

Epidemiology of stroke in the south west of Iran: A cohort study

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Abstract

Background: Stroke is the second common cause of death in the world. It imposes a huge amount of economic and social burden on individuals, families, communities, and governments. There are significant regional differences in stroke incidence even within countries. The last information about stroke incidence in Bushehr is related to 2002-2003. Life expectancy is increasing and as a result burden of non-communicable diseases including stroke is in progress, so the current study was conducted to obtain a better picture of stroke incidence in Bushehr district, Iran, in 2013-2014.

Methods: In a retrospective cohort study, hospital files of all the individuals admitted as stroke or transient ischemic attack in the Persian Gulf and Salman-e-Farsi Hospitals in 2013-2014 were studied. A list of patients with diagnosis of stroke was prepared using International Classification of Disease 10. Bushehr middle year population was estimated based on the census (2011-2012). Age standardization was done according to World Health Organization standard population. Incidence correction was done using sensitivity analysis.

Results: In the study year, 255 cases of stroke were registered in two hospitals. The mean age was 65.3 ± 14.14 years. Crude and standardized incidence of stroke were 92.71 (81.69-104.81) and 198.3 (189.68-207.22) per 100,000, respectively. Standardized incidence was higher in men as compared with women ($P < 0.001$).

Conclusion: Stroke incidence is high, especially in men, in Bushehr district. A population-based stroke registry is necessary for more accurate estimation of the rates over time.

Keywords: Cerebrovascular Disorders; Incidence; Iran; Noncommunicable Diseases; Stroke

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Introduction

Cerebrovascular accident is a clinical syndrome with vascular cause and rapid onset of focal and occasionally global neurological signs and symptoms lasting more than 24 hours or causing death (1). Patients with stroke face numerous

somatic, cognitive, mental, psychological, and social difficulties including depression, feeling of worthlessness, difficulty in speech and communication, personality change, losing friends, and dependence on others for daily activities.

These changes can potentially affect their quality of life (15). Stroke imposes a huge amount of economic and social burden on individuals, families, communities, and governments.

Stroke is the second common cause of death and disease burden (measured as disability adjusted life years) in people over 60 years in the world (6). Ranking of stroke in Iran based on the years of life lost changed from seventh to fourth between 1990 and 2010 (7). There are significant regional differences in stroke incidence even within countries (8). According to Auckland community stroke study, Europeans had the highest crude stroke incidence (9). Annual incidence was 2.8 per 1,000 in Scotland boundary in 2002-2004 (10). Based on Mashhad Stroke Incidence Study (MSIS), crude incidence of the first ever stroke were 139 per 100,000 and age adjusted rates were more than most countries in 2006-2007 (11). According to a hospital based study, age adjusted annual incidence for stroke were 77.31 and 116.71 per 100,000 in men and women, respectively, in Bushehr district in 2002-2003, which were more than the rates of developed European countries. In the last decades of the 20th century, the trend of decline in mortality from stroke, which had started in previous decades, became slower in some countries (12, 13). It is predicted that new cases of stroke grow more than twice between 2010 and 2050 (14).

In order to set priority in health policy and plan for preventing stroke, it is necessary to know its epidemiology. It is known that there are significant regional differences in stroke epidemiology even within countries (8). Furthermore, the last information about stroke incidence in Bushehr is related to 2002-2003. Since life expectancy is increasing and, as a result, burden of non-communicable and chronic diseases including stroke is in progress, this study aimed to determine stroke incidence in Bushehr district, Iran in 2013-2014.

Methods

In a cohort study, data on all patients who were admitted with diagnosis of stroke in the Persian Gulf and Salman-e-Farsi Hospitals in Bushehr Port between March 2013-March 2014 were collected in the period between January and October 2015. Also, all the deaths, whose underlying cause was marked as stroke in Bushehr district Death Registry System during the same interval, were recorded. These two hospitals are the only hospitals of Bushehr district which have neurology ward and all the stroke cases in the district are referred there.

Data collection started using hospital information system (HIS) of two hospitals by the same researcher. A list of patients with diagnosis of stroke was prepared using codes of the International Classification of Disease 10 (ICD 10), including I64, I61.9, I62.9, and G45.9. Among these patients, those who lived in Bushehr district were selected and using file numbers, these patients' hospital files were reviewed. Different items including admission order, reception and discharge sheets, medical and nursing reports, radiology, doppler sonography, and angiography reports as well as death certificates were used to get data on age, sex, residence, episode of stroke, brain Computerized Tomography (CT) scan or Magnetic Resonance Imaging (MRI) reports.

To ensure accuracy of diagnostic code, stroke was considered as abrupt onset of neurological signs and symptoms with vascular origin lasting at least 24 hours or ending in death (1). Cases with information in favor of uremia, hypoglycemia, blood dyscrasia, anticoagulant therapy, trauma, metastasis, tumor, and nonbacterial endocarditis were excluded. Also, patients with history of endarterectomy surgery, coronary artery bypass graft, aortic aneurism surgery, intracranial surgery, and angiography (12) as well as nationalities other than Iranian were excluded. Diagnosis of stroke and its types was based on hospital file reports, history, physical

examinations, CT scans, MRI reports, discharge sheets, and death certificates. Stroke types were classified as brain ischemia (IS), intracranial hemorrhage (ICH), and subarachnoid hemorrhage (SAH).

Those with the cause of death recorded as stroke in the study year were extracted from provincial death registry system and verbal autopsy forms. These deaths were included if stroke as cause of death occurred in the same year. Sensitivity analyses were performed for cases who died at home and whose dates of stroke were unknown. Obviously, these cases were not recorded in HIS and used in order to correct incidence rates.

Fasting blood sugar equal or more than 126 mg/dl, random blood sugar equal or more than 200 mg/dl (16), and total serum cholesterol equal or more than 180 mg/dl (17) were considered diabetes mellitus and hypercholesterolemia, respectively. Also, taking drugs which are used for the treatment of these two diseases was considered as a criterion to consider having diabetes mellitus and/or hypercholesterolemia.

In the present study, "incidence" stands for crude incidence and "standardized incidence" means age standardized incidence using World Health Organization (WHO) standard population as reference population. Also, stroke episode means whether stroke occurred once or more for one person.

Incidence was calculated as crude, age specific for age groups ≤ 14 , 15-34, 35-44, 45-54, 55-64, 65-74, 75-84, and ≥ 85 years and separately in males and females. Age and sex specific incident cases were used as numerator and age specific population measures were used as denominator, based on the data of statistical center of Iran.

Descriptive statistics (frequency, mean, standard deviation, and 95% confidence interval) were used to describe the sample. Crude total incidence and age, sex, type, and episode specific incidence were calculated per 100,000. Corrected rates

(using sensitivity analysis) were calculated in 100,000. Corrected incidence was calculated by adding two other type cases to the original cases. The number of patients whose death was due to stroke recorded in Bushehr Province death registry system, which were not in hospital files' finding and confirmed by phone interview with family of the deceased, was 17; also, the number of cases confirmed by verbal autopsy records was 6. Another corrected incidence was calculated using those mortality cases from death registry system which did not have phone number or contact was not possible (11 cases). Z test was used to compare incidence between men and women. *P* value less than 5% was considered significant in all analyses. Data analysis was performed using PASW Statistics for Windows, Version 18.0. and Stata Statistical Software: Release 13.

Stata was used to calculate age standardized rates. We accomplished age standardization because age can be a confounding factor when we compare incidence between different populations. Age standardization was done using direct method (18) based on standard population of WHO (Appendix 1) (19). Age Standardization was done for total and sex, type, and episode specific incidence rates. Bushehr mid-year population was estimated based on the national population and housing census 2011 in Iran (Appendix 2) and natural growth rate of Bushehr Province (3.11%) (20). The following formula was used for estimating the population of the study year: $P_{(t+n)} = P_t (1 + r)^n$, where "r" stands for natural population growth rate (0.0311), "t" for base year, "n" for the interval between the base year and the study year (2 years), and "P" for population number (21).

The study began after approval in ethics board at Bushehr University of Medical Sciences. The study was launched after obtaining permission from vice chancellor of research at Bushehr University of Medical Sciences and the head of the two hospitals. All data was used anonymously.

Results

Totally, 514 cases in the Persian Gulf Hospital and 360 cases in Salman-e-Farsi Hospital, who were registered as stroke or Transient Ischemic Attack (TIA), were extracted from HIS. The flowchart of identification of stroke and TIA incident cases is shown in Figure 1. The number of stroke cases was 255: 143 (56.1%) were males and 112 (43.9%) were females, and the mean age was 65.3 ± 14.14 years. The

median age was 66 years with the range between 17 and 100 years. Demographic variables for stroke cases are shown in Table 1. As shown, the highest mean age was for IS and the lowest for SAH. Brain CT scan was the most common method to determine the type of stroke (80%). MRI was used in 12.9% of cases and in 2% of cases both of these methods were used. In 5.1% of cases, no radiologic method was used to diagnose type of stroke.

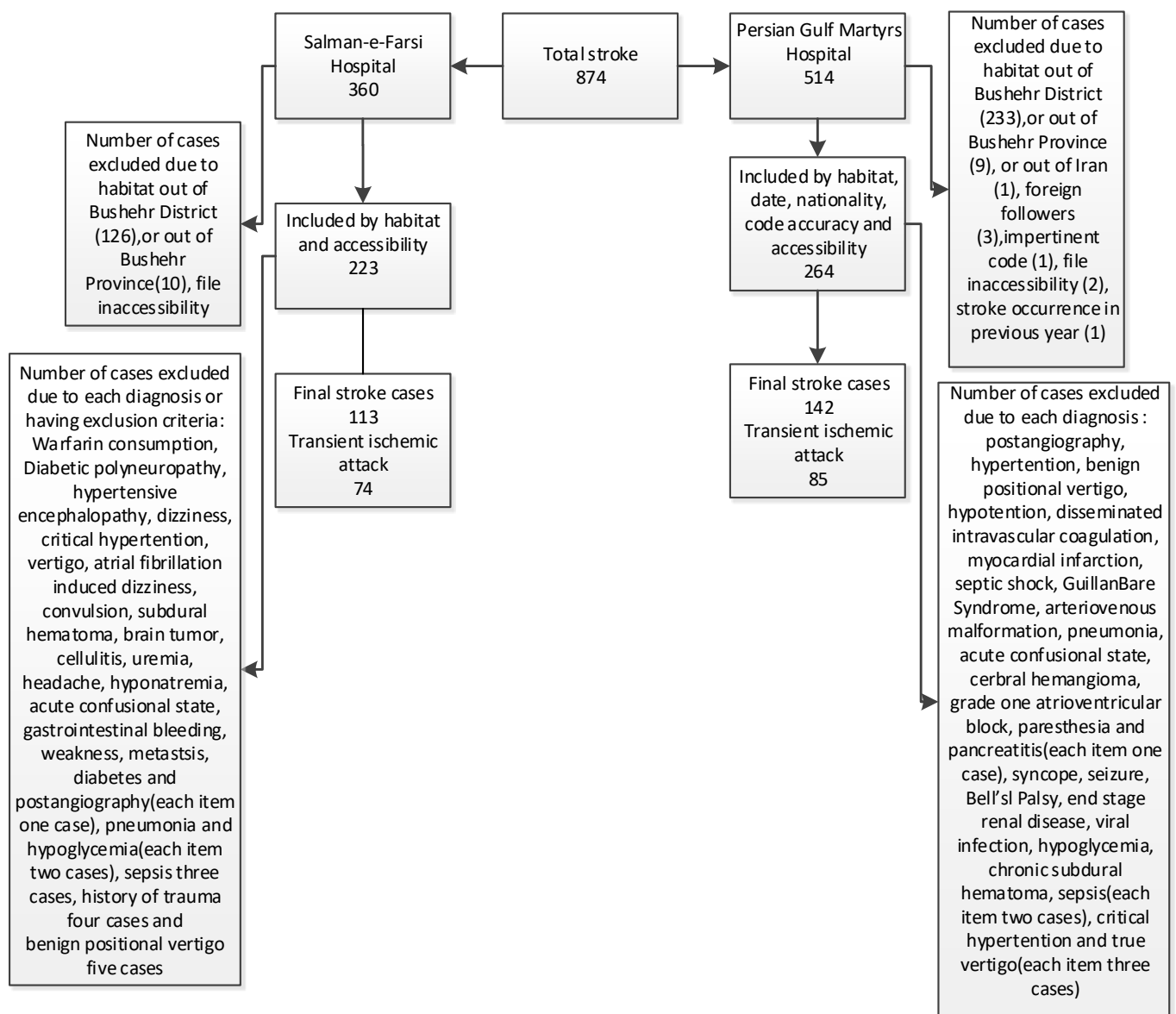


Figure 1. Flowchart of identification of stroke and TIA cases from two Bushehr Hospitals, Bushehr, Iran, 2013-2014

Crude and standardized incidences were 92.71 and 198.3 per 100,000, respectively. When the number of events instead of number of cases was considered as numerator, crude incidence was 99.26 per 100,000 (Table 2). Incidence was higher in men compared to women although it was

not statistically significant ($P=0.19$) (Table 3).

Incidence was the highest in 75-84 year-old age group (2532.1 per 100,000) and the lowest in 15-34 year-old age group (5.65 per 100,000) (Table 4).

Table 1. Baseline characteristics of stroke patients according to the type of stroke in Bushehr, Iran, 2013-2014

Variable		Type of event			
		IS	ICH	SAH	IS and/or ICH
Age (year)	Mean±SD	65.9±14.1	63.5±12.4	52.3±25.3	63.6±16.7
	Min-Max	27-100	37-84	17-76	41-82
Sex		N (%)	N (%)	N (%)	N (%)
	Male	125 (58.1)	15 (48.4)	1 (25)	2 (40)
	Female	90 (41.9)	16 (51.6)	3 (75)	3 (60)
Episode of stroke	Once	155 (72.1)	24 (77.4)	4 (100)	5 (100)
	More than once	60 (27.9)	7 (22.6)	0	0
Place of residence	Urban	179 (83.3)	30 (96.8)	4 (100)	5 (100)
	Rural	36 (16.7)	1 (3.2)	0	0

Table 2. Crude and standardized incidence of stroke (per 100,000 populations per year), in Bushehr, Iran, 2013-2014

	Incidence*	Number	Incidence per 100,000	95%CI
Crude		255 [‡]	92.71	81.69-104.81
		278 [†]	101.08	89.55-113.68
		289 [‡]	105.08	93.31-117.91
		273 [§]	99.26	87.84-111.75
Standardized		255 [‡]	198.3	189.68-207.22

* Population at risk 275039

‡ Number of stroke cases

† Corrected according to confirmed data of death registry of Bushehr Province and verbal autopsy records

‡ Corrected according to unconfirmed data of death registry of Bushehr Province

§ Number of Strokes

Table 3. Sex specific, crude and standardized incidence of stroke (per 100,000 populations per year) in Bushehr, Iran, 2013-2014

Sex	Crude rate	95%CI	<i>P</i>	Standardized rate	95%CI	<i>P</i>
Male	100.09	84.37-117.9		218.7	180.7-256.7	
Female	84.74	69.78- 101.95	0.19	178.1	144.1-212.2	<0.001
Total	92.71	81.69-104.81		198.3	189.68-207.22	

Table 4. Age specific, crude incidence of stroke (per 100,000 populations per year) in Bushehr, Iran, 2013-2014

Age group (year)	Population at risk	No. of cases	Incidence	95% CI
0-14	67539	0	0	0
15-34	123863	7	5.65	2.27-11.64
35-44	38510	12	31.16	16.1-54.43
45-54	23495	39	165.99	118.06-226.85
55-64	13611	60	440.82	336.56-567.06
65-74	4769	57	1195.22	906.47-1545.8
75-84	2646	67	2532.12	1967.62-3204.67
≥85	606	13	2145.21	1147.06-3640.45
Total	275039	255	92.71	81.69-104.81

Discussion

In order to determine epidemiologic status of stroke in Bushehr district, we decided to determine stroke incidence in 2013-2014. The crude and standardized stroke incidence were 92.71 (95% CI=81.69-104.81) and 198.3 (95% CI=189.68-207.22) per 100,000, respectively. In a hospital-based study in Bushehr district in 2003, 59 stroke cases (relevant to 7 months) in the Persian Gulf Hospital and Salman-e-Farsi Hospital were studied. Standardized stroke incidence was 77.31 per 100,000 in men and 116.71 per 100,000 in women. Total standardized stroke incidence was not reported. Leyden et al. found an age standardized stroke incidence rate of 96 per 100,000 in Australia in 2009-2010 (22). In a systematic review on the published studies between 1990-2008 in Iran, Hosseini et al. found a rate of 23-103 per 100,000 (23). On the basis of the study of global burden of diseases 2010, Feigin et al. obtained a rate of 257.96 per 100,000 for the world and 251.9-336.3 per 100,000 in the Middle East (24). In the current study, the age standardized incidence was more than those of Leyden et al. and Hosseini et al. and less than that reported in the study of global burden of diseases 2010. These differences are expectable considering disease epidemiologic transition trend in the developing countries. On the basis of this trend, burden of non-communicable diseases is increasing in these countries. In addition, a comparison with other parts of Iran by Hosseini et al., predicted worst

condition of the standardized stroke incidence in Bushehr (23).

Frequency of imaging among stroke patients was 90-100% in the systematic review by Hosseini et al. (23), 95% in study of Leyden et al. (22), 93.2% for the study of Palm et al. in Germany in 2006-2007 (8), and in a study in China was 85.4% in 1992-2012 (25). Frequency of imaging among our patients (94.9%) was comparable with other studies (8, 22, 23, 25).

The mean age of stroke was obtained to be 69.2 by Kissela et al. in United States in 2005 (26), 71.6 by Palm et al. (8), 75.5 for high income countries and 69.4 for low and middle income countries in global burden of diseases 2010 study (24), 68.33 and 69.6 in two different studies in Iran (27, 28). On the other hand, Safari in Shiraz, Iran, in 2001-2011, found a mean age of 63.4 years (29). In the present study, the mean age (65.32 years) was lower than those of other mentioned studies. The reason may be change in life style and increase in risk factors specially inactivity, overweight, obesity, hypertension, and smoking in lower age in Bushehr district Population.

Frequency of stroke in men was reported 51.1% by Palm et al. (8), and from 43.6-53.6% in different studies in Iran (23, 27-29). In the present study, frequency of stroke in men (56.1%) was more than those of all these studies indicating the possibility of higher frequency of risk factors of stroke in men compared to women in our population.

Frequency of stroke in men was higher than women which is congruent with other studies (8, 29). In other above mentioned studies, in contrast to our study, frequency of stroke in women was higher than in men (23, 27, 28).

Moreover, standardized incidence rate in men was higher than that in women in other studies (6, 8, 22, 31), which is consistent with our results.

The mean age was higher in ischemic stroke compared with other types, which is a normal finding regarding the basic knowledge and pathologic mechanism of different types of stroke. This rate was reported 66.84 and 66.3 in two studies in Iran (27, 29), and 57.1 years by Renjen et al. in India in 2004-2006 (30). The mean age of ischemic stroke (65.9) was higher in our study compared with Indians (30) and approximately similar to two above-mentioned studies in Shiraz. However, this rate for intracranial hemorrhage (63.5) was not congruent with the study in Shiraz (27). The mean age for intracranial hemorrhage was reported 66.22 by Daneshfard et al. (27) and 59 years by Safari et al. (29). The reason can be different frequencies of risk factors such as hypercholesterolemia which is more related to increased risk of ischemic but not hemorrhagic stroke compared to other risk factors.

Age-specific stroke incidence increased with each decade of age conforming with the results of studies of global burden of diseases 2010 and similar studies (6, 8, 24, 31). The only exception to this trend of increment was for age group above 85 years whose age-specific incidence was lower than that of age group 75-84. An explanation for this exception can be missing stroke due to other synchronous diseases as differential diagnosis.

Standardized incidence rate in Palm et al. study was reported to be 125 per 100,000 and 14 per 100,000 for ischemic and hemorrhagic stroke, respectively (8). This rates were 238 per 100,000 for ischemic and 76.5 per 100,000 for hemorrhagic stroke in a study by Li et al. (25).

Standardized incidence of ischemic and hemorrhagic stroke in our study were higher than that of Palm et al. and lower than the rate in the study of Li et al. indicating the embedment of our target population somewhere between developed and developing countries populations regarding burden of stroke and its risk factors. Standardized incidence rate of subarachnoid hemorrhage was four per 100,000 in the study of Palm et al. (8), which was higher than the rate in our study. The reason is not clear.

The highest standardized incidence among different stroke types in these two studies (8, 25) was similar to our results and was related to ischemic stroke.

The main limitation of the present study was inaccessibility to all the incident stroke cases due to hospital-based calculation of incidence. We compared mortality of stroke cases from death registry system of Bushehr Province with the mortality of cases obtained from two hospitals in order to investigate accuracy of data and also correction of incidence. Another limitation was inaccessibility to patients who referred to physician offices, mild cases, probability of referral to other provinces, misdiagnosis due to death before referring to hospital, or presence of other differential diagnosis, which could have led to selection bias, too. Since most of the time stroke presents as an acute illness with prompt start of neurological symptoms, it is unlikely that patients with stroke refer to physician offices, unless in the case of mild cases which may not even refer to physicians and thus it would be impossible to be recognized anyway. Also, it is improbable that stroke patients refer to hospitals in other provinces prior to referring to Bushehr hospitals. In the current study, there is the limitation about random error because of limitation in sample size, influencing accuracy of estimating incidence and width of confidence intervals. Also, there is the possibility of error in measurement of stroke type leading to misclassification of stroke.

Stroke incidence in Bushehr district especially in men is higher compared to other cities in the country. Moreover, stroke occurs in younger ages in Bushehr compared to other populations.

Taking into account epidemiological status of stroke in Bushehr, planning and implementing preventive strategies is so important; these issues should be considered in priority setting in health policy. Although healthcare coverage of different age groups of the community has been considered in inclusive health services centers, persuasion of people for attending health education and consultation in these centers sounds necessary. An additional program for health education of men in their workplaces can be helpful.

Considering the higher incidence of stroke in Bushehr compared to other parts of the country and demographic transition toward population aging, establishing a stroke registry system to make more accurate and reliable data available seems necessary. Furthermore, a stroke medical center is required to prevent secondary complications and better systematic rehabilitation of stroke patients.

The present study was a hospital-based investigation. Carrying out a population-based research would make it more probable to access stroke cases and more accurate rates would be obtained.

Conflict of interest

Authors declare no conflict of interests.

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