Journal of the Neurological Sciences 395 (2018) 17–24

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Incident stroke among Ghanaians with hypertension and diabetes: A multicenter, prospective cohort study

Fred S. Sarfo[a,b,*], Linda M. Mobula[c,d], Jacob Plange-Rhule[e], Daniel Ansong[a,b], David Ofori-Adjei[f]

[a] Department of Medicine, Kwame Nkrumah University of Science & Technology, Kumasi, Ghana
[b] Department of Medicine, Komfo Anokye Teaching Hospital, Kumasi, Ghana
[c] Johns Hopkins University School of Medicine, Baltimore, MD, USA
[d] Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD, USA
[e] Ghana College of Physicians and Surgeons, Accra, Ghana
[f] Department of Medicine & Therapeutics, University of Ghana School of Medicine and Dentistry, Accra, Ghana

ARTICLE INFO

Keywords:
Incident stroke
Risk factors
Prospective study
West Africa

ABSTRACT

Background: The burden of stroke among hypertensive and diabetic population in sub-Saharan Africa remains high. We sought to identify the risk factors associated with stroke occurrence in these high-risk population groups.

Methods: A prospective cohort study involving adults with hypertension and or type II diabetes mellitus at 5 public hospitals in Ghana who were stroke-free at enrollment. Patients were followed every 2 months at clinic for 18 months and assessed clinically for first ever stroke by physicians. We calculated crude incidence rates for stroke and assessed the factors associated with stroke occurrence using a multivariate Cox Proportional Hazards regression models.

Results: Of 3220 eligible participants with 3805 person-years of follow-up, there were 54 clinically confirmed new strokes. Incidence rate of stroke was 14.19 events per 1000 person-years [95% CI: 10.77–18.38], with rates among diabetics with hypertension being 16.64 [10.58–25.00], hypertension of 13.77 [9.33–19.64] and diabetes was 9.81 [3.59–21.74]. Two factors independently associated with stroke occurrence were previous cigarette smoking with adjusted HR (95% CI) of 2.59 (1.18–5.67) and physical inactivity, 1.81 (1.06–3.10). In secondary analysis, stage II hypertension compared with optimal BP was associated with aHR of 3.04 (1.00–9.27), $p = .05$ for stroke occurrence.

Conclusion: Incident stroke among Ghanaians with hypertension and diabetes is quite high. Stricter control of blood pressure and engaging in regular physical activities are strongly recommended to reduce the risk of strokes.

1. Introduction

Recent estimates indicate that sub-Saharan Africa (SSA) currently bear a high and rising burden of stroke on the globe [1–7]. Stroke in these regions is characterized by young age of onset, a high propensity of being hemorrhagic, a high mortality, and significant post-stroke complications including depression, cognitive impairment and social stigma [8–19]. Due to the pervasive lack of health personnel and weak health infrastructure to support stroke survivors in these regions, there is a dire need to identify the key risk factors for stroke occurrence to inform interventions aimed at stroke prevention at the population level.

The INTERSTROKE [11] and GBD studies [10] which included African participants provided some insights into the potential risk factors for stroke occurrence in SSA. The Stroke Investigative Research and Educational Networks (SIREN), the largest case-control study on stroke in Africa [12] to date have recently identified and characterized the associations between 11 dominant risk factors of stroke in decreasing order of population attributable risk as hypertension, dyslipidemia, regular meat consumption, elevated waist-to-hip ratio, diabetes mellitus, low consumption of green leafy vegetables, stress, table added salt, cardiac disease, physical inactivity and current cigarette smoking [12]. These cardio-metabolic and lifestyle risk factors associated with stroke occurrence provide a clear evidence of the impact of the epidemiologic transition, driven by rapid urbanization and adoption of

* Corresponding author at: Department of Medicine, Division of Neurology, Kwame Nkrumah University of Science and Technology, Private Mail Bag, Kumasi, Ghana.
E-mail address: stephensarfo78@gmail.com (F.S. Sarfo).

https://doi.org/10.1016/j.jns.2018.09.018
Received 1 August 2018; Received in revised form 6 September 2018; Accepted 12 September 2018
Available online 13 September 2018

westernized lifestyles, on the surge of Cardiovascular Diseases (CVD) among Africans.

Prospective studies aimed at identifying risk factors for stroke occurrence among indigenous Africans are also urgently warranted. While case-control studies can identify risk factors associated with stroke occurrence, causal inferences cannot be drawn. The prospective, community-based Tanzania Stroke Incidence Project (TSIP) study reported a yearly stroke incidence rate of 108.6 per 100,000 in rural Hai and 315.9 per 100,000 in urban Dar-es-Sallam [4]. Among the factors, the TSIP investigators identified as associated with stroke occurrence were previous cardiac event, HIV infection, high ratio of total cholesterol to HDL cholesterol, smoking and hypertension [20]. An emerging view supported by recent secular trends is that the growing burden of stroke in SSA is driven by a neglect in control of vascular risk factors such as hypertension and diabetes at the population level. In this regard, prospective data on stroke risk among high risk population such as those with hypertension and diabetes are needed to elucidate the key contributors to stroke occurrence to fine-tune primary prevention interventions. We therefore sought to evaluate the determinants of stroke among a prospective cohort Ghanaians with hypertension and diabetes mellitus. Participants were recruited as part of a pragmatic clinical trial aimed at improving access to medicines for the control of hypertension and diabetes by offering medications at differential pricing [21].

2. Methods

2.1. Study design and participants

The Ghana Access and Affordability Program (GAAP) pilot study is a prospective cohort study involving adults with hypertension only (HPT), hypertension with diabetes mellitus (HPT + DM) and diabetes mellitus only (DM) at public hospitals in Ghana. Participants were recruited from five study sites including the Agogo Presbyterian Hospital, (APH), Atua Government Hospital, (AGH), Komfo Anokye Teaching Hospital, (KATH), Kings Medical center, (KMC) and the Tamale Teaching Hospital, (TTH). Ethical approval was obtained from all study sites. The study protocol has been published elsewhere [21].

2.2. Evaluation of study participants

Trained research assistants obtained informed consent before participants were enrolled into the study. Demographic information including age, gender, educational attainment, employment status, and lifestyle behaviors such as alcohol use, cigarette smoking, level of physical activities, frequency and daily quantities of fruits and vegetable consumption as well as table added salt were assessed through interviews and responses collected on a questionnaire. A detailed medical history including duration of hypertension or diabetes diagnosis and doses of medications currently being taken were obtained. Anthropometric evaluations including measurement of weight, height and waist circumference were performed by Study nurses. Body mass index (BMI) of each participant was then derived by dividing the weight in kilograms by the square of the height in meters.

2.3. Laboratory measurements

To ensure standardization across all study sites, an International Organization for Standardization (ISO)-certified and quality-assured laboratory was contracted to run all biochemical panels which included serum creatinine, lipid profile and hemoglobin A1C for subjects with diabetes. Samples were transported to the laboratory by trained phlebotomists on the same day of collection often within 4 h or where not feasible (KMC and AGH sites), samples were stored in a freezer before transported to the laboratory the next day.

2.4. Stroke diagnosis

Stroke diagnosis was based on the World Health Organization definition [22], if participant had ever experienced sudden onset of weakness or sensory loss on one side of the body, sudden loss of vision, or sudden loss of speech. These questions were obtained from the 8-item questionnaire for verifying stroke free status (QVSFS) which has been validated locally [23–25]. QVSFS was used as neuro-imaging facilities were not available at any of the study sites at the time of the study. Study participants visited every 2 months for 18 months to assess control of hypertension and diabetes mellitus and to assess for vascular complications including stroke.

Individuals were classified as physically active if they were regularly involved in moderate exercise (walking, cycling, or gardening) or strenuous exercise (jogging, football, and vigorous swimming) for 4 h or more per week. Alcohol use was categorized into current users (users of any form of alcoholic drinks) or never/former drinker while alcohol intake was categorized as low drinkers (1–2 drinks per day for female and 1–3 drinks per day for male) and high drinker ($>$ 2 drinks per day for female and $>$ 3 drinks per day for male. 1 drink or 1 unit of alcohol = 8 g of alcohol) [26]. Smoking status was defined as current smoker (individuals who smoked any tobacco in the past 12 months) or never or former smoker [26]. Vegetable and fruit intake was assessed based on number of daily servings per week. The Ghana Statistical Services defines urban residence as settlements with population $>$ 20,000, peri-urban as settlements with population size between 5000 and 19,999 and rural residence as those with population $<$ 5000.

2.5. Statistical analysis

The main outcome measure was time to onset of new stroke during 18 months of prospective follow-up. Patients with a prior history of stroke before study onset were excluded from the present analyses. For baseline characteristics, means were compared using the Student's *t*-test for 2-group comparisons and proportions were compared using the Chi-squared tests or Fisher's exact test for proportions with subgroupings < 5. Crude incidence rates were calculated and expressed as events/1000-person years of follow-up and 95%CI calculated using the Mid-P exact test. A multivariate Cox Hazards Proportion regression analysis was fitted to identify factors independently associated with the risk of stroke. Patients were censored either at the date of stroke diagnosis, at the last visit for those who were lost-to-follow up, or at July 31, 2017 for the remainder. Independent variables evaluated included the following *socio-demographic factors*: age, gender, location of residence, employment status, *lifestyle/behavioral factors*: included previous cigarette smoking, current alcohol use, physical activity, table added salt, fruit and vegetable intake; *health system factors:* level of healthcare institution (primary, secondary or tertiary), *patho-biologic factors:* central obesity, duration of hypertension or diabetes, number of antihypertensive medications, and baseline systolic and diastolic BP as well as baseline HBA1C. Variable selection was based on clinical and empirical significance of covariates in the model. Variables were included in the multivariate analyses upon meeting a *p*-value cut-off of < 0.05 in bivariate unadjusted regression analysis. In all analyses, two-tailed *p*-values $< .05$ were considered statistically significant. Secondary analyses included the determinants of stroke among participants with any hypertension (HPT or DM/HPT) or diabetes (DM + DM/HPT). Model diagnosis and fit were assessed using residual plots analysis and visual inspection for collinearity of variables in the Cox models. Statistical analysis was performed using Graphpad Prism version 7 and SPSS version 20.