The Global Burden of Haemorrhagic Stroke- a summary of findings from the Global Burden of Diseases, Injuries, and Risk Factors 2010 Study

Rita Krishnamurthi[1], PhD, Andrew Moran[2], MD, MPH, Mohammad H. Forouzanfar[3], Ph.D., Derrick Bennett[4], PhD, George A. Mensah[5], M.D., Carlene Lawes[6], MBChB, PhD, FAFPHM, Suzanne Barker-Collo[7], PhD, Myles Connor[8], MBBCh, FCP(SA), FCNeurol (SA), PhD, FRCP, Gregory Roth[3], M.D.,M.P.H., Ralph Sacco[9], MD, MS, FAHA, FAAN, Majid Ezzati[10], PhD, Mohsen Naghavi[3], M.D., M.P.H., Ph.D., Christopher J.L. Murray[3], M.D., D.Phil., Valery Feigin[1], MD, MSc, PhD, FAAN

[1]National Institute for Stroke and Applied Neurosciences, Faculty of Health and Environmental Studies, AUT University, Private Bag 92006, Auckland, New Zealand

[2]Division of General Medicine, Columbia University Medical Centre, PH 9 East, room 105, 622 West 168th Street, New York, New York, U.S.A

[3]Institute for Health Metrics and Evaluation, University of Washington, Seattle, WA, USA

[4]Clinical Trial Service Unit and Epidemiological Studies Unit, Nuffield Department of Population Health, University of Oxford, Oxford, UK

[5]National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, USA

[6]National Institute for Health Innovation, University of Auckland, Private Bag 92019, Auckland, New Zealand

[7]School of Psychology, The University of Auckland, Auckland, New Zealand

[8]NHS Borders, UK; Division of Clinical Neurosciences, University of Edinburgh, UK; Bute Medical School, University of St Andrews, UK; and School of Public Health, University of the Witwatersrand, South Africa

[9]Miller School of Medicine, University of Miami, Clinical Research Building1120 NW 14th Street, Suite 1352, Miami, FL 33136, USA

[10]MRC-HPA Centre for Environment and Health, Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, Medical Faculty Building, Norfolk Place, London W2 1PG, UK

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Abstract

Background: This report summarizes the findings of the Global Burden of Diseases, Injuries, and Risk Factors (GBD 2010) Study for haemorrhagic stroke (HS).

Methods: Multiple databases were searched for relevant studies published between 1990 and 2010. The GBD 2010 Study provided standardized estimates of the incidence, mortality, mortality-to-incidence ratios (MIR) and disability-adjusted life years (DALYs) lost for HS (including intracerebral haemorrhage and subarachnoid haemorrhage) by age, sex, and income level (high income countries: HIC; low and middle income countries: LMIC) for 21 GBD 2010 regions in 1990, 2005 and 2010.

Results: In 2010, there were 5.3 million cases of HS and over 3.0 million deaths due to HS. There was a 47% increase worldwide in the absolute number of HS cases. The largest proportion of HS incident cases (80%) and deaths (63%) occurred in LMIC countries. There were 62.8 million DALYs lost (86% in LMIC) due to HS. The overall age standardised incidence rate per 100,000 of HS in 2010 was 48.41 (95% CI 45.44-52.13), in HIC and 99.43 (85.37-116.28) in LMIC and 81.52 (72.27-92.82) globally. The age standardised incidence of HS increased by 18.5% worldwide between 1990 and 2010. In HIC, there was a reduction in incidence of HS by 8% (1-15%), mortality by 38% (32-43%), DALYs by 39% (32-44%), and MIR by 27% (19-35%) in the last 2 decades. In LMIC countries, there was a significant increase in the incidence of HS by 22% (5-30%), while there was a significant reduction in mortality rates of 23% (-3 to 36%), DALYs lost of 25% (7-38%), and MIR by 36% (16-49%). There were significant regional difference in incidence rates of HS, with the highest rates in LMIC regions such as sub-Saharan Africa and East Asia, and lowest rates in high income North America and Western Europe.

Conclusion: The worldwide burden of HS has increased over the last 2 decades in terms of absolute numbers of HS incident events. The majority of the burden of HS is borne by LMIC. Rates for HS incidence, mortality, and DALYs lost, as well as MIR decreased in the past 2

decades in HIC, but increased significantly in LMIC countries, particularly in those younger than 75 years old. HS affected people at a younger age in LMIC than in HIC. The lowest incidence and mortality rates in 2010 were in High Income North America, Australasia and Western Europe, while the highest rates were in Central Asia, Southeast Asia and sub-Saharan Africa. These results suggest that reducing the burden of HS is a priority particularly in LMIC. The GBD 2010 findings may be a useful resource for planning strategies to reduce the global burden of HS.

Introduction

Haemorrhagic stroke (HS), including primary intracerebral and subarachnoid haemorrhage, accounts for 10-27% of strokes worldwide,[1] yet because of its high case fatality rate, contributes to a high proportion of stroke deaths, with a 30 day case fatality rate of over 50% for intracerebral haemorrhage and around 45% for subarachnoid haemorrhage.[2] HS has a poor short term and long term prognosis with the risk of death increasing with increasing age.[3] Those who survive 28 days have a 4.5 fold increased risk of death within the first year compared to ischaemic strokes (IS). HS are associated with higher rates of mortality risk and greater stroke severity than IS. [4, 5]

During the past few decades there has been an increase in life expectancy worldwide, along with a shift from death and disability related to communicable diseases and undernutrition to those related to chronic non-communicable conditions such as stroke and heart disease.[6] Industrialisation and urbanisation in developing countries have led to the increased prevalence of adverse dietary risk factors, increased smoking, and harmful use of alcohol.[7] This epidemiologic transition[8] may have contributed to increased disparities in stroke burden between low and middle income countries (LMIC) and high income countries (HIC). Importantly, it has been shown in a recent study that while the secular trends for IS and ischaemic heart disease are similar, they differ from that for HS.[9] An accurate evaluation of stroke burden by its pathological subtypes is essential for planning well informed and targeted prevention and treatment strategies to reduce stroke burden worldwide.

The Global Burden of Diseases, Injuries, and Risk Factors Study 2010 (GBD 2010) was a systematic analysis of the global, comparative magnitude of health loss due to diseases, injuries, and risk factors by age, sex, and country income level in 21 world regions for 1990, 2005 and 2010. [10] The GBD 2010 [11, 12] provided standardized estimates of the incidence, mortality, mortality-to-incidence ratios (MIR), a measure of stroke case fatality, and disability-adjusted life years (DALYs), an measure of population health burden from stroke, for total stroke and the first GBD estimates for IS and HS separately by age, sex, and country income level. [11, 12] The purpose of this report is to summarise the main findings for the burden of HS from the 2010 GBD study. [11]

Methods

Multiple databases (Medline, Embase, Scopus, LILACS, PubMed, Science Direct, Global Health Database, and regional databases) were searched for relevant studies published between 1990 and 2010. Studies were included for data extraction and analysis if they used the WHO definition of stroke, reported methods for ascertaining stroke cases, distinguished between first-ever stroke and recurrent stroke (only incident strokes were included in these analyses), reported an age-specific epidemiologic parameter of interest and the population denominator (i.e. stroke incidence and/or prevalence in 5 or 10-years age bands) with sufficient detail to enable an estimate of age-adjusted parameters. Incidence studies from HIC required complete stroke case ascertainment while less rigorous stroke case ascertainment was allowed for studies from LMIC in which no other relevant data were otherwise available. Pathological types of stroke were analysed only for studies that had computed tomography of the head, magnetic-resonance imaging (MRI) within 2 weeks of stroke onset, or brain autopsy findings available for at least 70% of stroke cases. All age groups were included in the analysis. To estimate the mortality rate, the GBD mortality database and an ensemble cause of death modelling approach (CODEm) were used.[10, 12, 13]. MIR was used as an ecological proxy estimation of stroke case fatality, because incidence and mortality data could not be linked at the level of individual cases. MIR was calculated as

the ratio of the number of deaths to the number of new cases of stroke within a specified period of time. DALYs are used as a summary measure of population health burden, and are the sum of years of life lost (YLL) due to death and years lived with disability (YLD).[14] YLL is the product of the number of deaths at each age by a standard life expectancy at that age according to standard life tables. The reference for life expectancy was made by the least observed mortality rate of each age group among countries in 2010. YLD is the prevalence of the disease multiplied by the disability weight for that disease. The disability weight is calculated on the basis of the level of health loss for the disease and reflects the severity of the disease on a scale from 0 (perfect health) to 1 (equivalent to death).[14] Each DALY is a year of healthy life lost due to disease, impairment or death. Age standardised incidence and mortality rates per 100 000 person-years and estimates of DALYs lost per 100 000 people were calculated with the direct method of standardisation with the WHO standard population as a reference. The GBD 2010 analytical technique DisMod-MR was used to estimate the overall number of incident strokes and the number of HS.[10] As the majority of data were for incidence and 28 days case fatality, DisMod-MR estimated the prevalence of acute stroke (28 days) by taking incidence of stroke, 28 day case fatality plus a high remission to keep duration, by definition, of acute stroke sequelae, under 30 days. Uncertainty of each step was tracked by saving and following one thousand draws of the posterior distribution of results from each step including prevalence, disability weight, reference life expectancy, envelope of all-cause mortality and stroke mortality. Mean and credible interval of the posterior distribution for each outcome measure was calculated using final 1000 draws. The detailed methodology for calculating all these estimates in the GBD 2010 Project has been described elsewhere. [10, 12]

Results

Worldwide, there were 5.3 million cases of HS in 2010 and the largest proportion (80%) of these occurred in LMIC countries, in contrast with IS, of which 63% occurred in LMIC. There were over 3.0 million HS deaths (84% in LMIC), and 62.8 million DALYs lost (86% in LMIC) due to HS).

Table 1. Age-standardised annual incidence and mortality rates (per 100,000 person-years), mortality-incidence ratio (MIR) and DALYs lost for haemorrhagic stroke by age groups in high-income countries, low to middle-income countries and globally in 1990, 2005 and 2010

The overall age standardised incidence rate per 100,000 of HS in 2010 was 48.41 (95% UI 45.44-52.13), in HIC, 99.43 (85.37-116.28) in LMIC, and 81.52 (72.27-92.82) globally (Table 1). There were large variations in age-standardised incidence and mortality rates by 21 GBD regions. The highest incidences of HS in 2010 were in the Central Asia and East Asia regions (101-158 per 100,000) and East and Southern sub-Saharan Africa (73-101 per 100, 000). The lowest HS incidence rates were in high-income North America, Central and Andean Latin America, Western Europe, and Oceania (25-40 per 100,000). At the country level, age standardised incidence of HS was lowest in Qatar (14.55) and highest in China (159.81). The highest mortality rate among the 21 GBD regions was in Southeast Asia, 90.12 (80.42-98.70).The highest mortality rates for males was in Southeast Asia, 104.98 (87.81-121.57) and also highest in Southeast Asia for females, 77.49 (67.99-85.96) (Figure 1). The lowest mortality rate for was on High Income North America for both males, 9.56 (7.13-11.35) and females, 9.14 (7.52-10.35). The age standardised mortality rate per 100,000 person years was lowest in the U.S. at 9.64 and highest in Mongolia at 210.56. DALYs lost due to HS per 100,000 ranged from 178.20 in Switzerland to 4,118.90 in Mongolia.

Figure 1 Age-standardised mortality rates of HS by 21 GBD regions

Between 1990 and 2010 there was in increase in the absolute numbers of incident HS in LMIC of 114%, and a 24% increase in HIC, and a 47% increase globally. The age standardised incidence of HS increased by 18.5% worldwide between 1990 and 2010. However, there were differing trends in stroke burden by country income level over the last two decades (Figure 2). In HIC, incidence of HS reduced by 8% (1-15%), mortality by 38% (32-43%), DALYs by 39% (32-44%), and MIR by 27% (19-35%). In LMIC countries, there was a 22% (5-30%) increase in the incidence of HS by. There was a significant reduction in mortality rates of 23% (-3 to 36%), DALYs lost of 25% (7-38%), and MIR by 36% (16-49%) in LMIC.

Figure 2. Global changes in haemorrhagic stroke burden from 1990 to 2010.

Trends in HS burden for different age groups varied for LMIC and HIC (Figure 3). There was a significant reduction (14.6%, p= 0.046) globally in the incidence of HS in the older age group (≥75 years). However, in LMIC countries, there was a 19% (5-30) increase in the incidence of HS in those younger than 75 years. In particular, in people aged 20-64 years, the incidence HS in LMIC countries increased significantly by 40.8% (p=0.001) compared to a 6.9% increase in the same age group in HIC. The mean age of people for incident HS was 69.1 (0.15) years in HIC compared to 63.8 (0.13) years in LMIC countries. In 2010, the mean age at fatal HS in HIC was 74.8 (0.32) years and was also higher by 6 years than in LMIC at 68.9 (0.31) years. Globally, in 2010, the mean age at HS incidence at 65.1 (0.15) years was 8 years younger compared to mean age at IS at 73.1 (0.10) years, and age at death for HS was 9.5 years younger than for IS deaths.

Figure 3. Change in age-standardised incidence rates of HS by age and income level.

Trends in HS burden varied between the 21 GBD regions. The greatest increases in HS rates between 1990 and 2010 were seen in eastern and central Europe, North and sub-Saharan Africa and the Middle East, whereas significant reductions were noted in North

America, western Europe, and tropical and southern Latin America. MIR for HS was lowest in high-income North America, while Oceania had the highest (0.94-1.27).

Discussion

The GBD 2010 study found that the global burden of HS in terms absolute numbers of incident cases and deaths and DALYs lost in 2010 is substantial, and that the bulk of stroke burden is disproportionately due to HS rather than IS.[11] HS burden is significantly higher in LMIC than in HIC. As shown in the GBD 2010 studies for stroke burden by subtypes,[11] compared to IS, incident HS occurred at a younger age on average, with the mean age of around half of those affected being less than 65 years of age. Age-standardised rates of HS incidence, mortality and DALYs lost have declined in HIC, in both younger and older age groups. In contrast, there was a significant increase in the incidence rates of HS in LMIC, particularly in the younger age groups (20-64 years) in the past 2 decades.

An encouraging finding was the decline in age standardised mortality rates, DALYs lost and MIR for HS in LMIC. This may reflect some changes towards better access to acute treatment and antihypertensive medication within some regions of LMIC.[15, 16] Wide regional differences in stroke burden by subtype have been reported in countries such as China[17], possibly reflecting the effect of socioeconomic and risk factor exposure heterogeneity on HS burden.

A recent meta-analysis found that there was no decrease in intracerebral haemorrhage incidence worldwide between 1980 and 2008 and both incidence and case fatality increased with age, with no decrease in case fatality seen over the study period [18]. Another study however found an increase in HS incidence in people ≥75 years old[19]. Previous studies have also shown that HS occurs at a younger age than IS and the risk of intracerebral haemorrhage in hypertensive people is greater if they are not compliant with antihypertensive medication, or are smokers [20-22] Our results are in line with other studies that have shown that the burden of HS relative to IS has increased in LMIC in many countries with poor access to medical care and hypertension control.[23]

Several factors may bring about the increasing disparities between regions of different income level [6]. Hypertension is the most important risk factor for HS [24, 25], and other important risk factors include smoking, and excessive alcohol intake.[26] The increased prevalence of risk factors such as smoking [27, 28] and harmful use of alcohol [29, 30] are also likely to be major contributors to the disproportionate increase in HS burden in LMIC. The significant disparity of HS burden in LMIC compared with HIC could be also attributed to differences in awareness of stroke risk factors, and low accessibility to diagnostic and therapeutic interventions for the prevention and treatment of HS. [31] An aging population has contributed to increased incidence of both HS and IS. While regional and temporal trends of IS are similar to those of ischemic heart disease, the trends for HS have been very different, suggesting important differences in causal factors in these two stroke subtypes.[9]

GBD 2010 included only studies that had CT of the head and MRI within 2 weeks of stroke onset, as crucial inclusion criteria for confirming the validity of stroke diagnosis; yet, it represents an important limitation for studies from LMICs where access to medical imaging is limited. However, this potential bias was minimised by approximating estimates of HS burden from studies reporting neuroimaging in at least 70% of cases for pathological subtype verification. The analysis of HS burden grouped together data for intracerebral haemorrhage and subarachnoid haemorrhage. The proportion of incident cases and aetiology of the 2 subtypes of HS differs; therefore results need to be interpreted in consideration of this limitation. Sex differences in stroke outcome, by pathological subtypes, are also an important consideration given differences in both incidence and outcomes for males and females.[32] The incidence and prevalence of intracerebral haemorrhage is higher in men while the incidence of subarachnoid haemorrhage is higher in women, and women also have more severe strokes than men. While the current report does not present analyses for sex differences in HS incidence and outcomes, this would be an important consideration for future reports.

The GBD 2010 study provides globally representative and reliable resource for information on stroke burden by pathological subtypes. This valuable resource provides detailed data on stroke burden for each subtype by age and country income level; hence it can be used for the planning of preventive strategies and future healthcare policies.

Contributions

RK wrote the first draft of the report. All members of the writing committee contributed to the critical revision of the manuscript for important intellectual content.

GBD Stroke Expert Writing Group members (alphabetical order)

Suzanne Barker-Collo, Derrick A. Bennett, Myles Connor, Majid Ezzati, Valery L. Feigin, Mohammad H. Forouzanfar, Rita Krishnamurthi, Carlene Lawes, George A. Mensah, Andrew Moran, Christopher J.L. Murray, Mohsen Naghavi, Gregory Roth, Ralph Sacco.

Conflict of interest

All the authors declare that they have no conflict of interest.

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