imaging (MRI) scan to confirm the infarct location and size. When clinically indicated and technically feasible, some patients had carotid Doppler ultrasound and/or magnetic resonance angiography (MRA) of the neck and brain vessels to rule out arterial stenosis or occlusion. Most patients had 2 D-transthoracic echocardiography to rule out a valvulopathy or left atrial/ventricular clot. Tests for hypercoagulable state or vasculitis were done when clinically indicated.

Each patient was assessed for risk factors for stroke. Hypertension, diabetes mellitus, and hyperlipidaemia were defined by standard guidelines [10–12]. Ischaemic heart disease, myocardial infarction and atrial fibrillation were confirmed by a 12-lead electrocardiogram (ECG) and with a cardiology consultation. History of prior

transient ischaemic attacks and smoking were also noted.

An assessment was made of the cause(s) of the stroke and these were classified into subtypes using the TOAST criteria [*13*] and according to whether the cause was determined or undetermined (2 or more possible causes or negative evaluation).

Management included treatment with antiplatelet drugs (aspirin 325 mg/day, ticlopidine 250 mg twice daily), anticoagulants (warfarin, maintaining an international normalized ratio of 2–3), physiotherapy, antioedema agents (mannitol), reduction of risk factors or supportive measures, each when indicated. None of the patients received thrombolytic drugs owing to the lack of supportive facilities at this hospital and late presentation to the emergency department (the mean time between onset of stroke and arrival at the emergency department was 21 hours, range 6–120 hours).

Outcome was classified broadly into: ambulatory with mild neurological deficit, moderate neurological deficit compromising activities of daily living (aphasia, hemiparesis, assistance in ambulation), and severe neurological deficit (hemiplegia) or vegetative state and death.

Results

There were 200 patients with ischaemic stroke, accounting for 3.5% of admissions to the medical ward/intensive care unit during the study period. The mean age was 61.2 years, range 29–95 years, comprising 112 males and 88 females (male to female ratio of 1.3). The age and sex distribution is shown in Table 1. Most of the patients (159/200) were between 51 and 80 years; however, there was a high proportion of patients with stroke aged under 55 years (41/200).

Table 1 **Age and sex distribution of 200 patients with first-ever ischaemic stroke**

Age (years)	Male No.	Female No.	Total No.
21–30	1	0	1
31–40	3	2	5
41–50	14	8	22
51–60	37	22	59
61–70	38	31	69
71–80	12	19	31
81–90	7	4	11
91–100	0	2	2
Total	112	88	200

The cause of stroke could be determined for 161 patients (80.5%); the majority of cases (51.5%) were lacunar infarcts (Table 2). Most of the etiologically undetermined cases, 30/39 (76.9%), had atherosclerotic and/or lacunar infarcts.

The risk factors for each stroke subtype are shown in Table 3. The most common risk overall was hypertension (76.0%) followed by diabetes mellitus (44.0%), smoking (35.0%), hyperlipidaemia (33.0%) and ischaemic heart disease (20.5%). Hypertension was also a major risk factor for lacunar infarcts in 87 out of 103 patients (84.5%) followed by diabetes mellitus in 49/103 (47.6%) and smoking in 30/103 (29.1%).

Among the 152 patients with hypertension, 100 had known hypertension, 23 were newly diagnosed and 29 had uncontrolled hypertension at the time of stroke. Among the 88 diabetic patients, 59 had known diabetes mellitus, 14 were newly diagnosed and 15 had uncontrolled diabetes mellitus at the time of stroke. Among the 66

Table 2 **Subtypes of ischaemic strokes among 200 patients with first-ever ischaemic stroke, classified using the TOAST criteria [13]**

Category	No. of patients (n = 200)	%
Cause determined		
Large artery atherosclerosis	40	20.0
Lacunes	103	51.5
Cardioembolism	16	8.0
Hypercoagulable state	2	1.0
Total	161	80.5
Cause undetermined		
Atherosclerosis and/or lacunes	30	15.0
Embolism with 2+ possible causes	3	2.0
Negative evaluation	6	3.0
Total	39	19.5
Total	200	100.0

n = *total number of patients.*

patients with hyperlipidaemia, 35 had known and 31 newly diagnosed hyperlipidaemia. Among the 70 smokers, 62 were males and 8 females. No risk factors except elderly age could be determined in 12 patients. Two patients had hypercoagulable state (primary antiphospholipid syndrome).

There were 16 patients (8.0%) with cardioembolic strokes. The majority (14/16) were female patients above the age of 50 years (7 above 70 years) with 12 out of 16 having chronic atrial fibrillation and at least 1 other risk factor (mainly hypertension and left ventricular hypertrophy). None of the patients with atrial fibrillation had therapeutic levels of warfarin before the stroke (2 patients discontinued warfarin, 4 were taking warfarin but were subtherapeutic, the remainder were not taking the medication).

Large artery atherosclerotic strokes (20.0% of cases) were predominantly in the carotid territory (22/37) as opposed to the vertebrobasilar region (15/37) and presented mainly with hemiparesis/hemiplegia with or without aphasia and lateral homonymous hemianopsia. MRI and/or CT brain scans showed infarcts located predominantly in branch vessels (13/22 in a branch of middle cerebral artery and 8/15 in the posterior cerebral artery). Strikingly, none of these patients had haemodynamically significant extracranial carotid or vertebral artery atherosclerosis (> 50% luminal narrowing) on carotid Doppler ultrasound and/or MRA of neck vessels. The most common clinical presentation of lacunar infarcts was pure motor stroke (67/103) followed by mixed sensorimotor stroke (26/103). The most common lacunar infarct location on CT and/or MRI brain was in the internal capsule (34/103) followed by multiple locations (25/103) and the periventricular area (17/103). Lacunes were shown on CT scan in 73 out of 103 patients (70.9%), but in 17/103 (16.5%) they were seen only on MRI and in 13/103 were shown on both scans.

Of the etiologically undetermined stroke subtypes, 30 patients had atherosclerosis and/or lacunes. Three patients had embolisms with 2 or more possible causes; 2 had atrial fibrillation and hypertension and the third cardiomyopathy and hypertension. There were 6 patients with a negative evaluation who had multiple risk factors (hypertension, diabetes mellitus, smoking).

A few treatment complications occurred. Four patients had bleeding duodenal ulcers due to aspirin and 2 had warfarin toxicity. With regard to outcome, most patients did well. After a mean follow-up of 18 months (range 3 to 24 months), 170 patients (85.0%) were discharged home. Among those discharged, 107 had mild

Table 3 **Risk factors for stroke among the 200 patients with first-ever ischaemic stroke according to subtype (most patients had more than one risk factor)**

Risk factor	Cause determined				Cause undetermined			Total (n = 200)	
	Large artery AS (n = 40) No.	Lacunes (n = 103) No.	Cardio-embolism (n = 16) No.	HC state (n = 2) No.	AS/ lacunes (n = 30) No.	Embolism plus[a] (n = 3) No.	Negative evaluation (n = 6) No.	No.	%
Hypertension	32	87	–	–	28	–	5	152	76.0
Diabetes mellitus	26	49	–	–	10	–	3	88	44.0
Smoking	16	37	–	–	14	–	3	70	35.0
Hyperlipidaemia	18	30	–	–	14	–	4	66	33.0
Ischaemic heart disease	10	22	–	–	9	–	–	41	20.5
Previous transient ischaemic attack	8	6	–	–	3	–	–	17	8.5
Obesity	3	3	–	–	–	–	–	6	3.0
Chronic atrial fibrillation[b]	–	–	12	–	–	3	–	15	7.5
Prosthetic valve	–	–	3	–	–	–	–	3	1.5
Myocardial infarct	–	–	1	–	–	–	–	1	0.5
Antiphospholipid syndrome	–	–	–	2	–	–	–	2	1.0
Nothing identified	–	5	–	–	6	–	1	12	6.0

AS = atherosclerosis.
HC = hypercoagulable.
n = *total number of patients.*
[a] *Embolism with 2+ possible causes.*
[b] *Associated with hypertension and/or diabetes mellitus.*

neurological deficit and 63 required assistance with ambulation. The latter group of patients had a prolonged stay in the hospital due to lack of a rehabilitation centre at Jordan University Hospital. Thirty patients (15.0%) died, 10 due to large infarcts in middle cerebral artery territory with herniation, 7 due to brainstem infarcts and 13 secondary to medical comorbidities (such as aspiration pneumonia, deep vein thrombosis with pulmonary embolism, sepsis, renal failure).

Discussion

Several points emerge from this retrospective study of 200 patients with first-ever ischaemic stroke admitted to Jordan University Hospital over a 2-year period. The stroke admission rate of 3.5% was similar to that from other Arab countries [*4–6,14*]. The mean age of our patients (61.2 years) was younger than in industrialized countries. For instance, in the Framingham study the mean age of stroke patients was 63.4 years for men and 66.1 years for women [*15*]. In the Northern Manhattan Stroke Study (NO-MASS) the mean age at ischaemic stroke was 70 years [*16*].

Concerning stroke subtypes, 161/200 (80.5%) of our patients had a stroke of determined cause, similar to the determined stroke rates 96/136 (70.5%) found by Conti [*17*]. The majority of determined strokes were lacunar infarcts (51.5%), which were more frequent compared with other Middle Eastern and Western studies [*2 8,14 18*]; the frequencies of lacunes in most populations ranged from 11% to 42%. Our higher percentage of lacunar infarcts may be due to the higher rate of hypertension in our patients compared with most populations. In addition, the proportion of large artery atherosclerotic strokes (20.0%) was similar to some studies [*17,19*] but less than in others (30% and 39.5%) [*18,31*]. Cardioembolic strokes in our series (8.0%) were less frequent in comparison with other studies (17.5% to 31%) [*17–19,27,31*]. The number of patients (3.0%) with a negative evaluation was less than that found by others [*17,31*] and furthermore these patients did not receive transesophageal echocardiography to rule out cardiogenic or aortic arch embolic sources. As demonstrated by Amarenco, as many as 38% of patients with no discernible cause for embolic strokes may have atherosclerotic plaques > 4 mm in diameter in the aortic arch [*20*].

The most frequent risk factor in our patients with non-cardioembolic strokes was hypertension (76.0%), followed by diabetes mellitus (44.0%). Hypertension was also a major risk factor for lacunar infarcts, as was diabetes mellitus and smoking. Similarly, in a population-based study in Minnesota, Sacco noted that hypertension was found in 81% of patients with lacunar infarcts [*21*]. Smoking and hyperlipidaemia were also important risk factors in our study, as in other Middle and Far Eastern studies [*14,26*].

Concerning cardioembolic strokes, the most common risk factor was chronic atrial fibrillation (12/16 patients) associated with other risk factors (diabetes mellitus, hypertension with left ventricular hypertrophy) occurring in women above the age of 50 years, which is in agreement with other studies [*22–25*]. Interestingly, we had few men with atrial fibrillation in this study.

With regard to clinical and imaging findings in non-cardioembolic strokes, there was a striking absence of severe extracranial carotid and/or vertebral atherosclerosis (> 50% narrowing) in all of our patients. This is similar to Qari's study, in which only 4 out of 71 Saudi Arabian patients had

severe carotid stenosis [*14*]. Other Middle Eastern reports [*4*] found a higher frequency of lacunar infarcts and a less frequent prevalence of extracranial large artery disease. On the other hand, pure motor stroke was the most common sign of lacunar infarct (67 of 103 patients, 65.0%), which is in accordance with other studies. [*16,26,27*]. The most frequent location was in the internal capsule (34/103). With respect to cardioembolic strokes, the most common clinical sign was hemiparesis/ hemiplegia with or without aphasia and all patients had cortical infarcts in accordance with Dulli et al. where the odds ratio for cortical stroke was highest for atrial fibrillation on ECG (OR = 4.77; CI: 2.08–10.94) [*28*].

In cardioembolic strokes, only 6 out of 16 of our patients were on warfarin prior to their stroke (2 had stopped recently prior to the stroke and 4 had sub-therapeutic levels). Thus 12 out of 16 patients (75%) were not properly treated with warfarin prior to stroke. The problem of undertreating patients with atrial fibrillation has been demonstrated by Ibrahim and Kwoh who found in a cohort of 2093 patients with heart failure and atrial fibrillation that only 414 patients (20%) received oral anticoagulants [*29*]. Old age was negatively associated with their use. Deplanque et al. also noted that among 137 patients with atrial fibrillation eligible for oral anticoagulation, 108 (78.8%) did not receive treatment [*30*].

With regard to outcome, after a mean follow-up of 18 months, 85% of patients were discharged home (two-thirds independent, one-third dependent) and 15% died. The mortality rate was in the lower range, similar to Vilalta and Arboix's Barcelona registry at 14% [*31*]. Ikebe et al. found among 315 stroke patients followed up for 1 year that 33% died, 13% were dependent and 54% independent in activities of daily living [*32*]. The relatively good outcome in our patients may be due to their relatively low mean age and the predominance of lacunar infarcts.

In conclusion, this study has shown, first, a younger age of stroke prevalence compared with developed countries; second, a distinctive predominance of lacunar infarcts with absence of severe extracranial atherosclerotic disease and a lower frequency of cardioembolic strokes; and, third, that the major risk factors for non-cardioembolic and cardioembolic strokes were hypertension and chronic atrial fibrillation respectively. Although this study has the limitations associated with being a small, retrospective, hospital-based study, our results suggest the morbidity and mortality of stroke would be greatly reduced by appropriate management of hypertension. The lacunar stroke and hypertension rate is higher than most regions, and should be a focus of public health in Jordan and the Arab world. Furthermore, more nursing homes and rehabilitation centres in Jordan may reduce the length of hospital stay. Future community-based stroke registry and clinical trials in the region would further elucidate the health needs of the population.

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