ORIGINAL ARTICLE

Predictors of Short-term Intra-Hospital Case Fatality Following First-ever Acute Ischaemic Stroke in Nigerians

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ABSTRACT

Objective: To determine the predictors of 30-day intra-hospital case fatality rate in patients with first-ever acute ischaemic stroke, attending a tertiary care hospital in Western Nigeria.

Study Design: A cross-sectional observational study.

Place and Duration of Study: This study was conducted at the Lagos University Teaching Hospital, Lagos, Nigeria between February 2003 and May 2004 (16 months).

Methodology: One hundred consecutively consenting patients admitted within 72 hours of onset of first-ever acute ischaemic stroke were studied. Uniform information was obtained using a standard format documenting demographic information, stroke-related symptoms and signs, risk factor profile, admission Glasgow Coma Score (GCS), stroke severity, admission Random Blood Glucose (RBG) and presence of complications. All patients were closely followed-up to monitor progress and document any complications. The end point was mortality or survival at 30 days from stroke onset.

Results: The 30-day case fatality rate was 28%. In univariate analysis, the factors predicting mortality were admission stroke severity, admission hyperglycaemia, admission level of consciousness, and presence of any complication during the hospitalization period. Of these factors, presence of complications had the strongest correlation with 30-day case fatality ($r = 0.52$; $p = 0.001$).

Conclusion: Presence of complications was the most important predictor of short-term mortality in Nigerians with first-ever acute ischaemic stroke. Prevention, early detection, and aggressive intervention to treat complications may reduce the unacceptably high mortality rate of ischaemic stroke in our environment.

Key words: *Ischaemic stroke. Predictors. Mortality. Nigerians. Complications.*

INTRODUCTION

Stroke is an important health problem in both developed and developing countries. It is the second leading cause of death worldwide, and this situation is projected to persist over the next two decades.[1-3] The World Health Organization (WHO) estimates that by 2030, 80% of strokes will occur in people living in low and middle-income countries, and stroke will account for 7.9% of all mortality in low-income countries, coming a close third after ischaemic heart disease and HIV/AIDS.[1,2] A recent community-based survey in Nigeria showed that the crude prevalence of stroke is 1.14/1,000 while hospital-based studies provide data indicating that it may account for upto 45% of neurological admissions and 5-17% of medical deaths,[4,5] with about 2 out of every 5 cases dying within 30 days of onset.[6] The factors that determine outcome following stroke include the stroke subtype, patient characteristics (age, gender), disease severity, physiological parameters (admission blood pressure, blood glucose, level of consciousness), and presence of complications.[7-9] Stroke outcome has also been shown to be better in cases managed in stroke units.

In order to improve stroke outcome, it is important to identify factors that predict poor outcome as a first step to applying interventions aimed at modifying or forestalling such factors. This is even more important in developing countries where management of the condition is still largely conservative and in general wards. Although, the case fatality rate of stroke is high in Nigeria, data on the predictors of this high fatality is sparse. This study aimed at determining the 30-day case fatality rate and its predictors in adult Nigerians, admitted to a tertiary health facility, for first-ever acute ischaemic stroke.

METHODOLOGY

The study was conducted over a period of 16 months from February 2003 to May 2004 at the Lagos University Teaching Hospital, a tertiary-care centre in the cosmopolitan city of Lagos in Western Nigeria. The research protocol was approved by the Research and

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Ethics Committee of the Hospital. Informed consent was obtained from each patient or a proxy (for patients unable to give consent).

Stroke was clinically defined according to the WHO definition as 'a focal (or global) neurological impairment of sudden onset, lasting more than 24 hours (or leading to death), and of presumed vascular origin.[10] The inclusion criteria were as follows: (i) first-ever stroke (based on historical account from the patient or relatives), (ii) presentation within 72 hours of symptom onset, (iii) ischaemic stroke confirmed by brain Computerized Tomographic (CT) scan (where available) or combined satisfaction of the WHO and Siriraj Stroke Score criteria for cerebral infarction in those who could not afford the cost of a CT scan.[11]

Demographic characteristics, temporal profile, symptoms at stroke onset, and history of risk factors were documented in a standardized format. Physical examination was conducted to document the baseline vital signs, level of consciousness on the Glasgow Coma Scale (GCS), neurological deficit, cardiovascular status, and presence of complications. Stroke severity on admission was assessed using the National Institute of Health Stroke Scale (NIHSS) and a score >13 was defined as severe stroke.[12] Random Blood Glucose (RBG) was measured on admission using the glucose oxidase method and hyperglycaemia was defined as RBG >140 mg/dl (7.8 mmol/L).[13] Ancillary investigations including electrocardiography, serum electrolytes, blood urea nitrogen, creatinine, and haematological parameters were routinely obtained.

All the patients were managed conservatively using the neurology unit's protocol adopted from existing international guidelines for management of acute ischaemic stroke.[14,15] Periodic reassessments were conducted to evaluate clinical status, document progress and monitor for development of complications. The primary outcome of interest was survival or death at 30 days after stroke onset. Those who were well before 30 days were discharged and re-evaluated in the Neurology outpatient clinic by the 30th day post-ictus.

Data analysis was done using the Statistical Package for the Social Sciences version 11.0® (SPSS Inc.). The Case Fatality Rate (CFR) at 30 days, means with standard deviations and medians were determined as appropriate for the relevant variables. Case fatality rate at 30 days was determined from the number of deaths recorded divided by the total number of patients studied. The significance of any inter-group difference in mean values was tested using Analysis of Variance (ANOVA). Chi-square test (with Yate's correction where necessary) was used for comparison of categorical variables while Pearson's correlation coefficients were determined for the potential predictors of 30-day CFR. A p-value < 0.05 was accepted as an indicator of statistical significance.

RESULTS

A total of 100 patients comprising 53 men (53%) and 47 women (47%) were studied. Their ages ranged from 16-96 years. Mean age was 58.6±14.1 years overall, and did not differ significantly by gender (p=0.09). The baseline demographic and clinical characteristics are shown in Table I. There was a history of hypertension in 71 (71%), Diabetes mellitus in 23 (23%), and cigarette smoking within the 12 months preceding the stroke in 13 (13%). All the cigarette smokers were male, and this was the only baseline characteristic with a significant gender difference (p < 0.001). The mean admission systolic blood pressure (BP) was 163.7±31.9 mmHg overall with a median of 165 mmHg, median admission NIHSS score 11, and median Glasgow Coma Score 13.5. Admission hyperglycaemia was present in 34 (34%) cases.

In the course of hospitalization, 44 (44%) of the patients developed at least one complication. The complications were characterized by aetiology into infectious and non-infectious complications as shown in Table II. Overall, infectious complications comprised 21/44 (i.e. 47.7%) while 23/44 (52.3%) had non-infectious complications. Of the non-infectious complications, aspiration pneumonitis accounted for 11/44 (25%), deep vein thrombosis and pulmonary embolism 5 (11.4%), heart failure 4 (9.1%), and raised intracranial pressure 3 (6.8%).

Twenty-eight out of the 100 patients studied died within 30 days of stroke onset giving a 30-day case fatality rate (CFR) of 28%. The CFR was 13/47 (27.7%) in women and 15/53 (28.3%) in men (p=0.94). The CFR in relation

Table I: Demographic and clinical characteristics of all stroke patients on admission.

Characteristic	Overall	Male (n=53)	Female (n=47)	p-value
Age range, years	16 - 96	16 - 81	37 - 96	-
Mean age ± SD, years	58.6±14.1	55.9±14.0	61.5±13.8	0.09
Median systolic BP, mmHg	165	170	160	0.63
Median Glasgow coma score	13.5	13	14	0.83
Median admission NIHSS score	11	10	11	0.80
Admission hyperglycaemia *	34	19	15	0.84
History of hypertension	71	39	32	0.70
History of diabetes mellitus	23	10	13	0.42
Cigarette smoking	13	13	0	0.0008

** Random blood glucose on admission ≥ 140 mg/dL (7.8 mmol/L)*

Table II: Frequency and aetiology of complications.

Complication	Total number (n=44)	Frequency (%)
Infectious	21	47.7
Urinary tract infection	12	27.3
Septicaemia	5	11.4
Pyomyositis/abscess	2	4.6
Pneumonia	2	4.6
Non-infectious	23	52.3
Aspiration pneumonitis	11	25.0
Heart failure	4	9.1
Raised intracranial pressure	3	6.8
DVT/Pulmonary embolism	5	11.4

DVT= Deep venous thrombosis

to patient characteristics is shown in Table III. It was significantly higher in patients with admission NIHSS scores > 13 (p=0.02) and complications (p < 0.001). The CFR in relation to the major complications were 72.7%, 60% and 16.7% for aspiration pneumonitis, septicaemia and urinary tract infection respectively.

Pearson's correlation coefficient was determined for potential predictors of 30-day CFR. The strongest correlate of 30-day CFR was the presence of complications (r=0.52; p < 0.001), followed by admission NIHSS score (r=0.34; p=0.001), admission blood glucose (r=0.22; p=0.03), and admission Glasgow Coma Score (r=-0.21; p=0.04).

Table III: Case fatality rates categorized according to clinical and demographic characteristics.

Variable	Alive	Dead	p-value
Mean age ± SD (years)	57.2 ± 14.1	62.2 ± 13.8	0.17
Gender			
Male (n=53)	38 (71.7%)	15 (28.3%)	
Female (n=47)	34 (72.3%)	13 (27.7%)	0.94
NIHSS score			
< 13 (n=65)	52 (80.0%)	13 (20.0%)	
> 13 (n=35)	20 (57.1%)	15 (42. 9%)	0.015
Glasgow coma score			
< 8 (n=2)	0 (0.0)	2 (100%)	
≥ 8 (n=98)	72 (73.5%)	26 (26.5%)	0.08*
Mean ± SD admission SBP (mmHg)	164.7 ± 30.0	161.2 ± 36.8	0.66
Admission RBG (mg/dL)			
< 140 (n=66)	52 (78.8%)	14 (21.2%)	
≥ 140 (n=34)	20 (58.8%)	14 (41.2%)	0.035
History of diabetes mellitus			
Present (n=23)	17 (73.9%)	6 (26.1%)	
Absent (n=77)	55 (71.4%)	22 (28.6%)	0.81
Complications			
Present (n=44)	20 (45.5%)	24 (54.5%)	
Absent (n=56)	52 (92.9%)	4 (7.1%)	0.00

*Note: *Fisher's exact test, SBP= systolic blood pressure, RBG- Random blood glucose*

DISCUSSION

Identification of predictors of case fatality, following acute ischaemic stroke, is important as it provides a basis for planning management protocols aimed at prevention, early intervention, and treatment of such factors in order to improve survival. This observational study is thus relevant in this regard, as it is one of the few studies in this population to prospectively assess factors that predict 30-day case fatality rate following first-ever acute ischaemic stroke. The 30-day case fatality rate of 28% in this study is lower than the 40% reported by Ogun *et al.* in a retrospective study in a similar tertiary hospital also in South-Western Nigeria.[6] This may, however, be attributed to the fact that the rates reported in that study represented both ischaemic and haemorrhagic strokes (the latter often having higher mortality), whereas this study included only ischaemic strokes. This CFR is comparable to rates reported from South Africa and India,[16,17] but higher than those reported from developed countries.[18] The higher CFR in developing countries has been attributed to a high complication rates because admission to the hospital often depends on stroke severity with a bias towards admitting the more severe and complicated cases.[19] Also, interventional strategies and treatment facilities are lacking in many developing countries like ours.

Presence of complications was documented in 44% cases and had the strongest correlation with 30-day CFR. This complication rate is comparable to the 43.1% reported from a retrospective study in the North-Western region of Nigeria in which it was also found that presence of complications was a strong predictor of 30-day case fatality.[20] Aspiration pneumonitis was found in 25% of these cases and it had the highest CFR of about 73%. The high rate of aspiration pneumonitis could possibly be as a result of feeding of these patients before they were brought to the hospital as it has been established that swallowing could be compromised in up to 45% of cases of acute stroke thus heightening the possibility of aspiration. In a study by Johnston *et al.*, it was found that complications are common after ischaemic stroke and that deaths attributable to complications have a bimodal peak with most of the deaths from the second week upwards being from medical complications.[9]

Other factors identified as being contributory to 30-day CFR in this study include severe stroke (defined by an NIHSS score >13), depressed level of consciousness (GCS <8), and admission hyperglycaemia. The positive correlation between stroke severity and mortality is in agreement with the finding of Heuschmann *et al.* in a study of predictors of in-hospital mortality in a multicentre study in Germany.[21] It is also consistent with the finding of Szczudlik *et al.* who demonstrated that severe neurological deficit at admission is associated with increased 30-day mortality.[22] This relationship is possibly as a result of the volume of infarct and the fact that complications are more likely to develop in those with severe stroke because of immobility.

The finding that admission hyperglycaemia is a predictor of mortality is not novel as some other studies have already established.[14,23] Admission hyperglycaemia leads to anaerobic glycolysis in the ischaemic penumbra with release of lactic acid and free radicals, subsequent direct membrane lipid peroxidation and cell lysis,[24] leading to extension of the area of infarction and worsening of the neurological deficit with high chances of developing complications.

While impairment of consciousness could be an accompaniment of stroke itself, it could also be a manifestation of complication especially raised intracranial pressure and it is not a surprise that Glasgow Coma Score had a significant negative correlation with 30-day case fatality. It is known that those who are conscious on admission have a better

outcome compared to unconscious patients and in those who are unconscious, the deeper the level of unconsciousness, the worse the outcome.[7]

The main strengths of this study lie in its prospective nature and the fact that studies on predictors of outcome in stroke in Nigeria are sparse although we appreciate that the study was limited by sample size, which is likely to have increased the possibility of type 2 error. Nonetheless, we believe that the objectives of the study were largely achieved.

The findings of this study have added to the body of existing information on predictors of outcome in acute ischaemic stroke especially in this part of the world, where stroke management is still largely conservative and will go a long way in guiding everybody involved in the management of stroke in the country on the acute and continued management of the disease.

CONCLUSION

The findings of high 30-day CFR and that presence of complications emerged as a strong predictor of this high CFR will assist in guiding healthcare providers in the country. It is, therefore, recommended that no effort should be spared in preventing complications from developing; however, if they develop, they should be managed aggressively in order to improve survival.

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