Excessive Incidence of Stroke in Iran

Evidence From the Mashhad Stroke Incidence Study (MSIS), a Population-Based Study of Stroke in the Middle East

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Background and Purpose—The epidemiology of stroke and its subtypes in the Middle East is unclear. Most previous studies have been performed in Western countries, and incidence rates are unlikely to apply in the Middle East. We aimed to determine the incidence of stroke in Mashhad, northeastern Iran.

Methods—During a 12-month period (2006–2007), we prospectively ascertained all strokes occurring in a population of 450 229. Multiple overlapping sources were used to identify people with stroke. A large number of volunteers assisted in finding stroke patients not admitted to hospital. Potential cases were reviewed by a group of stroke experts before inclusion.

Results—A total of 624 first-ever strokes occurred during the study period, 98.4% undergoing imaging. Despite a relatively low crude annual incidence rate of first-ever stroke FES (139; 95% CI, 128 to 149) per 100 000 residents, rates adjusted to the European population aged 45 to 84 years were higher than in most other countries: 616 (95% CI, 567 to 664) for ischemic stroke, 94 (95% CI, 75 to 113) for intracerebral hemorrhage, and 12 (95% CI, 5 to 19) for subarachnoid hemorrhage. Age-specific stroke incidence was higher in younger patients than is typically seen in Western countries. Comparison of age-specific incidence rates between regions revealed that stroke in Mashhad occurs approximately 1 decade earlier than in Western countries.

Conclusions—The results of this study provide evidence that the incidence of stroke in Iran is considerably greater than in most Western countries, with stroke occurring at younger ages. Ischemic stroke incidence was also considerably greater than reported in other regions. **(*Stroke*. 2010;41:e3-e10.)**

Key Words: Iran ■ Middle East ■ cerebrovascular disorders ■ incidence ■ stroke ■ population-based study ■ epidemiology

Stroke is a leading cause of death and disability worldwide.[1–3] Despite numerous epidemiologic studies of stroke, there is still scant population-based information in developing countries.[4] This is partly attributable to the high cost, lack of resources, and difficulty in undertaking this type of study because of the strict methods required. The majority of studies in these areas were hospital based and did not include patients not admitted to hospital.[5] This means that such studies do not provide comparable data on stroke incidence.

There are large geographic variations in stroke incidence and mortality around the world. There are also differences in the types of stroke occurring, the distribution of ischemic stroke subtypes, and the mechanism of stroke between white and Asian populations. For example, cerebral hemorrhage, small-artery disease, and intracranial carotid stenosis are more frequently noted in Asians than in whites.[6–9] Furthermore, most stroke deaths occur in developing countries, and the proportion is likely to increase with epidemiologic transition and the aging population.[4,10] Incidence rates and mortality vary, even within Western countries.[10,11] Therefore, population-based studies are a priority in stroke research to estimate the real burden of stroke and to help devise strategies for public health policy.

The Mashhad Stroke Incidence Study (MSIS) is a large, population-based study of stroke conducted in Mashhad, Iran. The main aims of the MSIS were to obtain an accurate measure of the incidence of stroke in Iran and to compare these incidence rates with those of other nations.

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Methods

Study Area and Population

The population denominator used in this study was obtained from a census conducted in October and November 2006. This census is conducted every 10 years and is conducted with a door-to-door approach. The MSIS was conducted in 3 different health districts of Mashhad, located in the province of Khorasan-Razavi, northeastern Iran. From November 21, 2006, for a period of 1 year, patients with recent stroke in the already defined study areas were identified. The study area was delineated by the main boulevards in Mashhad. According to the 2006 census, the study population comprised 450 229 inhabitants. The only neurology center in Mashhad is Ghaem Hospital, and all neurology emergency care is supplied at this hospital. Ghaem Hospital is 1 of the most important hospitals in the east of Iran. It is the referral hospital for eastern Iran (Khorasn, Sistan, and Baluchistan provinces) and for the region west of Afghanistan. Patients or next of kin calling the emergency services telephone number in Iran and who are identified as having a neurologic condition are transferred to Ghaem Hospital. When a patient with stroke is admitted to another hospital, after having been incorrectly diagnosed with another condition, they will then be transferred to Ghaem Hospital as soon as their diagnosis of stroke is made. This occurs when the hospital does not have a neurologist. In addition, some hospitals have a policy not to admit stroke patients because of the high associated mortality and morbidity and lengthy hospital stay. The other main hospital located in the study region is Hasheminejad Hospital, which has both internal medicine and neurosurgical wards. The 2 other smaller hospitals located within the region are 17 Sharivar (a welfare insurance hospital) and Imam Hosein (a military hospital).

Stroke Definition

According to the World Health Organization definition, stroke is defined as "rapidly developing signs of focal or global disturbance of cerebral function lasting >24 hours (unless interrupted by surgery or death) with no apparent cause other than a vascular origin."[12] With this clinical definition, silent stroke on imaging is not considered a stroke, and imaging confirmation is not required for stroke diagnosis.

Stroke Classification

First-ever stroke (FES) is defined as a stroke occurring for the first time during a patient's lifetime. Past history of stroke was determined by using all available information, including hospital records, information provided by patients, and family reports.

Neuroimaging was used to classify patients with definite FESs into ischemic stroke (IS), intracerebral hemorrhage (ICH), and subarachnoid hemorrhage (SAH) subgroups. All SAHs were included whether or not there were focal neurologic signs. IS was defined as a stroke for which either computed tomography (CT) performed within 28 days of symptom onset showed a normal appearance or CT or magnetic resonance imaging (MRI) showed an area of recent infarction corresponding to the incident symptoms and signs. ICH was defined as a stroke for which CT or MRI demonstrated blood within the brain parenchyma, with or without extension into the ventricles or subarachnoid space. SAH was defined as an abrupt onset of severe headache, loss of consciousness, or both, with or without focal neurologic signs. In addition, CT demonstrated subarachnoid blood. Lumbar punctures are performed in CT-negative patients with an appropriate history. Alternatively, ICHs, SAHs, or ISs were confirmed on autopsy.

An undetermined stroke is a stroke for which a patient did not undergo CT scanning within 28 days of the onset of symptoms and an autopsy was not performed. A possible stroke is considered as any acute episode of neurologic disturbance that is suggestive of stroke but for which there is insufficient information to establish whether the symptoms and duration (<24 hours or >24 hours) fully met the World Health Organization definition for definite stroke. "Possible" and "CT-only" strokes were not included in the incidence figures.

The presence of a past history of hypertension, diabetes, hyperlipidemia, atrial fibrillation, other cardiac disease, and transient ischemic attack (TIA) was obtained from medical records or from patient interview. In addition, information regarding the individual's smoking status, defined as never, ex-smoker, and current smoker, and their level of alcohol consumption, defined as nondrinker, occasional drinker (drinking at social occasions), daily drinker, and previous daily drinker, was ascertained.

Case Ascertainment

Multiple sources were used to identify stroke patients, particularly those who were not admitted to hospital. The following methods were used.

1. The medical records of all patients admitted to the 4 hospitals in the study area were examined every day by expert staff to determine any cases with stroke. Discharge diagnoses were also assessed as a backup procedure. We called every hospital in the study area daily to check for new admissions of patients with suspected stroke. All of these patients were visited by a member of the study team. Cases were included only if they lived in the study area. Two hospitals outside the study area were also contacted for potential cases, as it is possible that cases might have been seen at these hospitals. These cases were followed up in the same manner when a suspected stroke patient was identified. One of these, Imam Reza Hospital, is a main referral hospital with >800 beds, although there are no beds for either stroke or neurosurgery. Faraby is a smaller welfare insurance hospital. One of the authors (M.R.A.) provided consultations for difficult neurologic cases, and patients with stroke were referred to the study in return.
2. Despite a referral healthcare structure in Iran, there may be situations where people bypass a primary care contact and self-refer to specialists (private) and hospital outpatient clinics (public).[13] Therefore, family physicians, nursing care homes, outpatient clinics, and particularly neurologists in the study area were informed about the study and were asked to identify stroke patients who were not hospitalized. There are 35 neurologists in Mashhad, and they have official meetings on a 3- to 4-month basis. This served as an opportunity to remind neurologists about the study. Referral from neurologists was the major source of case-finding from the smaller military and welfare insurance hospitals (100 to 200 beds) where hospital records could not be checked. In addition, as an incentive to refer patients to the study, 1 of the authors (M.R.A.) accepted referrals free of charge for duplex and transcranial Doppler examinations from doctors at these hospitals.
3. Death certificates and reports were reviewed on a monthly basis to identify nonhospitalized fatal stroke cases. Cases were included when there was clinical evidence of a sudden, focal neurologic deficit before death. Further validation of stroke diagnosis was provided in cases where CT or MRI was conducted before death or when an autopsy was performed.
4. Local television (once) and newspapers (twice) provided an opportunity for the research group to inform residents about the study. People were invited to contact the study group if they had suffered a stroke.
5. In 1991, the Ministry of Health of Iran began a new healthcare system in urban areas with support from the United Nations Children's Fund and the United Nations Population Fund. The main aim of this system is to increase outreach capacity in urban health centers and build partnerships between health centers and the people so that the community itself could take a greater share of responsibility for its health. This was undertaken through the use of community health volunteers (CHVs). CHVs participate in several classes in different health-related aspects, such as water quality and family planning. There is evidence that CHVs have had significant impact on the health of their communities, and since 1994, CHVs have become an important part of the national health policy of Iran.[14]

For accurate estimation of nonhospitalized stroke patients, 980 trained CHVs who had enough general knowledge about stroke participated in this study. One of the authors (M.R.A.) undertook training sessions with the CHVs and their coordinators. Common presentations of stroke were outlined. CHVs lived in the study area, knew their neighbors, and were responsible for checking their neighborhoods for potential stroke cases. They were asked to refer any person with suspected symptoms of stroke. Each CHV was responsible for between 50 and 100 houses. This translates to ≈500 inhabitants, as the average household in Mashhad includes 5 people (>5 in poor areas). The CHVs provided door-to-door information about most of the inhabitants in the study area by visiting them at least every month. In addition, volunteers would see these neighbors every day in the street and in their homes or at religious meetings. Because these families knew the CHVs, they were comfortable reporting their health problems to them. The CHVs were responsible for reporting any people with a history of sudden onset of weakness, sensory disturbance, dizziness, language disturbance, visual loss, and sudden death to the study investigators. Subjects were then telephoned by the lead investigator (M.R.A.), and these subjects were invited to participate. The majority of these patients then attended the office of 1 of the investigators (M.R.A.) either with or without the CHV. Some individuals could not come to the hospital. In this instance, the investigator carefully checked the history of the event by telephone. Those with symptoms and signs consistent with stroke were then visited in their homes, and a neurologic examination was undertaken (visits were undertaken by M.R.A., M.T.F., R.K., and M.P.). This occurred on fewer than 10 occasions.

At the end of the study period, each CHV was asked to check each household for any potential stroke event that might have been missed. At this time, they were also asked to check the regions that did not have any volunteers; ≈20% of the region was not covered by CHVs. Any suspected cases of stroke or death from stroke in the previous year were identified, and a final diagnosis was made by the research team. It took 3 months to undertake this final surveillance.

Inclusion Criteria

All stroke events within the study period occurring among residents of the defined geographic region were counted in this study. Potential cases were reviewed by a panel of stroke experts before final inclusion. Cases were eligible only if they had been resident within the defined geographic area for at least 1 year before the stroke. This latter criterion was used because Mashhad has a large number of temporary residents not included in census figures. For example, farmers in neighboring areas might work for 6 to 8 months on their farms but then come and stay in Mashhad for the winter. Others, such as elderly people with chronic disease, live in neighboring cities and stay with their families in Mashhad for 2 to 3 months.

Data Collection and Entry

Three neurology residents (M.T.F., R.K., and M.P.), and a trained nurse (Mojgan Khaniani) abstracted the medical record of each patient and recorded all of the information regarding the patients' living arrangements, stroke symptoms and signs, risk factors, diagnostic studies, and treatment. Data entry was performed by a group of computer technicians and 4 medical students. A neurologist (M.R.A.) supervised the process from the patients' inclusion up to the time of data entry.

Calculation of Incidence

Incidence rates (number per 100 000 population per year) are reported as crude rates and as rates age-standardized to the "world" and "European" populations of Segi.[15] These standardizations allow unbiased comparisons between populations by eliminating the influence of different age distributions.[16]

Ethics

The study was approved by the ethics committee of Mashhad University of Medical Sciences (MUMS). Informed consent was obtained from each participant or the next of kin before any interview or neurologic examination was conducted.

Results

During the period of research, a total of 887 strokes were originally included. After careful review of their records, 2 were excluded because their signs and symptoms did not comply with the study definition of stroke, despite evidence of stroke on CT. There were a further 10 possible strokes, 43 TIAs, and 1 brain tumor case that were excluded. In addition, an additional 138 were found to live outside the study region, and in another 9, the stroke occurred outside the study time period. This left a total of 684 strokes that complied with the study definition. Four hundred ninety-one cases (71.8%) were admitted to hospital (92% in Ghaem Hospital and 8% in other hospitals), and 193 patients (28.2%) were managed in the community; these latter cases being mainly referred by volunteers and other neurologists (Table 1). The main ethnic

Table 1. Baseline Characteristics, Brain Imaging, and Sources of First Referral

Characteristics	Men* (n=353)	Women* (n=331)
Age, y, mean (SD)	65.2 (14.6)	64.2 (15.0)
FES	327 (92.6)	297 (89.7)
Risk factors		
History of hypertension†	182 (52.0)	234 (70.9)
History of diabetes†	105 (30.0)	103 (31.1)
History of hyperlipidemia†	76 (21.8)	93 (28.4)
History of atrial fibrillation†	26 (7.6)	31 (9.6)
History of TIA	26 (7.4)	23 (6.9)
Smoking†		
Current	64 (18.1)	41 (12.4)
Past	76 (21.7)	37 (11.2)
Alcohol consumption		
Occasional drinker	13 (3.8)	. . .
Daily drinker	6 (1.7)	. . .
Previous daily drinker	15 (4.4)	. . .
Imaging		
Imaging within 7 days of stroke onset	321 (90.9)	307 (92.7)
Imaging from 8 to 28 days of stroke onset	17 (4.8)	10 (3.0)
Imaging after 28 days of stroke	7 (2.0)	3 (0.91)
Time to imaging unknown	. . .	1 (0.30)
Source of first referral		
Public and private hospital admission	248 (70.3)	243 (73.4)
Emergency department discharge records	24 (6.8)	19 (5.7)
Death certificate	1 (0.3)	0 (0)
Neurology outpatient clinics	60 (17.0)	48 (14.5)
CHVs	21 (5.9)	21 (6.3)

*No. (%), unless otherwise indicated.

†Missing values: for hypertension, 3 men, 1 woman; diabetes, 3 men; hyperlipidemia, 5 men, 4 women; atrial fibrillation, 11 men, 9 women; alcohol consumption, 9 men, 4 women; smoking, 3 men, 1 woman.

Table 2. Age- and Sex-Specific Incidence Rates (per 100 000 Population per Year) for the FES Study in Mashhad, Iran (2006–2007)

	Men				Women				Men and Women Combined			
	Population at Risk	No.	Rate	95% CI	Population at Risk	No.	Rate	95% CI	Population at Risk	No.	Rate	95% CI
Age group, y												
0–14	59 161	0	0	. . .	56 720	0	0	. . .	115 881	0	0	. . .
15–24	55 458	4	7	0–14	57 130	4	7	0–14	112 588	8	7	2–12
25–34	42 266	9	21	7–35	40 865	5	12	2–23	83 131	14	17	8–26
35–44	29 202	13	45	20–69	28 541	23	81	48–114	57 743	36	62	42–83
45–54	20 681	51	247	179–314	19 915	42	211	147–275	40 596	93	229	183–276
55–64	10 146	69	680	520–840	9950	66	663	504–823	20 096	135	672	559–785
65–74	6820	83	1217	957–1477	6283	73	1162	897–1427	13 103	156	1191	1005–1376
75–84	3109	77	2477	1930–3023	2835	63	2222	1680–2765	5944	140	2355	1970–2741
>85	556	21	3777	2192–5362	591	21	3553	2061–5046	1147	42	3662	2575–4749
All ages	227 399	327	144	128–159	222 830	297	133	118–148	450 229	624	139	128–149
Standardized to world population*			208	180–236			198	170–226			203	175–231
Standardized to European population†			317	282–352			300	266–334			309	274–343
Standardized to European population 45–84 years‡			768	714–822			716	663–768			743	690–796

*Adjusted by age and sex to the world population.
†Adjusted by age and sex to the European population.
‡Adjusted by age and sex to the European population 45 to 84 years.

groups were Persian (82.5%), Turk (8.3%), Afghan (4.8%), Kurd (2.8%), Arab (1.2%), and other (0.4%).

A final diagnosis of FES was made in 624 (91.2%) individuals, of whom 52.4% were men and 47.6% were women. The crude annual incidence rate of FES was 139 (95% CI, 128 to 149) per 100 000; for men, 144 (95% CI, 128 to 159), and for women, 133 (95% CI, 118 to 148) (Table 2). No strokes were found in children age <15 years. The incidence rates increased significantly with each decade of life and were similar in men and women (Figure 1).

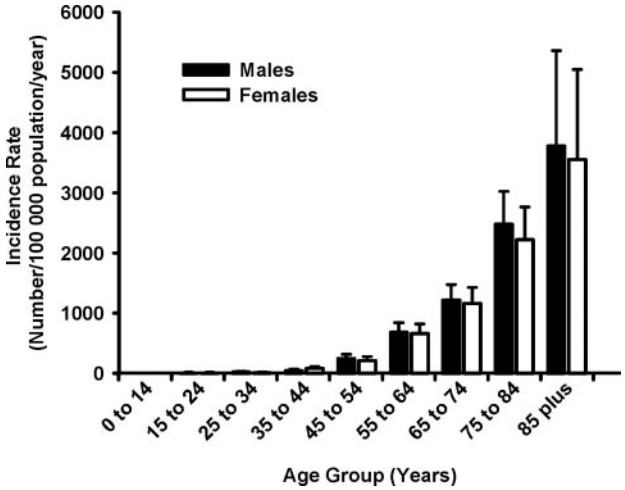

Figure 1. Age- and sex-specific incidences rates for FES. Error bars indicate 95% CIs.

A CT scan was performed for 661 events (96.6%). We used MRI as the only form of imaging in another 5 cases. Autopsy was performed in 2 cases, for whom we also had a prior CT, for a definite diagnosis of stroke subtype. Consequently, imaging/autopsy was performed for 666 cases (97.4%) of events (Table 1) and for 614 cases (98.4%) of FES. Pathologic subtypes of FES were classified in all 605 people who either had imaging within 28 days of stroke or had an autopsy examination: 511 (81.9%) patients had IS, 79 (12.7%) had ICH, and 15 (2.4%) had SAH. The crude annual incidence rate per 100 000 inhabitants was 113 (95% CI, 104 to 123) for IS, 18 (95% CI, 14 to 21) for ICH, 3 (95% CI, 2 to 5) for SAH, and 4 (95% CI, 2 to 6) for undetermined stroke (Table 3).

When adjusted to the world and European populations, stroke incidence rates were greater than those of crude incidence rates (Tables 2 and 3). Incidence adjusted to the European population aged 45 to 84 years was greater in Mashhad than in all other "ideal" studies conducted since 1995, apart from that in West Ukraine (Figure 2), and was largely attributable to a greater incidence of IS (Figure 3). The incidence of ICH also appeared to be greater in Mashhad than in all other regions apart from Tbilisi, Georgia (Figure 3). Adjusted incidence rates for each subtype of stroke were similar between men and women (Table 3).

Discussion

We found that the incidence of stroke, adjusted to the European population aged 45 to 84 years, in Mashhad, Iran,

Table 3. Subtype-Specific Incidence Rates (per 100 000 Population per Year) for FES by Age and Sex in Mashhad, Iran (2006–2007)

Age Group, y	Population at Risk	IS			ICH			SAH			Undetermined Stroke		
		No.	Rate	95% CI	No.	Rate	95% CI	No.	Rate	95% CI	No.	Rate	95% CI
Men													
0–14	59 161	0	0	. . .	0	0	. . .	0	0	. . .	0	0	. . .
15–24	55 458	3	5	0–12	1	2	0–5	0	0	. . .	0	0	. . .
25–34	42 266	6	14	3–26	1	2	0–7	2	5	0–11	0	0	. . .
35–44	29 202	10	34	13–55	0	0	. . .	1	3	0–10	2	7	0–16
45–54	20 681	41	198	138–259	8	39	12–65	2	10	0–23	0	0	. . .
55–64	10 146	48	473	340–607	17	168	88–247	1	10	0–29	3	30	0–63
65–74	6820	73	1070	826–1315	8	117	36–199	1	15	0–43	1	15	0–43
75–84	3109	64	2059	1559–2558	9	289	101–478	1	32	0–95	3	96	0–206
>85	556	18	3237	1766–4709	1	180	0–532	0	0	. . .	2	360	0–857
All ages	227 399	263	116	102–130	45	20	14–26	8	4	1–6	11	5	2–8
Standardized to world population*			167	142–193		29	19–40		4	0–8		7	2–12
Standardized to European population†			256	225–288		43	30–56		6	1–10		12	5–18
Standardized to European population 45–84 years‡			619	570–667		116	95–138		13	6–20		20	12–29
Women													
0–14	56 720	0	0	. . .	0	0	. . .	0	0	. . .	0	0	. . .
15–24	57 130	3	5	0–11	1	2	0–5	0	0	. . .	0	0	. . .
25–34	40 865	3	7	0–16	1	2	0–7	0	0	. . .	1	2	0–7
35–44	28 541	16	56	29–84	4	14	0–28	3	11	0–22	0	0	. . .
45–54	19 915	34	171	113–228	6	30	6–54	1	5	0–15	1	5	0–15
55–64	9950	54	543	398–687	7	70	18–122	2	20	0–48	3	30	0–64
65–74	6283	64	1019	770–1267	6	95	19–172	1	16	0–47	2	32	0–76
75–84	2835	56	1975	1463–2488	6	212	42–381	0	0	. . .	1	35	0–104
>85	591	18	3046	1660–4431	3	508	0–1081	0	0	. . .	0	0	. . .
All ages	222 830	248	111	97–125	34	15	10–20	7	3	1–5	8	4	1–6
Standardized to world population*			167	141–192		22	13–31		4	0–8		5	1–10
Standardized to European population†			254	223–285		33	21–44		5	1–10		8	2–13
Standardized to European population 45–84 years‡			612	564–660		71	55–88		12	5–18		21	12–30
Men and women combined													
0–14	115 881	0	0	. . .	0	0	. . .	0	0	. . .	0	0	. . .
15–24	112 588	6	5	1–10	2	2	0–4	0	0	. . .	0	0	. . .
25–34	83 131	9	11	4–18	2	2	0–6	2	2	0–6	1	1	0–4
35–44	57 743	26	45	28–62	4	7	0–14	4	7	0–14	2	3	0–8
45–54	40 596	75	185	143–227	14	34	16–53	3	7	0–16	1	2	0–7

(*Continued*)

Table 3. Continued

Age Group, y	Population at Risk	IS			ICH			SAH			Undetermined Stroke		
		No.	Rate	95% CI	No.	Rate	95% CI	No.	Rate	95% CI	No.	Rate	95% CI
55–64	20 096	102	508	409–606	24	119	72–167	3	15	0–32	6	30	6–54
65–74	13 103	137	1046	871–1220	14	107	51–163	2	15	0–36	3	23	0–49
75–84	5944	120	2019	1661–2376	15	252	125–380	1	17	0–50	4	67	1–133
>85	1147	36	3139	2130–4148	4	349	8–690	0	0	. . .	2	174	0–416
All ages	450 229	511	113	104–123	79	18	14–21	15	3	2–5	19	4	2–6
Standardized to world population*			167	142–192		26	16–36		4	0–8		6	1–11
Standardized to European population†			255	224–287		38	26–50		6	1–10		10	4–16
Standardized to European population 45–84 years‡			616	567–664		94	75–113		12	5–19		21	12–30

*Adjusted by age and sex to the world population.
†Adjusted by age and sex to the European population.
‡Adjusted by age and sex to the European population 45 to 85 years.

was greater than in most Western countries with the exception of the Ukraine.[17] Incidence rates were even higher than those of Novosibirsk, Russia, a region known for its high incidence of stroke.[18] Although population-based stroke studies are the best way to determine the real burden of stroke, these studies are scattered and have been performed mostly in developed countries. This is the first population-based study of stroke in a Middle East region that fulfils "ideal" criteria for a stroke incidence study.[19] The incidence of stroke was higher than expected. Indeed, the incidence was approximately double that of the majority of "ideal" studies conducted in the last decade (Figure 2).[17,20–37]

Importantly, the incidence of stroke was as high in women as in men. In a recent review of the differences between men and women, the overall incidence of stroke was 33% higher in men, apart from a few studies with small sample sizes and consequent low power.[38] The reason for this difference between Iran and most other countries is unclear.

Interestingly, although the adjusted incidence rates were high, the crude incidence rate of stroke was relatively low. Low crude incidence rates of stroke may occur when stroke incidence is low or when the source population is young; low crude incidence occurs in a young population because age is strongly associated with stroke incidence. However, despite the relatively young population in Mashhad, ISs are occurring approximately 1 decade earlier than in other countries (Figure 4). That is, a higher age-specific incidence is seen in younger age groups. This explains both the greater age-adjusted stroke incidence observed in Mashhad than in other countries (Figure 2 and 3) and the fact that a low crude stroke incidence is present in a setting of a high age-adjusted stroke incidence.

Another major finding is that the high incidence of total stroke is largely attributable to a high incidence of IS. This may be because some ICHs were misclassified as ISs because imaging was undertaken more than a few days after the

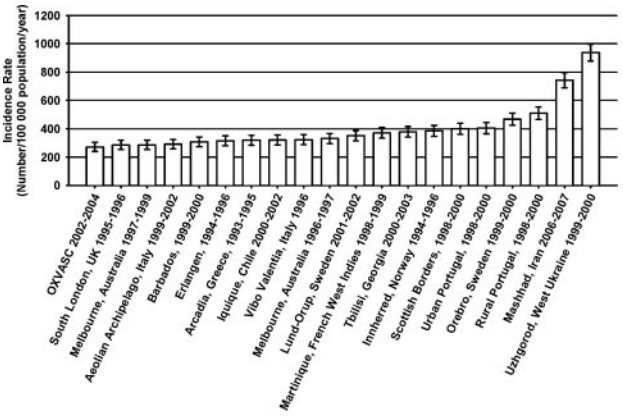

Figure 2. Incidence of stroke: summary of "ideal" stroke incidence studies conducted since 1995, adjusted by age and sex to the European population aged 45 to 84 years.[17,20–37] Error bars indicate 95% CIs.

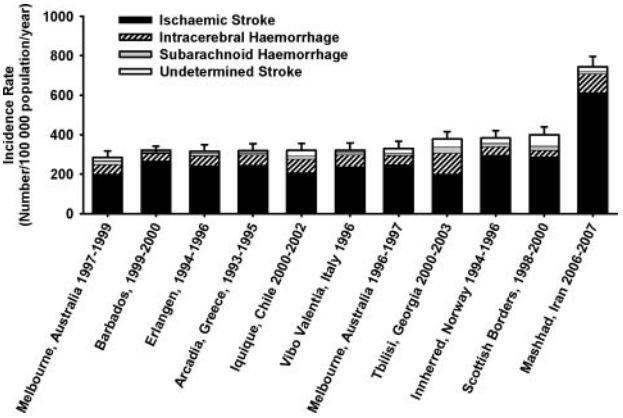

Figure 3. Incidence of stroke subtypes: summary of "ideal" stroke incidence studies conducted since 1995, adjusted by age and sex to the European population aged 45 to 84 years.[24–28,32,34,37,40] Error bars indicate 95% CIs.

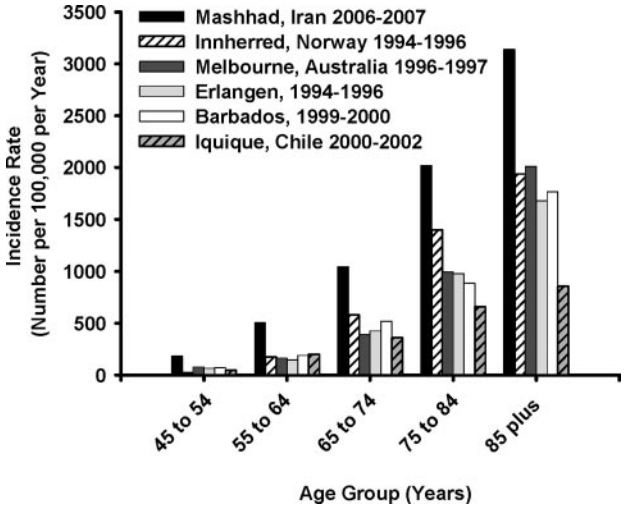

Figure 4. Age-specific incidence rates of IS: summary of selected "ideal" stroke incidence studies conducted since 1995.[24,25,27,33,37] (The studies are representative of all "ideal" studies conducted since 1995 in which stroke subtypes have been reported.)

stroke. However, this is unlikely to impact the findings significantly, as >90% of imaging was conducted within 7 days and 89.2% was conducted within 3 days. It also appears that the incidence of ICH is greater in Mashhad than in all other countries except Georgia.[32] Thus, both ICH and IS are considerable problems in this population. The low incidence of SAH may be due to incomplete ascertainment if lumbar punctures are not performed in CT-negative patients with an appropriate history. All of our cases with symptoms compatible with SAH had evidence of hemorrhage on their CTs. Furthermore, it is hospital policy to perform lumbar punctures in any cases with suspected SAH without any findings on CT scan. Therefore few, if any, cases are likely to have been missed.

The reason for the high incidence of stroke in Mashhad and the fact that stroke occurs at younger ages are not clear. It might be related to race-ethnic differences,[21] different types of vascular risk factors and their control, and the effect of socioeconomic status on stroke.[22] When assessing risk factors, the proportion of people with diabetes appears to be greater than in other stroke studies.[39] There also seems to be a large proportion of stroke patients, particularly women, with a history of hypertension. Although the proportion of patients with hypertension is not higher than that reported by others, strokes are occurring at a younger age, so it appears that hypertension is also developing at a younger age. It may also be that risk factors were not well controlled in our population and that this has contributed to the high incidence. In support of this, we found that 193 (46.4%) with hypertension, 76 (36.5%) with diabetes, and 104 (61.5%) with hyperlipidemia reported poor compliance with their treatment. Therefore, poor compliance with treatment may partly explain the relatively high stroke incidence in Mashhad.

We require prompt, preventive action on the part of health authorities to address this high incidence of stroke, particularly in the young. This has major implications for families, with many strokes occurring in those who are still of working age. There are also major implications for the provision of long-term care for stroke patients. The high incidence of stroke in the elderly will impact families, as most families will provide their own care for their elderly disabled relatives.

Our study has a number of limitations. Although there are different types of public and private healthcare systems in Iran, the public hospitals are not completely free of charge. In addition, substantial numbers of people do not have any type of healthcare insurance. This may result in a significant proportion of stroke cases being managed in the community and not admitted to a public hospital. These cases are traditionally hard to find. The fact that we used CHVs to find the majority of these cases may have overcome these limitations. However, there were some areas that could not be completely covered by CHVs. This is partly because most CHVs were women, and women are unable to go to every part of the city, particularly poor areas. In addition, rich people were not always cooperative and may have been missed because they would only attend a private clinic or would travel to other major centers, such as Tehran. The areas that were not covered by CHVs comprised no more than 20% of the study area, but it remains likely that some cases were missed in these areas. Another limitation is that the Emergency Departments are extremely busy, and some stroke patients may have been discharged before a complete evaluation was undertaken. This may be another source of missing cases. Finally, we confirmed strokes by autopsy in only 2 cases because of religious beliefs and customs. This limited our ability to find stroke patients who had died before reaching hospital. This could not be reliably supplemented by death certification because vague reasons for death, such as pneumonia, are usually recorded rather than underlying causes.

Our study has a number of strengths, including the use of CHVs to conduct a house-to-house search for cases, a very high proportion of cases who were imaged, and the lack of other centers of neurology in Mashhad, thereby ensuring that the majority of cases would have been referred to Ghaem Hospital. The fact that CHVs referred some cases with Bell's palsy, myocardial infarction, and psychiatric disorders (that were then excluded) indicates the overinclusive approach taken in finding cases in the community (data not shown, as these data were not systematically recorded).

In summary, the MSIS has provided valid and comparative data on the incidence of stroke in Iran as an area in the Middle East. The incidences of stroke, IS, and ICH were greater than those reported in most other regions of the world, and strokes occurred at younger ages. Further research may clarify the similarities and differences between the mechanism, genesis, and final outcome of stroke to develop a regional health policy for stroke. Culturally appropriate primary preventive strategies are required to reduce the burden of stroke in this region of the world.

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