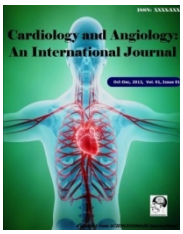

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Cerebrovascular Diseases and Associated Risk Factors in WHO Eastern Mediterranean Countries

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Authors' contributions

This work was carried out in collaboration between all authors. Author AB searched papers by Medline and Science Direct, checked for inclusion-exclusion and wrote the final version, author MD searched French abstracts and wrote the first draft, author WB searched for papers from other sources than Medline Science Direct and checked for overlapping, author MENL checked for inclusion-exclusion, wrote the flow diagram and table with country, date, author. All authors read and approved the final manuscript.

Review Article

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ABSTRACT

Background: In the WHO Eastern Mediterranean region, nearly one million deaths are caused by cardio-vascular diseases every year. During the last decade, the number of deaths caused by stroke increased by 23%. Most cardiovascular diseases can be prevented by addressing behavioural risk factors such as tobacco use, alcohol, unhealthy diet, physical inactivity, and metabolic risk factors like obesity, high blood pressure, diabetes and raised lipids.
Methods: This is a systematic review on cerebrovascular diseases and associated risk factors in WHO Eastern Mediterranean countries. Medline, Science Direct, and other sources were used to get peer reviewed papers dealing with the review theme. The search was limited to publications between 1990 and 2013 (30th June).
Results and Discussion: According to the inclusion criteria, 45 papers were included in the present review. The prevalence was found greater than 50% in 38 studies for hypertension, greater than 25% in 36 studies for diabetes, greater than 15% in 26 studies for smoking and greater than 25% in 19 studies for dyslipidemia. It was also indicated that

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incidence of stroke increases with ageing. The majority of studies found a prevalence of stroke higher in men than in women with a ratio male: female reaching 3.55:1 in one study.

Conclusion: Although at different levels of importance, all the studies reveal that hypertension, diabetes, dyslipidemia and smoking are crucial risk factors for stroke. This review also indicates a lack or scarcity of studies in many countries with an uneven contribution by country since 33% of studies are from Pakistan whereas North Africa (Egypt, Morocco, Libya, Tunisia) contributed with only 2 papers.

Keywords: Stroke; risk factor; hypertension; diabetes; smoking; dyslipidemia; Eastern Mediterranean.

1. BACKGROUND

Once associated with economic development and considered as diseases of the rich, cardio-vascular diseases (CVDs) are now affecting developed and developing countries alike [1,2].

According to the World Health Organisation (WHO) [3], cardiovascular diseases caused 17.3 million deaths (30% of all global deaths) in 2008 and this number is expected to reach 23.3 million by 2030. Over 80% of CVDs deaths occur in low- and middle-income countries with a percentage of premature death (before the age of 60) exceeding 40% in low-income countries, nearly three times the proportion in high-income countries (13%). The WHO statistics indicate that stroke is the second killer in the world with 6.2 million deaths representing 11.4% of the 54.6 deaths that occurred in 2011. A systematic review on worldwide stroke incidence showed a divergent trend in stroke incidence rates during the last four decades. While stroke incidence decreased by 42% in high-income countries, it increased by more than 100% in low to middle income countries [4]. Another review on global variation in stroke burden and mortality indicated raised mean systolic blood pressure and greater prevalence of smoking as predictors of stroke mortality but the national per capita income was the strongest predictor of mortality [5].

Most cardiovascular diseases can be prevented by addressing behavioural risk factors such as tobacco use, alcohol, unhealthy diet, physical inactivity, and metabolic risk factors like obesity, high blood pressure, diabetes and raised lipids. The risk of coronary heart disease and ischaemic stroke increases steadily with overweight/obesity and there is a continuous relationship between blood pressure and the risk of developing heart attacks and stroke [2]. Studies have shown that the risk of CVD doubles for each incremental increase of 20/10 mmHg of blood pressure starting as low as 115/75 mmHg [6]. Alcohol caused about 2.5 million deaths (3.8%) in 2004 with CVDs, liver cirrhosis and cancer responsible for 50% of these deaths. Although tobacco use is a totally avoidable risk factor, smoking is responsible for 10% of CVDs.

Most countries of the WHO Eastern Mediterranean region are engaged in an epidemiological transition, experiencing high rates of non communicable diseases in general and CVDs in particular. In this region, non communicable diseases caused 2.3 million deaths in 2008(53% of the regional annual mortality) of which 55%, 14%, 9% and 5% were due to CVDs, cancer, respiratory diseases and diabetes respectively.

According to the data released by the International Diabetes Federation in 2011, the Middle East and North Africa region has the highest comparative prevalence of diabetes (11%). Six

of the top 10 countries with the highest prevalence of diabetes (in adults aged 20 to 79 years) are in this region: Kuwait (21.1%), Lebanon (20.2%), Qatar (20.2%), Saudi Arabia (20.0), Bahrain (19.9%) and UAE (19.2%) [7,8]. The region is also known to have high rates of overweight/obesity [9-11] and hypertension [11].

The rationale for systematic reviews is based on the need of researchers and health policy makers to get an integrated scientific publication that gathers, compares and analyses the results yielded by a large number of studies in a certain field. Consequently, systematic reviews reduce large quantities of data into one accessible paper, provide information on the consistency of the results given by different studies and indicate if findings are limited to a particular area or can be generalised.

Following a previous review on multi-morbidity of non communicable diseases and equity in WHO Eastern Mediterranean countries [12], this review is dedicated to the association between cerebrovascular diseases and the risk factors (hypertension, diabetes, smoking and dyslipidemia or high cholesterol) in the WHO Eastern Mediterranean region which comprises the following 23 countries: Afghanistan, Bahrain, Cyprus, Djibouti, Egypt, Iran, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, The Occupied Territories (Palestine), Pakistan, Qatar, Saudi Arabia, Somalia, Sudan, Syria, Tunisia, United Arab Emirates (UAE), and Yemen Arab Republic.

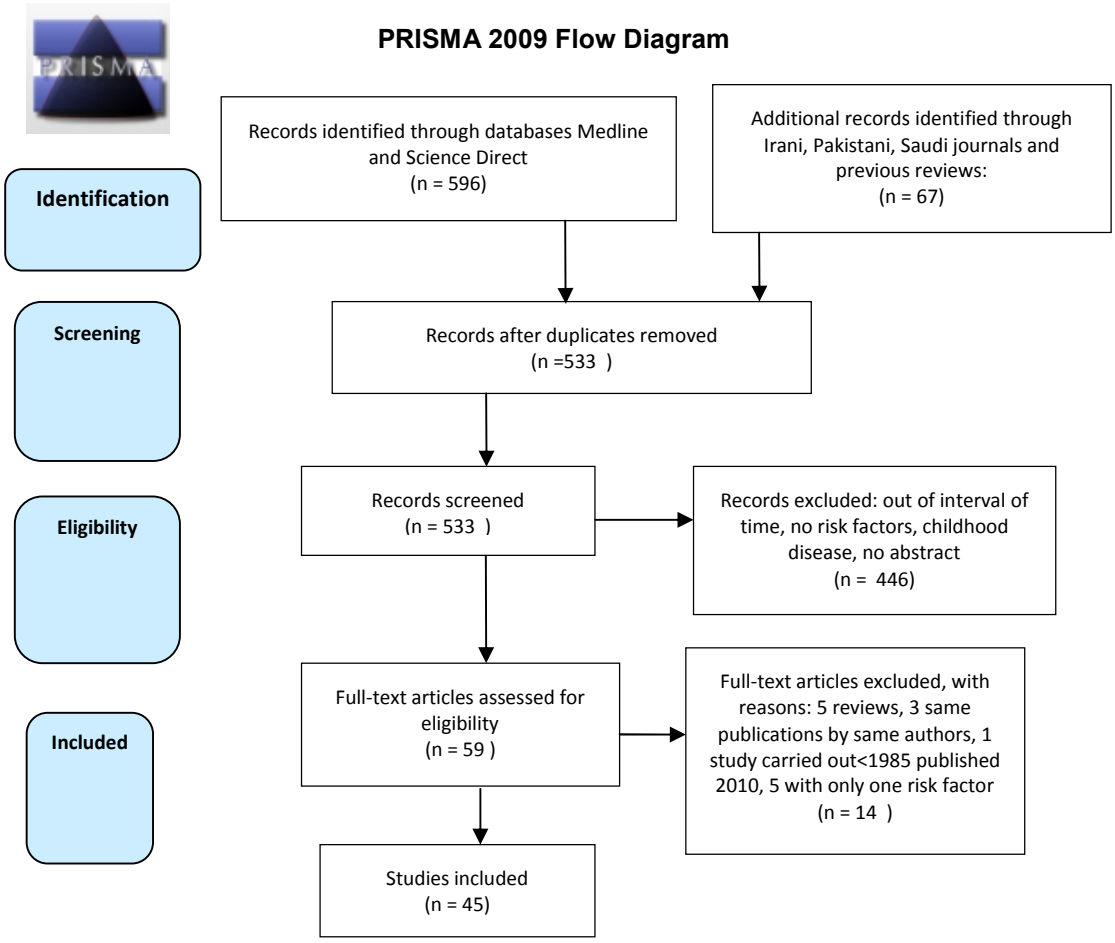
2. METHOD

This is a systematic review on cerebrovascular diseases and known associated risk factors in WHO Eastern Mediterranean countries. Medline/PubMed, scopus/ScienceDirect, and other sources were used to get peer reviewed papers dealing with the review theme.

The words/strings used for search and inclusion criteria were: cerebrovascular disease, stroke, ischemic stroke, haemorrhagic stroke, Arab and name of countries belonging to the WHO Eastern Mediterranean Region. The search was limited to publications between 1990 and 2013(30th September).

For a paper to be included in the review, five criteria were jointly required 1) Stroke, cerebrovascular diseases, 2) WHO Eastern Mediterranean country, 3) Hypertension, diabetes, dyslipidemia and smoking as risk factors (at least 2 risk factors), 4) Availability of abstract in English or French. 5) Childhood disease (age under 20 years) was not considered. When more than a paper was selected with the same authors and the same topic, only one paper was included in the review. Studies carried out before 1985 and published after 1990 [13], and reviews [14-17] were used for reference mining but they were not included.

A total of 596 records were identified through Medline and Science Direct using stroke/ cerebrovascular disease and name of country. The use of WHO Eastern Mediterranean region instead of countries by name gives insignificant information. Sixty seven other records were added through other sources like health journals edited in Iran, Pakistan and Saudi Arabia and previous reviews in Iran, Pakistan, and Arab World. After eliminating duplicated records and excluding 446 (for reasons of time of publication, availability of abstract, less than one risk factor, studies dealing with childhood disease), fifty nine full-text articles were assessed and a final set of 45 studies was included (See flow diagram additional file).



3. RESULTS AND DISCUSSION

According to the inclusion criteria, a total of 45 papers were included in the present review: Bahrain(1), Egypt(1), Jordan(1), Iraq(2), Iran(7), Kuwait(3), Libya(1), Qatar(3), Palestine(2), Pakistan (15), Saudi Arabia(7), Sudan (1), UAE(1) Table1.

Pakistani studies (15) represent one third of the selected studies whereas North Africa (Egypt, Morocco, Libya, Tunisia) contributed with only 2 papers.

First of all, it should be stressed that we must be very careful in comparing between the 45 studies because the populations considered vary from samples of 25 individuals in a study in Saudi Arabia [60] to 1392 individuals in another study in Iran [27]. Secondly, we concentrate on the risk factors most reported by the majority of studies, namely: Hypertension, diabetes, smoking and dyslipidemia (or hypercholesterolemia). Other risks like overweight/obesity, heart disease and physical inactivity were cited in few studies. Thirdly, the two broad categories of stroke (ischemic and hemorrhagic) and their pathological subtypes were considered globally because there was no consistent classification throughout the 45 studies.

Table 1. Mean age, male to female ratio and risk factors associated with stroke in WHO Eastern Mediterranean countries

Country (Author, date of publication)	Size of Sample	Mean Age	Ratio M:F	High blood Pressure (%)	Diabetes (%)	Smoking (%)	Dyslipedimia (%)
1. Bahrain (Al-Jishi et al.2000)[18]	144	60	1.62 :1	52	20	29	29
2. Egypt (Khedr et al.2013)[19]	57	59.1	1.7 :1	66	38.6	NA	NA
3. Jordan (Bahou et al.2004)[21]	200	61.2	1.27 :1	76	44	35	33
4. Iraq (Al-Mahdawi 2005) [20]	100	63.6	2.4 :1	34	28	44	24
5. Iraq (Al-Heeti 2003) [22]	188	NA	NA	76.1	25	47.3	18
6. Iran (Delbari et al.2011)[23]	460	69.6	1 : 1	74.6	55.7	5.4	15.2
7. Iran (Delbari et al.2010) [24]	953	68	1 :1.04	64	36	20	32
8. Iran (Ahangar et al.2005)[25]	250	68	1 :1.09	54	24	26	26
9. Iran (Ghandehari et al.2006) [26]	96	66.8	1: 1.18	60.4	20	14	23
10. Iran (Ghandehari et al.2007) [27]	1392	65.6	1 :1.12	53.2	13.5	15.2	8
11. Iran (Parniya et al.2006)[28]	157	66	1 :1.37	36.6	5.1	9.5	2.5
12. Iran (Fahimfar et al.2012)[29]	69	60	1.46 :1	48.6	22.9	23	42.8
13. Kuwait (Al-Shammri et al. 2003)[30]	62	64.1	1 :1.06	72.5	69.4	1.6	30.6
14. Kuwait (Abdul-Ghaffar et al.1997)[31]	241	NA	NA	53	42	23	61
15. Kuwait (Ashkanani et al. 2013)[32]	*151*	*NA*	*NA*	*68.9*	*56.3*	*NA*	*57*

Table 1 Continued.....

16. Libya (Zunni et al.1995)[33]	921	63	1.2 : 1	51	24.6	33	NA
17. Pakistan (Vohra et al. 2000) [30]	796	56	1.3 :1	50	18	17	NA
18. Pakistan (Ansari et al. 2001) [35]	100	NA	NA	64	29	29	15
19. Pakistan (Basharat et al.2002)[36]	100	NA	NA	61	33	53	32
20. Pakistan (Iqbal et al. 2003) [37]	189	60.8	1.05: 1	82	44	NA	62
21. Pakistan (Syed et al.2003)[38]	596	60.5	1.67 :1	66.2	41.5	NA	22.1
22. Pakistan (Alam et al. 2004) [39]	100	59	1.78: 1	60	28	22	28
23. Pakistan (Khan H et al.2006)[40]	211	58.5	1.48 :1	55.5	32.7	10.9	19.4
24. Pakistan (Hasan S et al. 2007)[41]	90	58.7	1.4 : 1	60	25.5	44.4	18.8
25. Pakistan (Khan SN & Vohra 2007) [42]	281	62	1.05 :1	65.8	41.3	43	25.5
26. Pakistan (Kamal et al.2009)[43]	119	50	1.8 : 1	64	30	21	NA
27. Pakistan (Khan NI et al.2009)[44]	55	41.4	3.55 :1	65	36.3	32	32.7
28. Pakistan (Marwat et al. 2009) [45]	88	65.9	2.38: 1	75	54.5	13.6	13.6
29. Pakistan (Taj et al. 2010) [46]	159	57	1.89 :1	78	40.3	NA	31.5
30. Pakistan (Aquil N et al. 2011) [47]	100	63.5	1.4 :1	85	49	9	22
31. Pakistan (Basharat et al.2012)[48]	281	65	1.3 : 1	86.8	59.8	18.1	59.1
32. Palestine (Sawalha 2008) [49]	153	69	1.2 : 1	66	45.8	19.6	NA

Table 1 Continued…

33. Palestine (Sweileh et al.2008) [50]	186	69	1.04 :1	69.9	45.2	21	NA
34. Qatar (Hamad et al.2001)[51]	217	60	2.6 : 1	63	42	NA	NA
35. Qatar (Deleu et al. 2006) [52]	303	61.2	2.6 : 1	69	51	26	57
36. Qatar (Khan FY et al. 2008)[53]	270	57	2.7 : 1	74.8	58.9	35.9	44.4
37. SA (El Sayed et al. 1999) [54]	329	61.2	1 : 1	24.9	40.4	1.8	NA
38. SA (Yaqub et al.1991)[55]	174	NA	NA	41	25	NA	NA
39. SA (AlRajeh et al. 1993)[56]	500	63.2	2.2 : 1	56	42	6	NA
40. SA (Alrajeh et al.1998)[57]	488	NA	1.4 : 1	38	37	19.3	NA
41. SA (Awada A, et al.1999)[58]	1000	59	2.1 : 1	52	42	10	NA
42. SA (Qari FA. 2000) [59]	71	63	3.4 : 1	61	27	28	4
43. SA (Hatem, 2001) [60]	25	61.2	1.7 : 1	80	72	NA	36
44. Sudan (Sokrab et al.2002)[61]	96	NA	NA	46.9	14.6	NA	NA
45. UAE (McLachlan 2002) [62]	63	NA	NA	75	55	31	53

3.1 Gender

Among the 37 studies indicating the stroke ratio male to female, the majority (29) found stroke to be more prevalent among men than women with ratios varying from 1.3:1 to 2:1 in 14 studies [18,19,29,34,38-41,43,46-48,56,60], from 2:1 to 3:1 in seven studies [21,45,51-53,57,58] and from 3:1 to 3.55:1 in 2 studies [44,59]. As stressed by one of the authors [51], the high male to female ratios found in studies from Qatar (2.6:1, 2.7:1) and from Saudi Arabia (1.7:1,2.1:1,2.2:1,3.4:1) need explanation. Curiously, five of the six studies that found stroke to be slightly more common in women were from Iran (1:1.04, 1:1.09,1:1.18,1:1.12,1:1.37) [24-28]. In contrast, the 13 Pakistani studies for which data was available reported a proportion of men greater than that of women, with ratios varying from 1.05:1 to 3.55:1[34,37-48] and again, no explanation was given for the highest ratio 3.55:1. Studies from Bahrain [18], Egypt [19], Jordan [20], Iraq [21], Libya [33] and Palestine [49] all found men more susceptible to stroke than women with ratios varying from 1.2:1 to 2.4:1. Finally, few studies from different countries indicated an equal prevalence of stroke or a non significant difference between men and women, taking into account that women live longer than men [23-25,30,37,42,50,54].

3.2 Mean Age

The quasi-totality of studies reported that stroke risk increases with aging. Twenty six studies indicated a mean age in the sixth decade [18,20,21,23-30,33,37,38,42,45,47-52,54,57,59,60], eight studies found a mean age between 56 and 59 years [19,34,39-41,46,53,58], and only two studies reported a mean age of 41.4 years [44] and 50 years [43]. Increasing age was generally indicated as a strong determinant of acquiring stroke but many studies stressed the younger mean age compared to developed countries. A study in Saudi Arabia found that 15.9% of patients were younger than 45 years at stroke onset as compared to 3-5% in western epidemiological studies [58]. Similar proportions of patients younger than 45 years were reported in studies from Bahrain (11.8%) [18] and Qatar (18%) [51]. In contrast, studies from Iran [24] and Palestine [50] found that the proportion of younger patients (less than 45 years) with stroke was less than 5% and 1% respectively. As stressed by one of the authors [50], although prevalence of stroke may vary between different ethnic groups of various geographic areas, this sharp variation in neighbouring countries needs explanation.

3.3 Risk Factors

As indicated in the introduction, the general population of the Eastern Mediterranean region is known to suffer from high rates of diabetes and hypertension and the problem is accentuated by the late diagnosis and the high proportions of people who are unaware of their disease. Consequently, one expects a high correlation between stroke and risk factors like diabetes and hypertension. Indeed, although at different levels, all the studies stressed the importance of hypertension and diabetes as risk factors of stroke.

The prevalence of hypertension was equal to or greater than 75% in nine studies [20,22,37,45-48,60,62], between 50% and 75% in 29 studies [18,19,23-27,30-36,38-44,49-53,57-59], between 25% and 50% in six studies [21,28,29,55,56,61] and only one study reported a prevalence of hypertension less than 25% (24.9%) [54].

The burden of stroke can be reduced by acting on hypertension as one of the most modifiable risk factors. Indeed, according to the World Health Organisation, for every 10 people who die of stroke, four could have been saved if their blood pressure had been regulated. In particular, although stroke is uncommon in people under 40 years, high blood pressure is its main cause in this age category [63].

The prevalence of diabetes was less than 25% in nine studies [18,25-29,33,34,61] between 25% and 50% in 27 studies [19-22,24,31,35-44,46,47,49-51,54-59] and equal to or grater than 50% in 9 studies [23,30,32,45,48,52,53,60,62].

Studies have shown that diabetes is a clear risk factor for stroke and that tight control of blood pressure in people with diabetes can reduce the incidence of stroke significantly [64].
Smoking was indicated in 36 studies and varied from 1.6% to 53% with a prevalence greater than 30% in ten studies [20-22,33,36,41,42,44,53,62], between 15% and 30% in 16 studies [18,24,25,27,29,31,34,35,39,43,48-50,52,56,59] and less than 15% in ten studies [23,26,28,30,40,45,47,54,57,58].

While smoking is among the most modifiable risk factors, about 40% of deaths from stroke are linked to smoking in the population of people aged under 65 [63].

Finally, dyslipidemia or hypercholesterolemia was reported in 32 studies and varied from 2.5% to 62%. In six studies [31,32,37,48,52,62], the prevalence was greater than 50% whereas a prevalence between 25% and 50% was indicated in 13 studies [18,20,24,25,29,30,36,39,42,44,46,53,60] and finally, a proportion of patients with dyslipidemia less than 25% was found in 13 studies [21,22,23,26,27,28,35,38,40,41,45, 47,59].

Hypercholesterolemia and dyslipidemia are also risk factors for stroke. However, they are not as well established as risk factors for first or recurrent stroke in contrast to what is seen in cardiac disease [64].

The incidence of stroke has reached an epidemic level in low to middle income countries [4], while it is declining in many developed countries mainly as a result of better control of high blood pressure and reduced levels of smoking [4,63]. The authors of a review devoted to the epidemiology of stroke in the Middle East and North Africa reported an extensive variation of incidence of stroke between different countries. During the period 1980-2007, the age-standardised incidence rate of stroke (per 100000) in Saudi Arabia, Iran, Palestine, Kuwait, Bahrain, Libya and Qatar was 38.5, 61.5, 62.7,92.2,96.2,114.2 and 123.7 respectively [65].

Every year, stroke affects 15 million people worldwide, causes 5.5 million deaths (3 million women and 2.5 million men) and knocks another 5 million people with permanent disability [63].

In the WHO Eastern Mediterranean region, nearly one million deaths are caused by cardio-vascular diseases every year. During the last decade, the number of deaths caused by stroke increased by 23%, jumping from 250558 deaths in 2000 to 308050 deaths in 2011 [63]. Health decision makers should pay a particular attention to the high burden of stroke due to ageing and risk factors like hypertension, diabetes, smoking, dyslipidemia, overweight/ obesity and physical inactivity.

4. CONCLUSION

This systematic review presents 45 studies carried out in 13 different countries of the WHO Eastern Mediterranean region. Although at different levels of importance, all the studies reveal that hypertension, diabetes, smoking and dyslipidemia are crucial risk factors for stroke. The studies also indicate the increase of incidence rates of stroke with ageing, attracting attention of health decision makers in a region where most countries are engaged in a multidimensional transition (economic, demographic, epidemiological and geographical). Like a previous review on multi-morbidity of non communicable diseases in the same region [17], this review shows a lack or scarcity of studies in many countries with uneven contribution by country since 33% of studies are from Pakistan whereas North Africa (Egypt, Libya, Morocco, Tunisia) contributed with only 2 studies.

5. LIMITATION

We tried to use data analysis (for instance Principal Component Analysis) but the large difference between the size of samples (from 25 individuals in one study to 1392 individuals in another study) restricted our comparing possibilities. Different structures of age was another limitation for an advanced analysis of the results provided by the 45 studies.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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