STROKE MORTALITY IN ACCRA: A STUDY OF RISK FACTORS

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SUMMARY

We studied risk factors in consecutive autopsy cases of fatal strokes in persons aged 20 years and above at the Korle Bu Teaching Hospital, Accra. The presence of the following modifiable risk factors was noted: Hypertension, atherosclerosis, diabetes mellitus, cardiac diseases and obesity. Non-modifiable risk factors noted were age and sex. We calculated the age-adjusted proportionate mortality for each sex and assessed sex differences using the χ^2 with Yates correction.

Mortality from stroke rose with age, increasing suddenly after 39 years, peaking at 50-59 years in males and 70-79 years in females, and declining thereafter. There were sex differences in mortality with male proportionate mortality exceeding females up to 39 years after which female proportionate deaths were higher than in males. Haemorrhagic stroke was a more common cause of death than infarctive stroke before 70 years in males and 60 years in females. After these ages, there was a reversion with more deaths from infarction than haemorrhage.

Hypertension was the dominant risk factor of stroke mortality being involved in 77% of all cases. However, cerebral atherosclerosis was the main risk factor for infarctive stroke, but appeared unimportant in cerebral haemorrhage. Other risk factors such as diabetes mellitus, thrombotic phenomena, and pre-existing cardiac disease were present in a minority of cases. Obesity as a risk factor for stroke appeared to be more of a female problem than a male one.

The results of the study are compared with those of studies conducted elsewhere and the role of each risk factor in stroke is discussed.

Keywords: Stroke, cerebral haemorrhage, cerebral infarction, mortality, risk factors, Korle Bu Teaching Hospital, Ghana.

INTRODUCTION

The findings of a large number of prospective, observational studies and intervention studies involving populations from a variety of geographic regions have yielded a number of major determinants or risk factors of stroke. These risk factors are of two types: those that are modifiable and those that are not[1]. Non-modifiable determinants include age, sex, heredity and race. Modifiable risk factors include hypertension, hypercholesterolaemia, cigarette smoking, diabetes mellitus, atherosclerosis, physical inactivity, socio-psychological stress, obesity, and excessive alcohol consumption. Others include cardiovascular diseases such as ischaemic heart diseases, infective endocarditis, atrial fibrillation, peripheral vascular disease and hematological diseases affecting haemostasis.

The incidence and prevalence of stroke increases with age[2,3]. Sex differences also exist in incidence of stroke. Incidence is higher in men than in women[1] but when age-specific incidence rates are examined higher rates are seen in older women than in older men[4,5]. Stroke is more common in individuals with a family history of stroke than those without[1]. Both stroke morbidity and mortality rates are higher in black than in white Americans[6].

Hypertension has long been recognized as the most important risk factor for stroke. Several studies have shown the relationship between high diastolic blood pressure and stroke[7]. Systolic hypertension, irrespective of the levels of diastolic pressure, is a powerful predictor of future strokes[8].

Atherosclerosis, whether intracranial or extracranial, is associated with ischaemic stroke[6,9].

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There is clearly an increased risk of stroke in persons with cardiac disease. The Framingham study has shown a clear association between atrial fibrillation, especially among those with rheumatic heart disease, and increased risk of ischaemic stroke[10]. Stroke is 3 times more likely to develop in a person with coronary heart disease than in a person without that disorder[11]. Stroke is a well-known complication of infective endocarditis[12,13].

Diabetes mellitus accelerates atherosclerosis and would be expected to be an important risk factor in ischaemic stroke. However, there is considerable variation in the incidence of ischaemic stroke among persons with diabetes, depending on the presence of other risk factors. One study of a cohort of diabetics showed that non-hypertensive diabetics had no significant increase in stroke incidence compared with non-diabetics and the increased frequency of stroke in diabetics could be accounted entirely for by the presence of hypertension[14]. Others, however, indicated a positive relationship between stroke and diabetes[15-17]. Obesity is associated with increased risk of stroke development[18].

Although these risk factors may have independent impact on the development of stroke, they interact with each other to impact on stroke development. Thus hypertension is commoner in blacks than whites[5]. Hypertension and diabetes are both risk factors for atherosclerosis. Obesity is associated with both hypertension and diabetes. Hypertension especially isolated systolic hypertension, and atherosclerosis tend to increase with age.

The purpose of this paper is to examine the risk factors in consecutive autopsy cases of fatal stroke seen at the Korle Bu Teaching Hospital. The Department of Pathology serves the city of Accra and has a high autopsy rate with about 3,500 autopsies, including coroner's cases, performed annually.

MATERIALS AND METHODS

Cases Studied

Postmortem records of the Department of Pathology, University of Ghana Medical School and Korle Bu Teaching Hospital in Accra were examined for the five-year period 1994 -1998. The total number of natural or non-traumatic deaths was determined for each year for those 20 years of age and above. Deaths from stroke were determined and recorded according to type as haemorrhagic or infarctive. We noted the presence of the following modifiable risk factors: Hypertension, atherosclerosis, diabetes mellitus, cardiac diseases and obesity. Non-modifiable risk factors noted were age and sex. Other modifiable risk factors such as alcohol intake, smoking, and physical inactivity could not be assessed for lack of information. All cases of unnatural deaths, undetermined causes and deaths of subjects under 20 years of age were excluded.

Statistical Analysis

Ages were grouped into decades starting from 20 years. We calculated the age-adjusted proportionate mortality for each sex. Differences between genders were assessed using the χ^2 with Yates correction. Results were considered as statistically significant at $P<0.05$. The 95% confidence intervals (CI) were calculated using the Confidence Interval Analysis microcomputer program (CIA, available from British Medical Journal, London).

RESULTS

A total of 9,760 deaths of persons aged 20 years and above from natural causes were autopsied during the five year period 1994 to 1998 at the Korle Bu Teaching Hospital mortuary. These comprised 5831 males and 3929 females. During the period, 1,086 cases of stroke, made up of 594 males (10.2% of total male deaths) and 492 females (12.5% of total female deaths), were autopsied at the Hospital mortuary (Table 1).

Table 1 Age and sex distribution

Age Group	Total No. of Autopsies 1994-1998		No. of Stroke Deaths Diagnosed at Autopsy 1994-98		Proportion of Deaths Due to Stroke (%) At Autopsy 1994-98	
	Male	Female	Male	Female	Male	Female
20-29	750	834	28	28	3.73	3.36
30-39	939	750	45	31	4.90	4.13
40-49	1173	588	129	85	11.00	14.46
50-59	1097	579	163	114	14.86	19.69
60-69	984	561	134	109	13.62	19.43
70-79	589	363	60	79	0.19	21.76
80-89	220	185	23	35	0.45	18.92
>90	50	63	5	8	10.00	12.70
Age not Stated	29	6	7	3	-	-
TOTAL	**831**	**3929**	**594**	**492**	**0.19**	**12.52**

The overall difference in mortality between the sexes was statistically significant (χ^2=12.7114, P<0.001, 1df; 95% CI=1.04 - 3.63). The age was stated in 587 of the males with a mean of 54.48 years (SD 14.22) while it was stated in 489 females with a mean of 57.57 years (SD 15.83).

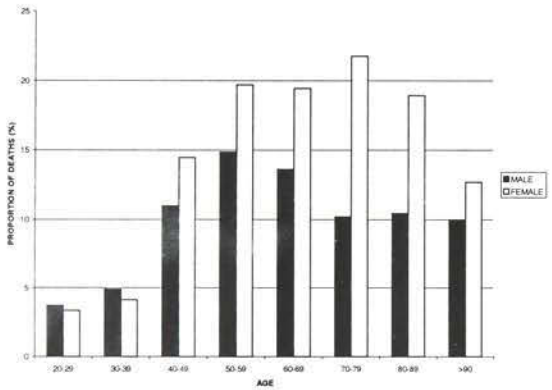

Figure 1 Age-adjusted sex-specific proportional mortality from stroke

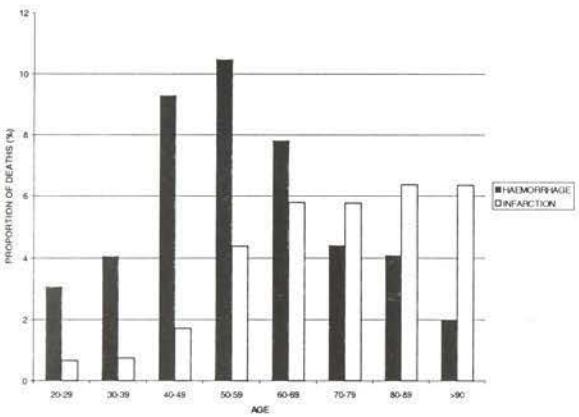

Figure 2 Age-adjusted proportionate mortality and type of stroke in males

Figure 1 shows the age-adjusted sex-specific mortality pattern. Age-adjusted proportional mortality stroke rises suddenly in both sexes after age group 30 to 39. However, male mortality peaks at 50-59 years and falls to a plateau from 70-79 years while female mortality peaks two decades later and declines thereafter. Female mortality is higher than male mortality in all age groups above 40 years. To assess the possibility that a change in the type of stroke might explain these patterns of mortality, strokes were divided into subtypes and tabulated against age groups and sex (Figures 2,3,4). Strokes from haemorrhage were more common than from infarction in males in age groups 20-29 to 60-69. Thereafter, there were more deaths from infarctive compared to haemorrhagic strokes. A similar trend was seen in females but here the change in pattern occurred from the 60 to 69 age group onwards where deaths from infarction exceeded those from haemorrhage. When age-adjusted proportionate mortalities from haemorrhagic stroke in males and females were compared (Figure 4), it was seen that more males died from haemorrhage than females in the first two decade groups and thereafter more females died from haemorrhage than males. This pattern mirrors that of the overall age-adjusted proportional mortality for both sexes (figure 1).

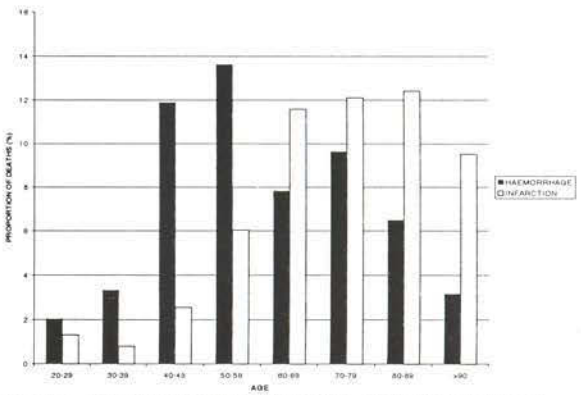

Figure 3 Age-adjusted proportionate mortality and type of stroke in females

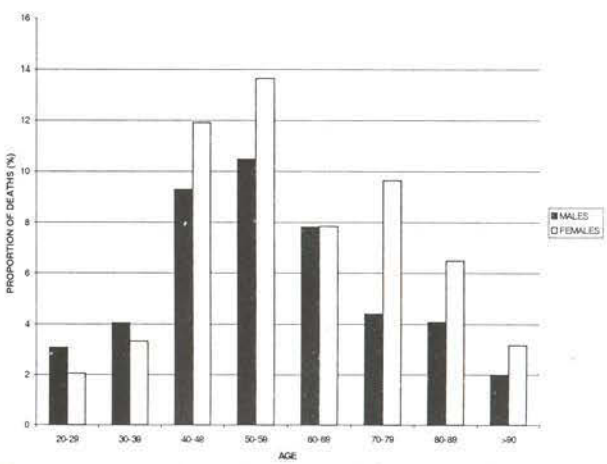

Figure 4 Age-adjusted sex-specific proportionate mortality from haemorrhage stroke

Hypertension was the dominant factor in the development of stroke being involved in 77.3% of cases. It was involved in 619 cases of haemorrhagic stroke, 195 cases of infarctive stroke and 22 of combined haemorrhagic and infarctive strokes (Table 2). One hundred and eighteen of these cases also had cerebral atherosclerosis, 15 chronic renal disease, 9 eclampsia, 6 had diabetes mellitus and 3 also had ruptured berry aneurysms of cerebral vessels. Severe cerebral atherosclerosis was involved

in 59.95% of infarctive strokes. Indeed it was the sole factor in 140 persons dying from infarctive stroke (35.26% of cases) but the sole factor in only one case of haemorrhagic stroke. Six persons had combined hypertension, severe cerebral atherosclerosis and diabetes mellitus while another 6 had atherosclerosis and diabetes. Thus in all there were 18 cases of diabetes (1.7%) with two-thirds dying from infarctive stroke.

Table 2 Risk factors and types of stroke

Causes	Haemorrhage (%)	Infarction (%)	Combined (%)
Hypertension	596 (89.5)	94 (23.7)	22 (95.7)
Hypertension + Diabetes	3 (0.5)	3 (0.8)	0 (0.0)
Hypertension + C. Ather.	20 (3.0)	92 (24.7)	0 (0.0)
Hpt. + C. Ather. + Diabetes	0 (0.0)	6 (1.5)	0 (0.0)
Cerebral Atherosclerosis	1 (0.2)	134 (33.8)	0 (0.0)
C. Ather. + Diabetes	0 (0.0)	6 (1.5)	0 (0.0)
Bacterial Endocarditis	3 (0.5)	6 (1.5)	0 (0.0)
Others	15 (2.3)	23 (5.8)	0 (0.0)
Not Determined	28 (4.2)	33 (8.3)	1 (4.3)
Total	666 (100)	397 (100)	23 (100)

C. Ather. = Cerebral Atherosclerosis
Hpt. = Hypertension

In 21 persons there were thrombotic phenomena in the form of 8 cases of cerebrovascular thrombosis and 13 thrombo-emboli from mural cardiac thrombi (8 from atrial fibrillation and 5 from myocardial infarction). Six and 3 persons respectively developed infarction and haemorrhage as a result of septic emboli from bacterial endocarditis. There was one case of combined aortic stenosis and incompetence causing infarctive stroke. Thus in all there were 18 cases of cardiac disease associated with stroke in this study. No cause could be found for 28 cases of haemorrhagic strokes, which were deemed to be spontaneous haemorrhages, and 33 infarctive strokes.

One hundred and sixteen (23.6%) females were described as obese while only 17 making up 2.9% of males were described as obese. The sex difference was statistically significant (χ^2 = 105.53, 1 d.f.; P<0.001; 95% C.I. = 16.7-24.7).

DISCUSSION

Mortality from stroke and age-sex-specific mortality rate for stroke both increase with age for both sexes in most countries of the world[5]. Proportional hazards analysis in one study indicated that advanced age is a factor significantly related to increased risk of death from stroke[19]. In this study, the mortality from stroke increases with age up to 59 years in males and 79 years in females and then declines. This apparent difference may be due to the fact that this particular study examined only cases seen at autopsy. In Western countries age-sex-specific male mortality is higher than female mortality in all age groups up to 74 years after which female mortality exceeds male mortality but the sex-specific mortality rate for all ages is higher in females[5]. The overall age-adjusted sex-specific proportionate mortality is significantly higher in females than in males in the present report. In a study from Burkina Faso, a neighbouring country, Zabsonre et al found significantly higher stroke mortality in females than in males (P<0.0001)[20]. Matenga reported a higher case-fatality rate in women (40%) compared to men (31%) in Harare[2]. Nonetheless, a study from the United States showed that elderly women (65 years and above) had a better 1-year survival after stroke than elderly males[21] while a Canadian study indicated that males were more likely to die from index stroke than females[19].

The age-adjusted sex-specific mortality pattern in this study showed a higher mortality for males in the first two decades with a higher female mortality thereafter. This is mirrored by the observation that more proportionately males died from haemorrhagic stroke than females in the first two decades while proportionately more females died from cerebral haemorrhage in the older age groups. Case fatality rates for stroke secondary to haemorrhage are substantially greater than those for infarction[22] and thus may explain this trend. However, this may only be in part. A comparison of Figs. 1 and 2 shows that the pattern of the overall age-adjusted male mortality is similar to that of haemorrhagic stroke in males the decline in mortality after age 59 is less steep than the decline in incidence of haemorrhagic stroke. Furthermore, when the pattern of overall age-adjusted proportionate female mortality (Fig. 1) is compared with that of the type of stroke (Fig. 3), the incidence of haemorrhagic stroke is higher in age group 50-59 than in age group 70-79 where mortality peaks. Indeed more infarctive strokes occur after 59 years than haemorrhagic. These suggest that other factors, such as site and size of the lesions, may play a role in mortality.

The results of this study confirm the statement that hypertension is the most powerful risk factor in the development of stroke[23] and are comparable to other studies in black Africans[24]. The effect of hypertension is not simply an increased risk of stroke over a certain level of blood pressure but an in-

creasing risk from the lowest to the highest levels of blood pressure[25]. The combined results of 7 prospective observational studies have shown no evidence of any "threshold" below which lower levels of diastolic blood pressure were not associated with lower risks of stroke[26-7]. There was an approximately 'log-linear' relationship between the risk of stroke and blood pressure suggesting that the proportional difference in stroke risk associated with a given difference in blood pressure is similar at all levels of blood pressure studied. Thus the usual diastolic blood pressure was strongly and positively related to risk not only among those who might be considered "hypertensive" but also among those who would usually be considered "normotensive"[26-7]. Prolonged differences in usual diastolic blood pressure of 5, 7.5 and 10 mm Hg were estimated to be associated with 34%, 46% and 56% difference in risk of stroke respectively[11].

Although systolic and diastolic blood pressures are usually closely correlated, the risk of stroke is at least as high in systolic hypertension as in diastolic and the effect of systolic hypertension occurs in the absence of diastolic hypertension[26-7]. Epidemiological studies show that isolated systolic hypertension increases risk of stroke by at least three times[27,26].

Twenty-two out of 23 persons who had both cerebral infarction and haemorrhage were hypertensive. In the Harare study all 4 patients who had combined lesions were hypertensive[2]. About 24% of cerebral infarctions were due solely to hypertension. These probably resulted from thrombotic arterial occlusion due to arterionecrosis induced by hypertension.

From this study atherosclerosis appears to exert its influence in stroke by causing cerebral infarction rather than haemorrhage. In a prospective study Reed et al found that autopsy-verified cerebral infarction was strongly associated with increasing severity of atherosclerosis involving the circle of Willis and its branches[28,27]. Large cerebral infarctions (such as might result in death) have been shown to be caused by atherosclerosis with or without thrombosis in the proximal circumflex (cortical) cerebral arteries[29,28]. Out of the 141 persons who had cerebral atherosclerosis only 1 had haemorrhage while out of the 118 who had hypertension and cerebral atherosclerosis 98 had infarction and 20 had haemorrhage. These findings are in agreement with a similar study from this hospital, which showed that severe cerebral atherosclerosis is less involved in the pathogenesis of cerebral haemorrhage in Ghanaians[30].

Diabetes is positively related to stroke incidence and has a similar effect on stroke mortality[15]. It is a major risk factor for infarctive stroke[16,17] Fifteen of the 18 diabetics (83%) in this study had infarctive stroke while the remaining 3, who also had hypertension, died from cerebral haemorrhage. The proportion of diabetic cases seen in this study (1.7%) is less than the 3 out of 93 stroke cases (3.25%) seen by Matenga et al in the black population in Harare, Zimbabwe[24]. This may be because this study looked at stroke mortality only while the Harare study examined incidence with mortality. The mechanism of stroke production in diabetics may be due to cerebrovascular atherosclerosis, cardiac embolism or rheologic abnormalities[16]. The results in this study show that in 6 cases there was a combination of hypertension and diabetes with 3 haemorrhagic strokes, most probably the effect of the hypertension, and 3 infarctive strokes, most likely due to rheologic abnormalities in the brain. The remaining 12 cases had atherosclerosis as well as diabetes and suffered infarctive strokes. No cardiac embolism was seen in any of the diabetics.

Data from the Framingham Study show a clear association between atrial fibrillation and increased risk of cerebral infarction[31,30]. Unpublished data quoted by Whisnant indicate that the relative risk of stroke for a person with coronary heart disease is 3, for persons with atrial fibrillation is 6, for those with congestive cardiac failure is 5 while those with valvular disease have a relative risk of 2[11]. In patients with endocarditis, two-thirds of emboli involve the brain[12] resulting in cerebrovascular accident (CVA) with or without haemorrhage. Of these neurologic complications of endocarditis, embolic CVA without haemorrhage is the most common, affecting 42% of patients in one series[13]. The proportion of cases due to atrial fibrillation, myocardial infarction and endocarditis in this study is small (5.5% of all cases of infarction) compared to 12 cardiac source of embolism out of 62 cases of cerebral infarction seen by Matenga in Harare[24].

Obesity increases the risk of stroke in both sexes[18] and appears to be more predictive of cerebral infarction than haemorrhage[32,31]. When the relation between lifelong maximum reported body mass index and stroke was examined in a study, the risk for stroke appeared to be established early suggest-

ing that avoiding overweight and obesity during adult life would offer protection against stroke[33,32]. Significantly more females were described as obese than males in this study. This suggests that, at least, the risk of stroke due to obesity is more of a Ghanaian female than male problem, which is in agreement with the observation in black American women[34,33].

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