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ORIGINAL ARTICLES

Temporal trends of stroke incidence over 14 years in Iran: Findings of a large-scale multi-centric hospital-based registry

[1]Masoumeh Sadeghi *MD*, [2]Marjan Jamalian *MSc*, [3]Fatemeh Nouri *PhD*, [4]Hamidreza Roohafza *MD*, [5]Shahram Oveisegaran *MD*, [2]Marzieh Taheri *PhD*, [3]Nizal Sarrafzadegan *MD*, [6]Habib Rahban *MD*

[1]Cardiac Rehabilitation Research Center, [2]Heart Failure Research Center, [3]Isfahan Cardiovascular Research Center, [4]Interventional Cardiology Research Center Isfahan, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran; [5]Rush Alzheimer's Disease Center, Department of Neurological Sciences, Rush University Medical Center, Chicago, IL, USA; [6]Internal Medicine PGY-2, Cardiovascular Research Foundation of Southern California, Southern California Medical Education Consortium, Universal Health System, USA

Abstract

Background: The burden of stroke is high worldwide, especially in low-middle income countries. We aim to explore the temporal trends of the incidence rate (IR) of stroke over 14 years in Iran's central areas. *Methods:* Stroke registry as part of cardiovascular disease (CVD) registry in Isfahan that focused on hospitalized patients (≥15 years) with first or recurrent stroke from 2001 to 2015. Factors included date of symptoms, demographics, management, survival at 28 days, date of admission, history of stroke, and other CVD and clinical diagnosis according to Computer Tomography Scan. We calculated age-, sex, and place-of-residence-adjusted IR based on multiple reference populations. Data were analyzed by bootstrap robust zero-truncated negative binomial regression models using R Statistical Software. *Results:* From 19,174 registered patients with stroke assessed by ICD-10; 18,010 (93.93%) cases were identified based on WHO-MONICA. Approximately 51% of hospitalized stroke patients were women. The average annual increase in stroke incidence based on ICD-10 ranged from 1.56% (95% CI, 0.14, 2.97) to 2.67% (95% CI, 1.25, 4.09) for different reference populations. In addition, a similar trend was also observed for stroke IR based on WHO-MONICA during the study period for the whole reference population, with an average annual change of 2.5% (95% CI, 1.28, 3.72) to 3.64 % (95% CI, 2.47, 4.82).
Conclusion: Given that temporal trends of stroke have increased in both sexes, especially in Iran's urban areas, prevention programs are needed for public awareness and physician motivation in order to identify risk factors as well as primary and secondary prevention.

Keywords: Stroke, ischemic heart disease, temporal trend, incidence, Iran

INTRODUCTION

Stroke, considered to be the second leading cause of death worldwide, imposes a significant disease burden and is the third most prevalent factor resulting in disability-adjusted life years (DALYs) in 2019.[1] Globally, almost 1 in 8 (12%) deaths are caused by stroke[2], and estimates show that disability and early death by stroke will almost double by 2030.[3]

Stroke leads to a transient or permanent change in one or more brain regions' function.[4] It is likely that stroke incidence will increase with an aging population[5], and a significant rise in stroke-related deaths has been seen in low/middle-income countries during the past four

Address correspondence to: Fatemeh Nouri, Isfahan Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran. Tel: +983136115233, Email: nouri.fatemeh2000@gmail.com; Nizal Sarrafzedegan, Isfahan Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran, Tel: +983136115314, Email : nsarrafzadegan@gmail.com

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decades especially in younger age.[6] Additionally, according to epidemiological reports, stroke trends are influenced by gender, region (urban/rural), and variability trends over years.

Stroke was ranked as the second leading cause of death in countries with upper/middle and lower/middle incomes and the fourth and third cause of death in countries with low income and high income, respectively.[7] Each year, nearly 60% of all stroke instances are in people younger than 70 years and 52% occur in men.[8,9] In some countries, stroke rates are decreasing or being controlled, while on the rise in others.[10] This variance can depend on lifestyle, risk factors, and intervention program differences.[11] In the Eastern Mediterranean Region (EMR) between 1980 and 2007, deaths occurring within 28 days after a stroke vary from 10% in Kuwait to 31.5% in Iran.[12]

Given the evidence for increased stroke incidence and mortality worldwide, especially in EMR countries, recognizing trends over a long period of time is of great importance. Previous reports were examined based on two criteria: the number of years during which the trend was examined and statistical modeling to calculate both the point estimate and confidence interval of annual changes in stroke hospitalization. Therefore, the present study investigated how the incidence of stroke in Iran changed during a 14-year period from 2001 to 2015 per 10,000 cases using MONICA and clinical diagnosis (ICD-10) methods.

METHODS

The Monitoring Trends and Determinants in Cardiovascular Diseases (MONICA) Project was a study to determine international incidences of stroke in various populations.[13] In accordance with the WHO-MONICA study, regardless of age limitations, we monitored ischemic heart disease (IHD) incidence and stroke in Isfahan, Iran, compiling information using disease registries of patients age 15 and over who were hospitalized for stroke from 2000 to 2015. Isfahan is a major industrial and central city in Iran, south of Tehran. In 2001, Isfahan's district population was 1,253,338 (51.6% males; 48.4% females), made up of 90.6% urban residents and 9.4% rural citizens. As of 2015, it had grown to 1,791,621 citizens. As the capital of its province, Isfahan hospitals receive referrals from other district and province cities. Since 2000, Isfahan's health registration system has aimed to measure local stroke incidence and fatality rates; this paper focused on stroke patients.

Public, private, and academic hospital records were evaluated in this registration system. Records of patients hospitalized with either complete or partial neurologist supervision in a number of Isfahan hospitals were assessed for potential symptoms. This search was done using overlapping methods: looking through discharge diagnoses, records of attendee name, and hospitalization wards. Data were collected in the Isfahan Cardiovascular Research Center (ICRC); all records were assessed by a number of nurses trained in receiving and recording patient information who summarized records in special checklists. After collecting basic patient information, the case fatality period (survival after a stroke) was defined as 28 days so as to make events distinguishable. Factors including date of onset, gender, date of birth, management, survival at 28 days, date of admission, hospital name, risk factors, history of stroke, MONICA diagnostic category, and clinical diagnoses based on the International Classification of Diseases (ICD 10) were included as core data. Subgroups of stroke based on ICD-10 were Subarachnoid haemorrhage (I60); Intracerebral haemorrhage (I61); Other nontraumatic intracranial haemorrhage (I62); Cerebral infarction (I63); Stroke, not specified as haemorrhage or infarction (I64); Occlusion and stenosis of precerebral arteries, not resulting in cerebral infarction (I65); Occlusion and stenosis of cerebral arteries, not resulting in cerebral infarction (I66); Other stroke (I67); stroke disorders in diseases classified elsewhere (I68); and Sequelae of stroke (I69). Regarding fatal events, details of the death, death certificate diagnoses, and autopsy results were recorded.

Per the MONICA project, whose diagnostic criteria were applied to this registry, events are defined as either first-event or recurrent and as either fatal or nonfatal. Stroke events were analyzed from the first occurrence until midnight between the 27th and 28th day to determine fatality or nonfatality, where fatal cases are those in which death occurs within 28 days of the onset of an event. According to the MONICA diagnostic criteria, events were classified as *definite*, *not stroke*, or *unclassifiable*. In the present study, only instances of definite stroke, where available information allowed for clinical stroke diagnosis, were analyzed. Details of the MONICA diagnostic categories have been previously reported.[14,15]

Hospitalized patients living in urban/rural areas in Isfahan province with first or recurrent stroke

were included in the present study. Eligible cases were identified retrospectively (cold pursuit) in accordance with relevant ICD diagnoses according to hospital discharge reports and death. Clinical stroke diagnosis was based on initial diagnoses or the underlying cause of death and also by including the secondary diagnoses at hospital discharge or contributory cause of death from death certificate based on ICD10 (I60-I65) and definite events based on MONICA diagnostic categories.

Statistical analysis

Age-, sex-, and place-of-residence-adjusted stroke IR was calculated for 10,000 patients from April 2001 to March 2015. The annual figures recorded in Isfahan for different age groups, places of residence, and genders were utilized as the denominators for all IR calculations. A direct method was taken using five populations to adjust the age, sex, and place of residence distribution differences among the studied years: the Iran population and the Isfahan province population on the 2006 and 2011 censuses, and the Isfahan district population from April 2001 to March 2015. To examine the trend of stroke incidence across time, bootstrap robust zero-truncated negative binomial regression models were used for analytical purposes with year as the independent variable and crude rate and age-, sex-, and place-of-residence-adjusted IR as the dependent variable. The negative binomial regression model addresses overdispersion, requiring fewer assumptions about variance patterns than does Poisson regression. The data of dependent variables in regression model truncated at zero were obtained by adjusting IR. To put it another way, zero truncated negative binomial regression was used since the zero value is not included in the dependent variables. Additionally, in this study, all hospitalized patients with first and recurrent stroke events were included, in which an intra-group correlation was expected. A common method to address intra-group correlation is to strengthen the standard error of regression coefficients using different methods; here, robust bootstrap was used to address the misspecification resulting from intra-group correlation. In this regression model, trends across individual calendar years can be estimated to obtain the average annual percentage of change. Considering the corresponding estimated regression coefficient and standard error, an annual change in stroke might be derived along with the 95% confidence interval (CI). The exponent of the estimated regression coefficient is the relative risk (RR) per each calendar year; the regression coefficient of year multiplied by 100 gives the average annual incidence change in percentages. The collected data were analyzed using R Statistical Software version 3.5.3 (R Core Team, 2019).

RESULTS

From April 2001 to March 2015, a total of 19,174 cases of both first and recurrent stroke incidents were collected in Isfahan, Iran. Among those with stroke as clinical diagnosis based on ICD10 (I60-I69), 18,010 were identified as definite cases of MONICA diagnostic categories. Table 1 shows patients' demographic data patients. Nearly 51% of patients hospitalized for stroke were females, 45% of whom were between 55 and 75 years, with approximately 1.4% being younger than 35 years, and approximately 94% of whom were from urban areas. The average age for women and men was 70.67±13.04 years and 68.71±13.25 years, respectively, showing that men experienced stroke at a younger age than women. More details about the characteristics of participants are presented in Table 1.

Tables 2 and 3 show specific stroke IR associated with age, sex, and place of residence based on clinical diagnosis (ICD-10) and WHO-MONICA methods, respectively, during three observation periods: April 2001 to March 2006, April 2006 to March 2011, and April 2011 to March 2015. In urban areas for those older than 75 years, stroke IR based on both diagnostic methods was considerably higher than that of rural areas for both genders in all observation periods. While during the first observation period, the stroke IR based on both diagnostic methods were higher for the studied urban areas than that of the rural areas in men aged 45-75 and women aged 65-75 years, these rates were reversed in the last observation period. In urban areas, the stroke IR based on both diagnostic methods was higher in women over 75 years than in men of the same age during the three observation periods. However, in rural areas, stroke IR based on both diagnostic methods in men over 65, 60, and 45 years was higher than that of women of the same age during the same three observation periods. The stroke IR based on clinical diagnosis (ICD-10) and WHO-MONICA methods increased with age in both areas and sexes in all studied periods. Stroke IR in people over 60 years was considerably higher than those 35 to 60 years, as expected.

Figure 1 and Appendix 1 summarize the crude rate and age-, sex-, and place-of-residence-adjusted stroke IR (per 10,000 cases) based on the clinical diagnosis (ICD-10) method. The five above-mentioned populations were used to adjust the stroke IR. Also, crude and adjusted trends of estimated IR are graphically depicted in Figure 2, while Appendix 2 provides data on different standard populations for stroke diagnosed by WHO-MONICA criteria. The lowest and highest adjusted stroke IR in both diagnosis methods were in the adjustment based on Iran's 2006 census and Isfahan province's 2011 census as reference across time periods, respectively. Accordingly, adjusted stroke IR based on clinical diagnosis (ICD-10) ranged from 6.59 to 8.91 and 11.17 to 13.82 (per 10,000 cases) from April 2001 to March 2002, and from April 2014 to March 2015, respectively. Likewise, the adjusted IR based on WHO-MONICA ranged from 6.05 to 8.2 and 10.99 to 13.61 during the same periods. In Figures 1 and 2, following an initial relative fall from 2006 to 2010, the stroke IR for all reference populations relatively rose over the study period. Table 4 shows the average yearly changes using different diagnostic methods and different reference populations for adjustment. The average annual increase based on clinical diagnosis (ICD-10) ranged from 1.56% (95% CI, 0.14, 2.97) to 2.67% (95% CI, 1.25, 4.09). Additionally, a similar trend was also observed based on WHO-MONICA. On average, the annual increase in incidence of stroke ranged from 2.5% (95% CI, 1.28, 3.72) to 3.64 % (95% CI, 2.47, 4.82).

Table 1: Characteristics of registered hospitalization stroke patients based on diagnostic methods

Characteristics		**Clinical Diagnoses** (I60-I69)	**WHO-MONICA Diagnostic Categories**
Total cases		19174	18010
Sex N (%)	Female	9742(50.8)	8888(49.4)
	Male	9432(49.2)	9122(50.6)
Place of Residence N (%)	Urban	17949(93.6)	16844(93.5)
	Rural	1225(6.4)	1166(6.5)
Age (years), Mean (SD)	Female	70.67±13.04	68.74±13.16
	Male	68.71±13.25	70.75±12.99
	Urban	69.74±13.17	69.80±13.11
	Rural	68.67±13.24	68.73±13.17
	Total	69.67±13.18	69.73±13.11
Age Groups N (%)	15-19y	27(0.1)	22(0.1)
	20-24	54(0.3)	47(0.3)
	25-29	86(0.4)	80(0.4)
	30-34	124(0.6)	111(0.6)
	35-39	188(1.0)	178(1.0)
	40-44	354(1.8)	323(1.8)
	45-49	622(3.2)	579(3.2)
	50-54	1066(5.6)	999(5.5)
	55-59	1408(7.3)	1325(7.4)
	60-64	1997(10.4)	1883(10.5)
	65-69	2339(12.2)	2217(12.3)
	70-74	2969(15.5)	2785(15.5)
	>=75 y	7940(41.1)	7461(41.4)

Table 2: IR (per 10,000 cases) of hospitalization stroke based on clinical diagnosis (ICD-10: I60-I69) in Isfahan, Iran, from April 2001to March 2015

Years		April 2001- March 2006		April 2006 - March 2011		April 2011 - March 2015	
Sex	Age group	Rural	Urban	Rural	Urban	Rural	Urban
		IR(95%CI)	IR(95%CI)	IR(95%CI)	IR(95%CI)	IR(95%CI)	IR(95%CI)
Female	15-19y	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)
	20-24	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)
	25-29	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)
	30-34	0(0,0)	1(0.6,1.4)	1(0,2.2)	0(0,0)	0(0,0)	0(0,0)
	35-39	1(0,2.3)	1(0.6,1.4)	1(0,2.3)	1(0.7,1.3)	2(0.2,3.8)	1(0.7,1.3)
	40-44	1(0,2.4)	2(1.4,2.6)	2(0,4.1)	2(1.5,2.5)	2(0.0,4.0)	1(0.7,1.3)
	45-49	4(1.0,7.0)	5(3.9,6.0)	6(2.1,9.9)	4(3.2,4.8)	2(0,4.3)	2(1.5,2.5)
	50-54	7(2.6,11.4)	10(8.4,11.6)	11(5.3,16.7)	7(5.8,8.2)	6(1.7,10.3)	6(5.0,7.0)
	55-59	15(7.8,22.2)	17(14.6,19.4)	22(12.7,31.3)	13(11.1,14.9)	12(5.5,18.5)	13(11.2,14.8)
	60-64	34(21.6,46.4)	32(28.4,35.6)	23(12.6,33.4)	25(22.0,28.0)	19(9.5,28.5)	22(19.3,24.7)
	65-69	35(21.6,48.4)	52(46.8,57.2)	32(18.1,45.9)	40(35.6,44.4)	43(27.4,58.6)	40(35.7,44.3)
	70-74	36(21.6,50.4)	89(81.8,96.2)	36(21.0,51.0)	58(52.4,63.6)	63(41.2,84.8)	52(46.8,57.2)
	>=75 y	50(36.6,63.4)	136(128.3,143.7)	84(65.9,102.1)	144(136.4,151.6)	90(72.0,108.0)	151(143.3,158.7)
Male	15-19y	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)
	20-24	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)
	25-29	0(0,0)	0(0,0)	0(0,0)	0(0,0)	1(0.0,2.0)	0(0,0)
	30-34	1(0,2.1)	0(0,0)	0(0,0)	0(0,0)	0(0,0)	1(0.7,1.3)
	35-39	1(0,2.2)	1(0.6,1.4)	1(0,2.2)	1(0.7,1.3)	0(0,0)	1(0.7,1.3)
	40-44	3(0.6,5.4)	3(2.3,3.7)	1(0,2.4)	2(1.5,2.5)	2(0.1,3.9)	2(1.5,2.5)
	45-49	3(0.4,5.6)	5(4.0,6.0)	6(2.2,9.8)	4(3.2,4.8)	6(2.2,9.8)	4(3.3,4.7)
	50-54	12(6.1,17.9)	11(9.4,12.6)	9(3.8,14.2)	8(6.8,9.2)	11(5.3,16.7)	8(6.9,9.1)
	55-59	9(0,25.5)	18(15.6,20.4)	16(7.6,24.4)	14(12.1,15.9)	27(17.0,37.0)	17(15.1,18.9)
	60-64	22(11.6,32.4)	33(29.4,36.6)	25(13.4,36.6)	27(24.0,30.0)	35(21.4,48.6)	32(28.9,35.1)
	65-69	40(25.7,54.3)	46(41.5,50.5)	45(28.3,61.7)	38(34.0,42.0)	44(27.2,60.8)	39(35.1,42.9)
	70-74	55(36.8,73.2)	83(76.0,89.9)	73(52.2,93.8)	57(51.8,62.2)	69(45.9,92.1)	50(45.2,54.8)
	>=75 y	61(45.5,76.5)	115(107.8,122.2)	84(64.8,103.2)	130(122.6,137.4)	112(91.2,132.8)	139(131.6,146.4)

IR: Incidence rate, CI: confidence interval

DISCUSSION

The present study aimed to describe stroke hospitalization IR and shed light on the trends in age-, sex- and place-of-residence-adjusted stroke IR in Iran. Five standard populations were considered as reference for adjustment, with two diagnostic methods—MONICA and clinical diagnosis (ICD-10) —from April 2001 to March 2015. An increasing trend in stroke was seen for all reference populations with adjustment for age, sex, and place of residence, with an average annual change between 1.56 and 3.64%. For women over 75 years, stroke IR was higher than that of men and stroke IR in men over 60 years was higher than that of women in urban and rural areas, respectively.

Stroke IR varies regionally and over time. In some countries, this rate is increasing and in others it is decreasing or being controlled. Previous studies have shown that stroke IR has decreased in several Western nations due to training programs and better risk factor management, while the rate has grown in recent decades in Eastern Asia.[16] Stroke hospitalization IR is increasing in the United States, while subarachnoid hemorrhage (SAH) stroke hospitalization decreased from 1995 to 2008.[17] Per the Canadian Institutes for Health Information (CIHI), based on ICD-10 codes, the

Table 3: IR (per 10,000 cases) of hospitalization stroke based on WHO-MONICA diagnostic categories in Isfahan, Iran, from April 2001to March 2015

Years		April 2001- March 2006		April 2006 - March 2011		April 2011 - March 2015	
Sex	Age group	Rural	Urban	Rural	Urban	Rural	Urban
		IR(95%CI)	IR(95%CI)	IR(95%CI)	IR(95%CI)	IR(95%CI)	IR(95%CI)
Female	15-19y	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)
	20-24	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)
	25-29	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)
	30-34	0(0,0)	0(0,0)	1(0,2.2)	0(0,0)	0(0,0)	0(0,0)
	35-39	1(0,2.3)	1(0.6,1.4)	1(0,2.3)	1(0.7,1.3)	2(0.2,3.8)	1(0.7,1.3)
	40-44	1(0,2.4)	2(1.4,2.6)	2(0,4.1)	1(0.6,1.4)	2(0.0,4.0)	1(0.7,1.3)
	45-49	4(1.0,7.0)	4(3.1,4.9)	6(2.1,9.9)	3(2.3,3.7)	2(0,4.3)	2(1.5,2.5)
	50-54	6(1.9,10.1)	9(7.5,10.5)	11(5.3,16.7)	7(5.8,8.2)	6(1.7,10.3)	6(5.0,7.0)
	55-59	15(7.8,22.2)	15(12.8,17.2)	19(10.3,27.7)	13(11.1,14.9)	12(5.5,18.5)	13(11.2,14.8)
	60-64	30(18.4,41.6)	29(25.5,32.5)	21(11.1,30.9)	24(21.1,26.9)	19(9.5,28.5)	22(19.3,24.7)
	65-69	33(20.0,46.0)	47(42.1,51.9)	32(18.1,45.9)	39(34.7,43.3)	43(27.4,58.6)	40(35.7,44.3)
	70-74	35(20.8,49.2)	80(73.2,86.8)	34(19.4,48.6)	54(48.6,59.4)	59(37.9,80.1)	51(45.9,56.1)
	>=75 y	48(34.9,61.1)	123(115.7,130.3)	82(64.1,99.9)	137(129.6,144.4)	89(71.1,106.9)	147(139.4,154.6)
Male	15-19y	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)
	20-24	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)	0(0,0)
	25-29	0(0,0)	0(0,0)	0(0,0)	0(0,0)	1(0.0,2.0)	0(0,0)
	30-34	1(0,2.1)	0(0,0)	0(0,0)	0(0,0)	0(0,0)	1(0.7,1.3)
	35-39	1(0,2.2)	1(0.6,1.4)	1(0,2.2)	1(0.7,1.3)	0(0,0)	1(0.7,1.3)
	40-44	3(0.6,5.4)	3(2.3,3.7)	0(0,0)	2(1.5,2.5)	2(0.1,3.9)	2(1.5,2.5)
	45-49	3(0.4,5.6)	4(3.1,4.9)	6(2.2,9.8)	4(3.2,4.8)	6(2.2,9.8)	4(3.3,4.7)
	50-54	8(3.2,12.8)	10(8.4,11.6)	9(3.8,14.2)	7(5.9,8.1)	11(5.3,16.7)	8(6.9,9.1)
	55-59	8(2.5,13.5)	16(13.7,18.3)	16(7.6,24.4)	14(12.1,15.9)	26(16.2,35.8)	17(15.1,18.9)
	60-64	21(10.8,31.2)	29(25.6,32.4)	25(13.4,36.6)	26(23.0,29.0)	35(21.4,48.6)	32(28.9,35.1)
	65-69	38(24.0,52.0)	41(36.8,45.2)	45(28.3,61.7)	36(32.1,39.9)	44(27.2,60.8)	39(35.1,42.9)
	70-74	44(27.7,60.3)	74(67.4,80.6)	73(52.2,93.8)	55(49.9,60.1)	67(44.2,89.8)	49(44.2,53.8)
	>=75 y	50(36.0,64.0)	102(95.2,108.8)	80(61.3,98.7)	121(113.9,128.1)	109(88.4,129.6)	134(126.8,141.2)

IR: Incidence rate, CI: confidence interval

absolute numbers of stroke admissions in Canada were stable or declined in most provinces from April 2003 to March 2013. Results of this study showed that stroke IR did not change dramatically over time.[18]

According to a GBD study, age-standardized stroke IR reduced in Japan, Singapore, and Korea between 1990 and 2010.[5] In a report issued by the Korean Stroke Society, the incidence of ischemic stroke increased over time, whereas the incidence of hemorrhagic stroke decreased.[19] A systematic review study of epidemiology stroke showed an increase in stroke IR in the Middle East during the last decades.[16] Similarly, a study conducted in Bahrain with the ICD-10 diagnostic criterion reported an increase over the previous years.[20]

Middle eastern countries have reported lower mean ages than developed countries regarding stroke IR, which might be associated with the fact that the population in these countries is rather young and life expectancy is low due to the prevalence of non-communicable diseases.[21] Furthermore, unhealthy behaviors and risk factors have increased among young patients compared with older patients, resulting in a lower mortality rate among older patients over the last few decades.[17,22]

Another study reported that the IR of stroke decreased from 1990s to 2015 among women and men in the United States.[23] A study in Isfahan (2007) showed that age and sex characteristics

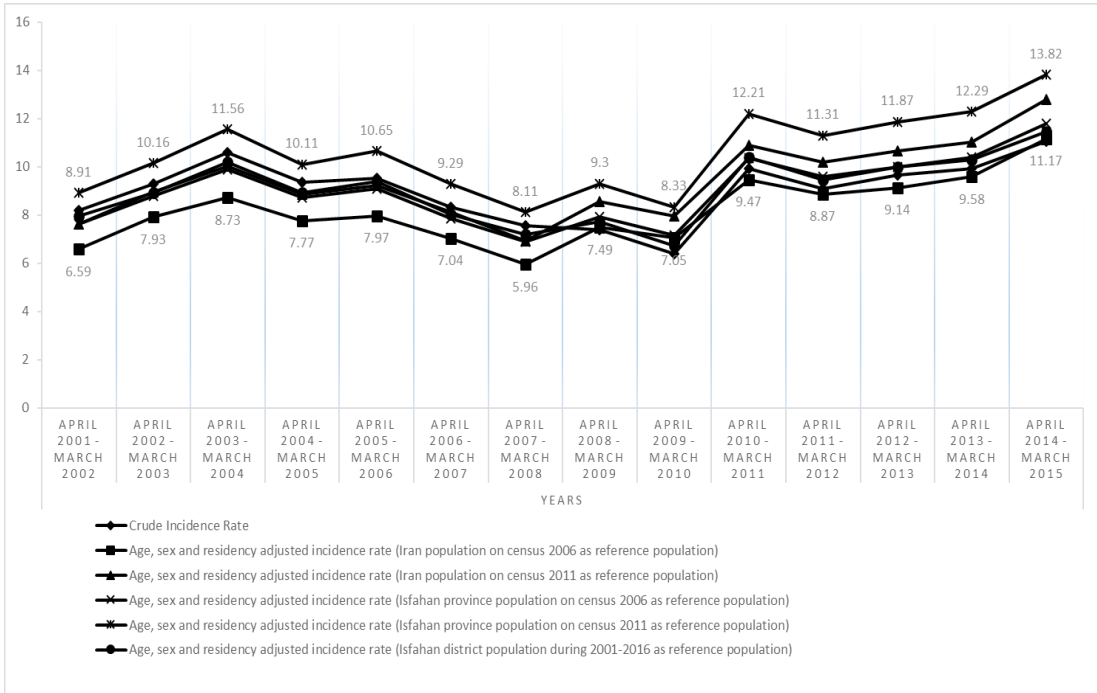

Figure 1. Crude rate and age-adjusted IR (per 10,000 cases) of stroke hospitalization based on clinical diagnosis (ICD-10: I60-I69) in Isfahan, Iran, from April 2001 to March 2015.

were similar to developed countries; however, it was the mortality rate which was similar to developing countries in the current study.[24] The maximum incidence was in the age range of 80 to 89 years, and the number of stroke admissions for younger patients rose.

In southern Germany, the stroke IR in women rose dramatically from 1994 to 1995.[25] In the current study, stroke IR increased in both sexes. The incidence of this disease was higher in men than women in 2013 in China[26]; in the UK, the average age at first stroke was reported as 77

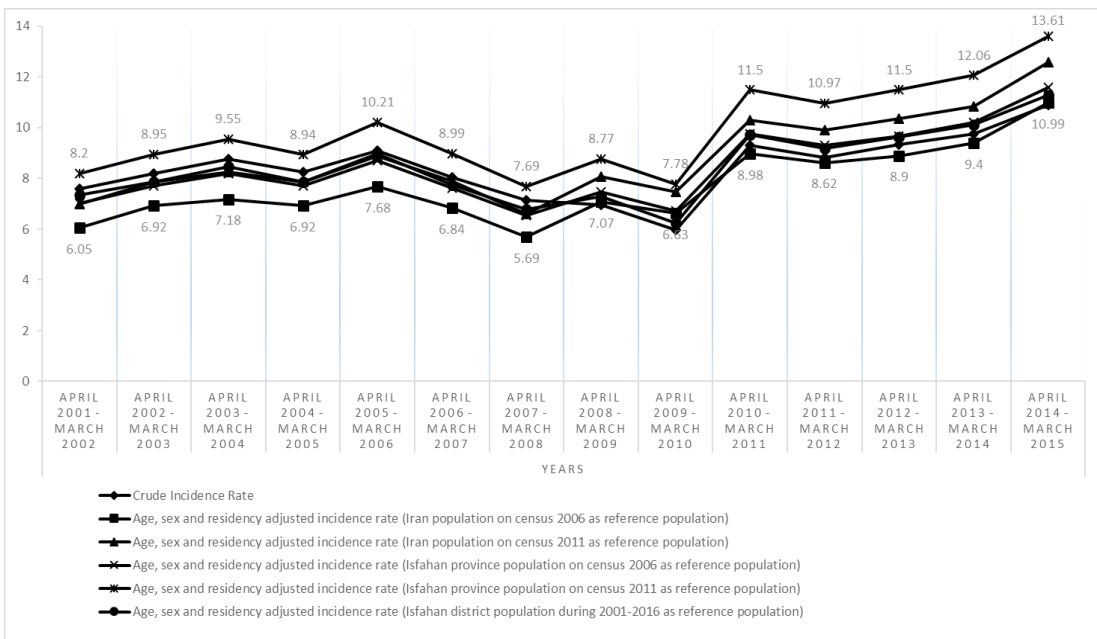

Figure 2. Crude rate and adjusted IR (per 10,000 cases) of hospitalization stroke based on WHO-MONICA diagnostic categories in Isfahan, Iran, from April 2001 to March 2015.

Table 4: Annual percentage of change in the incidence of hospitalization stroke in Isfahan, Iran, from April 2001to March 2015

	Clinical Diagnosis (ICD-10: I60-I69)			WHO-MONICA Method		
	Annual Percentage of change (% per year) (95% CI)	p-value	Relative Risk (95% CI)	Annual Percentage of change (% per year) (95% CI)	p-value	Relative Risk (95% CI)
Model 1	0.73(-0.79,2.26)	0.35	1.01(0.99,1.02)	1.68(0.38,2.98)	0.011	1.02(1.004,1.03)
Model 2	2.64(1.16,4.13)	<0.001	1.03(1.01,1.04)	3.63(2.41,4.85)	<0.001	1.04(1.02,1.05)
Model 3	2.67(1.25,4.09)	<0.001	1.03(1.01,1.04)	3.64(2.47,4.82)	<0.001	1.04(1.03,1.05)
Model 4	2.05(0.62,3.47)	0.005	1.02(1.01,1.03)	3.00(1.81,4.19)	<0.001	1.03(1.02,1.04)
Model 5	2.18(0.80,3.56)	0.002	1.02(1.01,1.04)	3.12(1.96,4.28)	<0.001	1.03(1.02,1.04)
Model 6	1.56(0.14,2.97)	0.031	1.01(1.001,1.03)	2.50(1.28,3.72)	<0.001	1.03(1.01,1.04)

Notes: Bootstrap Robust Zero-Truncated Negative Binomial Regression models were used with year as an independent variable and crude IR as a dependent variable in Model 1. Age-, sex-, and place-of-residence-adjusted IR (Iran population on census 2006 as a reference population) as a dependent variable in Model 2. Age-, sex-, and place-of-residence-adjusted IR (Iran population on census 2011 as a reference population) as a dependent variable in Model 3. Age-, sex-, and place-of-residence-adjusted IR (Isfahan province population on census 2006 as a reference population) as a dependent variable in Model 4. Age-, sex-, and place- of-residence-adjusted IR (Isfahan province population on census 2011 as a reference population) as a dependent variable in Model 5. Age-, sex-, and place-of- residence-adjusted IR (Isfahan district population during 2001-2016 as a reference population) as a dependent variable in Model 6. The regression coefficient of year multiplied by 100 gives the average annual change of incidence as a percentage.

years in women and 71 years in men.[27]

A study conducted in 155 urban and rural centers in China showed stroke IR and mortality rates rose in the past 3 decades, especially in rural areas.[28] In Saadat *et al*.'s study conducted in northern Iran, stroke cases were higher in rural areas.[29]

In the current study, both diagnostic methods showed a reduction in crude rates and adjusted stroke IR from 2006 to 2009. One reason for these changes could be associated with the 6-year program "IHHP - Isfahan Healthy Heart Program," which was implemented to prevent cardiovascular diseases by changing the lifestyles of Isfahan and Najafabad populations between 2001 and 2016.[30-32] Previous studies have shown that the strategies adopted in the IHHP program proved useful in reducing risk factors such as metabolic lifestyle behaviors and improving patient survival. A large number of IHHP interventions were integrated into the health system once the program completed in 2007. However, since 2010, the impact of IHHP interventions has gradually faded. Hence, it seems crucial to devise a plan to adopt similar strategies in this community.[33]

Strengths of this study include a long follow-up period, enabling the reporting of accurate and up-to-date information on stroke IR. Secondly, strokes were registered from a wide range of private and state sectors. Thirdly, this study used two standard diagnostic methods (ICD-10:160-169 and MONICA) for comparison and a variety of reference populations helping to identify heterogeneity and variability. Finally, a comprehensive statistical approach was used.

However, this study does not enjoy comprehensive, community-based research, which is important in stroke surveys. Secondly, samples were taken from a limited area in Iran. As the occurrence of the disease depends on how commonplace the risk factors are, it seems more practical to collect information from other Iranian cities and study stroke IR more broadly.

One of the limitation was increasing trends due to other reasons the study could not/did not measure eg change in prevalence and control of vascular risk factors, in the other hand increase awareness of stroke and health seeking behavior in the population, increased access to healthcare facilities due to greater proximity or affordability, increased diagnosis by the medical teams due to their greater awareness or availability of investigations, e.g., scans.

In conclusion, stroke is a major healthcare problem in Iran, its pattern showing geographical diversity and evolution over time, and seems to be more dangerous for men than for women. Stroke in the younger population shows that we might face an increasing trend for this disease in the future and, as this disease has negative effects

on patients' quality of life, it is necessary to raise citizen awareness and think of management and treatment measures to improve patient health.

DISCLOSURES

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