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Research Article

Multilevel Modelling of The Predictors of Post-Stroke Depression in South-West Nigeria

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ABSTRACT

Recent decline in stroke mortality engendered by improved treatment has led to an increase in post-stroke morbidity and related healthcare cost. Most of post-stroke morbidity is due to depression. Few studies have examined the association of contextual factors with post-stroke depression (PSD) using a multilevel framework. This study used multilevel modelling to examine both individual and contextual predictors of PSD in southwest, Nigeria. The study used secondary data from a comparative cross-sectional study of one hundred and thirty (130) stroke survivors. Participants were consenting adult (aged ≥ 18 years) residing in southwest Nigeria who have survived stroke in the last 3 to 24 months preceding the time of the study. Data were preliminarily analyzed using descriptive statistics including percentages and frequency tables. Bivariate association tests were carried out using Chi-square test. Multivariate analyses were performed using multilevel logit modeling and results were presented as odds ratio and their 95% Confidence Intervals (95% CI). All analyses were performed at 5% significance level. The mean (\pm standard deviation) age of participants was 59.54 ± 11.08 and most participants (53.6%) were female. Exactly half of the participants were retirees while most of them were currently married (82.3%), resided in urban (76.7%), and never used alcohol (73.8%). Prevalence of PSD in this study was 41.5%. Post-stroke depression was more likely among younger stroke survivors (OR=1.47; 95% CI: 1.16, 1.85), female (OR=1.37; 95% CI: 1.16, 1.60), alcohol users (OR=1.21; 95% CI: 1.04, 1.47), and the retired (OR=1.23; 95% CI: 1.04, 1.45). PSD was significantly associated with history of stressful life events and all depressed stroke survivors had considered suicide. Post stroke depression was common in younger survivors. Female survivors and alcohol users were more depressed. History of stressful life event is predictive of post stroke depression in this sample. Interventions focusing on women, alcohol users and people with history of stressful life events that had survived a stroke may reduce the burden of post stroke depression and possibilities of suicide.

Keywords: *Post-stroke depression, Stroke survivors, stressful life events, Multi-level analysis*

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INTRODUCTION

Stroke is the leading cause of severe physical disability in the elderly, the second most common cause of dementia and the third most common cause of mortality after cardiovascular disease and cancer in industrialized countries (Titianova, Velcheva, & Stamenov, 2010). However, current global trends of population ageing and decline in stroke mortality result in increased incidence of post-stroke cognitive impairment, depression and anxiety, thus significantly increasing health care expenditure. This has resulted in increasing numbers of survivors left with physical and mental impairment as well as

depressive mood (Ojagbemi, Owolabi, Atalabi, & Baiyewu, 2013).

Post-stroke Depression (PSD) is described as a depressed mood or loss of pleasure or interest in activities which developed after stroke (APA, 1994). Post-stroke Depression may interfere with the ability of patients to effectively self-manage stroke risk factors contributing to recurrent stroke and increased stroke burden. Well established correlations have been made between PSD and increased stroke mortality (Bartoli *et al.*, 2013), decreased activity, recurrent stroke, and decreased quality of life with no apparent non-vascular cause (Yarbrough, 2016).

Generally, prevalence of PSD has been estimated to be 30% globally (Ayerbe *et al.*, 2011) and ranged between 9% to as much as 60% as reported in different studies (Qamar, 2012). Stroke Association has reported that at least one of every three (33.3%) stroke survivor has depression (Stroke Association, 2012). In Nigeria, however, prevalence of PSD ranges between 25% to 45% (Aiyejusunle *et al.*, 2009; Oladiji *et al.*, 2009; Ojagbemi *et al.*, 2013). Studies have shown that there is a significant human and financial costs associated with PSD among stroke survivors (Perry & Strine, 2005).

Early studies found PSD to be associated with a number of stroke related factors including location of stroke and focal disturbance of neurotransmitter pathways (Robinson, Shoemaker, Schlumpf, Valk, & Bloom, 1975) as well as patient related factors including sex, age, personality, quality of life, coping abilities, enhanced disability and poor rehabilitation outcomes, higher rate of mortality, extended use of healthcare, suicidal ideation and social support provided are also associated with post-stroke depression (Qamar, 2012).

In Nigerian, selected studies have implicated physical disability, stroke severity, cognitive impairment, past history of depression, social isolation, functional impairment, dysphasia, age, gender, previous stroke and onset of stroke as having significant impact on PSD among stroke survivors (Ojagbemi, Akpa, Elugbadbo, Owolobi, & Ovbiagele, 2017; Aiyejusunle, Aina, Oladui, & Okafor, 2009; Oladiji *et al.*, 2009; Ojagbemi, Akinyemi, & Baiyewu, 2014). Unfortunately, literature search yielded no results for studies on PSD in Nigeria with multilevel analysis framework.

The present study focused on studying the effect of personal- and background/historical level characteristics on post-stroke depression among stroke survivors using multilevel analysis framework.

MATERIALS AND METHODS

Study Design and location

This study used secondary data from a hospital-based comparative cross-sectional study among stroke survivors. The settings for this study were in the Neurology Unit of the Department of Medicine, University College Hospital, Ibadan, and the Neurology Unit of the Department of Medicine, Federal Medical Center Abeokuta. The study examined depression among one hundred and thirty (130) stroke survivors and a comparative group include one hundred and thirty (130) age, sex and level of education matched, healthy unrelated caregivers or spouses of patients attending the outpatient clinics at the study locations.

Study Variables

Outcome Variable: The outcome variable considered in this analysis was experience of post-stroke depression which is a latent variable measured using adapted instrument from adopted Schedules of Clinical Assessment in Neuropsychiatry (S.C.A.N), Modified Rankin Scale (M.R.S), and Cognitive Assessment Instruments and categorized as “Present” or “Absent”.

Explanatory Variables: The choice of variables and identification of risk factors from the data source was based on previous published studies and literature review on post-

stroke depression (Costello, 1982; Oladiji *et al.*, 2009; Qamar *et al.*, 2010; Stanley, 2013). The explanatory variables used in the analysis were measured at two levels which included level 1 (comprising of individual characteristics: age, sex, place of residence etc.) and level 2 variables (comprising of background characteristics such as family history of chronic diseases, past medical history, and past history of stressful life events) (Figure 1).

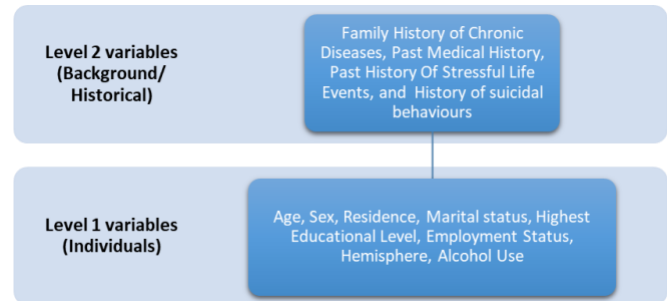


Figure 1: Distribution of the explanatory variables across the levels

Level 1 (Individual) Variables: The individual (level 1) variables consisted of age group, sex, residence, current marital status which is categorized as (currently married and not currently married), highest educational level in categories (no education, primary, secondary and tertiary), employment status (employed and retired), hemisphere (right/left), and alcohol use (yes/no)

Level 2 (Background) Variables: The background (level 2) characteristics pertain to family history of chronic diseases (yes/no), past medical history categorized as (none, any one, more than one), history of suicidal behavior, and past history of stressful life events which include marital separation, business failure, violence, major injury, and death of spouse (none, any one, more than one).

Overview of Data Management and Analysis

Descriptive statistics were used to assess the distribution of respondents by the key variables. Values were expressed as absolute number (percentages) and mean (standard deviation) for categorical and continuous variables respectively.

Chi-square test was used to investigate factors (covariates) associated with post-stroke depression among stroke survivors. Due to the hierarchical structure of the data, all variables were further analyzed in a multilevel framework using a multilevel logit model to further investigate the predictors of post-stroke depression among stroke survivors in southwest Nigeria. Results were presented as odds ratio with 95% Confidence Interval (95%CI). P-value less than 5% were considered to be statistically significant across analyses.

Multilevel Model Specifications

In the following model specifications, y_{ij} represents the dependent variable and $X_{ij} \equiv (x_{1ij}, x_{2ij}, \dots, x_{12ij})^T$ is a vector containing 12 fixed effect predictors such as age, sex, alcohol use, residence, current marital status, employment

status, highest educational level and hemisphere. The $u_j \sim N(0, \sigma_u^2)$ is a random intercept varying over backgrounds (level 2) which were assumed to be independent of each other. In other words, it is assumed that there was a random heterogeneity in respondents' underlying risk of post-stroke depression that persists throughout the entire duration of the study. The models are all specified as random-intercept. The modeling strategies will be approached in three ways as follows:

An unconditional (empty) random intercept two-level logistic model (Model 0): In this null model, no predictor was included. This served as a baseline for comparing other models. It first assesses the mean of the outcome variable and then the amount of outcome variation that exists in individual and background levels. High variation suggests that certain amount of variation in PSD could be explained by the predictors at that level. The null model (model 0) considers that the overall level of violation is allowed to vary over individuals, households and communities with no controlling factors and covariates and was expressed as follows:

$$y_{ij} \sim \text{Bernoulli}(p_{ij}), \text{ with} \quad (1)$$

$$\text{logit}\{\text{Pr}(y_{ij} = 1|X_{ij})\} = \text{logit}(p_{ij}) = \beta_0 + u_j$$

Here $X_{ij} \equiv \{\phi\}^T$ is an empty matrix.

This implies post-stroke depression follows a binomial distribution with two possible outcomes (present/absent) and was modelled with a binary logistic model. The predictors of post-stroke depression in the Model 0 were the intercept (β_0) and the error term (u_j). It is therefore an empty model with no predicting variable.

The first level of the two-level logistic model (Model 1): These models consider that the overall level of post-stroke depression was allowed to vary over individuals after controlling for other factors and covariates. Fixed effects variables are included in this model:

$$y_{ij} \sim \text{Bernoulli}(p_{ij}), \text{ with}$$

$$\text{logit}\{\text{Pr}(y_{ijk} = 1|X_{ij}, u_j)\} = \text{logit}(p_{ij})$$

$$= \eta_{ij} + \beta_1 x_{1ij} + \beta_2 x_{2ij} + \dots + \beta_8 x_{8ij} \quad (2)$$

This implies post-stroke depression follows a binomial distribution with two possible outcomes (present/absent) and was modelled with a binary logistic model. The predictors of post-stroke depression in Model 1 are individual level variables including age, gender, residence, marital status, educational status, employment status, alcohol use, and hemisphere.

A two-level logistic fixed effects random intercept model (Models 2): Where the intercept η_{ij} varies between backgrounds j. Denoting the eight covariates the individual level as x_{1ij}, \dots, x_{8ij}

The four covariates at the background level (family history of chronic diseases, past medical history, history of suicidal behaviors and self-harm and past history of stressful life events) as w_{1j}, w_{2j}, w_{3j} and w_{4j} the background level (level-2) model for the intercept becomes

$$\eta_{ij} = \pi_1 + \pi_{11}w_{1j} + \pi_{12}w_{2j} + \pi_{13}w_{3j} + \pi_{14}w_{4j} + u_j \quad (3)$$

The model (2) above can then be specified for the latent response y_{ij}^* as

$$y_{ij}^* = \beta_0 + \beta_1 x_{1ij} + \beta_2 x_{2ij} + \dots + \beta_{12} x_{12j} + u_j + \epsilon_{ij} \quad (4)$$

where ϵ_{ij} is a residual error term that has a logistic distribution.

Modelling Procedure for the Analysis

Model 0: The unconditional random-intercept model (Equation 1 above) was fitted firstly to serve as baseline for comparing other models.

Model 1: In this model, all fixed effects variables at level 1 i.e. age, sex, residence, marital status, highest educational level, employment status, hemisphere, alcohol use were included in model 0 in order to develop a fixed effects random-intercept model for level 1 variables.

Model 2: Finally, model 1 was adjusted for the fixed and random effect variables respectively at level 2 i.e. family history of chronic diseases, past medical history, past history of stressful life events, and history of suicidal behaviours. This helped to investigate the extent to which background characteristics influenced the prediction of post-stroke depression among stroke survivors in southwest Nigeria.

Each model, models 0, 1 and 2, determined its respective Individual (level 1), and Background (level 2) variance, σ_u^2 .

From these variances, the variability $\rho(\text{individual, background})$ to within individual factors influencing PSD was estimated. The results of the fixed part of the models were presented as odds ratios together with their 95% confidence intervals (95% CI); while for the random part of the models, Variance partition coefficient (%) for each random effect was presented.

The model goodness of fit was determined using the deviance statistic -2x Log Likelihood (-2LL) test; on the assumption that the model with the least -2LL fit the data best

RESULTS

Unadjusted Association between participants' Personal and background Characteristics

Our results show that majority of the stroke survivors are older than 60 years (44.6%) and were mostly female (53.8%). In addition, 76.7% of the respondents reside in urban areas while 82.3% are currently married. Furthermore, about one third (32.3%) of the respondents have tertiary education, 73.8% never used alcohol and 55.3% had stroke in the right hemisphere of their brain. Bivariate analysis showed that post-stroke depression was significantly higher in younger older-adults (≤ 50 years old), 70.4% and among female (55.7%) (Table 1).

On the other hand, 37.7% of stroke survivors has family history of chronic diseases (hypertension, stroke, diabetes, etc.) while 40.8% of them had post-stroke depression (Table 2). Past history of stressful life events (divorce, business failure, major illness/injury, death of spouse, etc.) showed significantly association as all stroke survivors with more than one stressful life events had post-stroke depression. Proportion with depression was significantly higher among stroke survivors (41.5%) compared to the control group (13.8%) (Table 3). Post-stroke depression was also significantly higher among survivors with history of suicidal thought and self-harms (94.1%) (Table 2).

Table 1:
Personal Characteristics of Respondents and Unadjusted Association

Variable	Stroke Survivors (n=130)	Depression Present (%)	Chi-Square _s	P-Value
Current Age				
50 and below	27 (20.8)	19 (70.4)	11.747	0.003
51 to 60	45 (34.6)	16 (35.6)		
More than 60	58 (44.6)	19 (32.8)		
<i>Mean ± SD</i>	<i>59.54 ± 11.08</i>			
Gender				
Male	60 (46.2)	15 (25.0)	12.551	<0.001
Female	70 (53.8)	39 (55.7)		
Residence				
Rural	30 (23.3)	9 (30.0)	2.259	0.133
Urban	99 (76.7)	45 (45.5)		
Marital Status				
Currently Married	107 (82.3)	42 (39.3)	1.302	0.254
Separated	23 (17.7)	12 (52.2)		
Educational Status				
None	26 (20.0)	10 (38.5)	2.480	0.479
Primary	17 (13.1)	8 (47.1)		
Secondary	45 (36.8)	22 (48.9)		
Tertiary	42 (32.3)	14 (33.3)		
Employment Status				
Retired	65 (50.0)	32 (49.2)	3.168	0.075
Employed	65 (50.0)	22 (33.8)		
Alcohol Use				
Ever use	34 (26.2)	17 (50.0)	1.357	0.244
Never use	96 (73.8)	37 (41.5)		
Hemisphere				
Right Hemisphere	72 (55.4)	28 (38.9)	0.467	0.495
Left Hemisphere	58 (44.6)	26 (44.8)		

§ - Chi-square test compares proportions across rows

Table 3:
Prevalence of depression among stroke survivors

	Major Depression	Non Depressed	Total	X ₂ (P-Value)	Odd Ratio (95% CI)
Stroke Survivors (%)	54 (41.5)	76 (58.5)	130 (100.0)	24.894; (p<0.01)	4.42 (2.41 - 8.12)
Controls group (%)	18 (13.8)	112 (86.2)	130 (100.0)		

§ - Chi-square test compares proportions across rows

Multilevel Analysis

The result of the random effects model is shown in Table 4 (Empty Model 0). There is significant variation in the log odds of experiencing post-stroke depression with background random variance ($\tau = 0.23, p < 0.05$). According to the intra-community correlation coefficient implied by the estimated intercept component variance, 24% variance in the odds of experiencing post-stroke depression could be attributed to background-level. There was a significant variation even after controlling for individual-level factors (Model 1) as well as both individual and background-level characteristics (Model 2). This can be clearly judged by proportional change in variance. Individual compositional factors (Model 1) and both individual compositional and contextual factors (Model 2) explained 54% and 67% of the variance in the log odds of experiencing post-stroke depression variance across background characteristics respectively. The variation remained substantial even in Mode 1 and after controlling for both individual and background-level characteristics (Model 2). Also, the proportional change in variance, 54% and 67% of the variance in the log odds of experiencing post-stroke depression variance across background characteristics was explained by Model 1 and both Model 2 respectively.

Table 2:
Historical/Background Characteristics of Respondents and Unadjusted Association

Variable	Stroke Survivors (n=130)	Depression Present (%)	Chi-Square _s	P-Value
Family history of chronic diseases (hypertension, stroke, diabetes, etc.)				
No	81 (62.3)	34 (42.0)	0.017	0.897
Yes	49 (37.7)	20 (40.8)		
Past Medical History (diabetes, hypertension, HIV, cancer, obesity, etc.)				
None	15 (11.5)	6 (40.0)	0.589	0.745
Any one	92 (70.8)	40 (43.5)		
More than one	23 (17.7)	8 (34.8)		
History of suicidal behaviors and self-harm				
No	113 (86.9)	38 (33.6)	22.265	<0.001
Yes	17 (13.1)	16 (94.1)		
Past History Of Stressful Life Events (divorce, business failure, major illness/injury, death of spouse, etc.)				
None	102 (78.5)	5 (100.0)	8.182	0.017
Any one	23 (17.7)	11 (47.8)		
More than one	5 (3.8)	38 (37.3)		

§ - Chi-square test compares proportions across rows

Table 4:

Multilevel Logistic Models of the Predictors of Post Stroke Depression among Stroke Survivors in South-West Nigeria

	FIXED PART	MODEL 0 OR (95% CI)	MODEL 1 aOR (95% CI)	MODEL 2 aOR (95% CI)
PERSONAL VARIABLES				
Current Age	50 and below		1.66 (1.31 – 2.09)*	1.47 (1.16 – 1.85)*
	51 to 60		1.06 (0.89 – 1.27)	1.00 (0.85 – 1.19)
	More than 60		Reference	Reference
Gender	Male		Reference	Reference
	Female		1.40 (1.18 – 1.66)*	1.37 (1.16 – 1.60)*
Residence	Rural		Reference	Reference
	Urban		1.10 (0.93 – 1.32)	1.08 (0.90 – 1.27)
Marital Status	Currently Married		1.01 (0.82 – 1.23)	1.00 (0.83 -1.21)
	Separated		Reference	Reference
Educational Status	None		Reference	Reference
	Primary		1.14 (0.87 – 1.49)	1.10 (0.84 – 1.44)
	Secondary		1.05 (0.83 – 1.31)	1.02 (0.81 – 1.28)
	Tertiary		1.01 (0.80 – 1.28)	1.06 (0.85 – 1.33)
Employment Status	Retired		1.29 (1.08 – 1.55)*	1.23 (1.04 – 1.45)*
	Employed		Reference	Reference
Alcohol Use	Ever use		1.25 (1.05 – 1.50)*	1.21 (1.04 – 1.47)*
	Never use		Reference	Reference
Hemisphere	Right Hemisphere		Reference	Reference
	Left Hemisphere		1.04 (0.90 – 1.21)	1.07 (0.92 – 1.23)
BACKGROUND VARIABLES				
Family history of chronic diseases	No			Reference
	Yes			1.01 (0.90 – 1.17)
Past Medical History	None			Reference
	Any one			1.09 (0.86 – 1.38)
	More than one			1.04 (0.77 – 1.39)
History of suicidal behaviors and self-harm	No			Reference
	Yes			1.53 (1.24 – 1.89)*
History Of Stressful Life Events	None			Reference
	Any one			1.02 (0.84 – 1.22)
	More than one			1.38 (1.04 – 2.01)*
Intercept		1.67 (0.11–3.72)	0.89 (0.64 – 1.12)	0.84 (0.57 – 1.24)
RANDOM PART	Background variance (SE)	0.236 (0.030)	0.169 (0.022)	0.144 (0.018)
	Variance partition coefficient (%)	6.7	11.3	8.7
	Explained Variance (%)	reference	46.7	49.7
	Deviance (-2LL)	184.716	136.706	116.513

*- Significant 95% confidence interval.

In addition, larger deviance information criterion for the individual compositional factors (Model 1) compared to individual compositional and background variables (Model 2) revealed increased multivariable multilevel model's ability to explain variation in the log odds of experiencing post stroke depression, as indicated by lower deviance of model 2.

The results of fitting the model including individual-level variables are shown in Table 4 (Model 1). The results of the inclusion of individual- and contextual factors is shown in Table 4 (model 2). Inclusion of the background-level variables had minimal effect on the contribution of individual- level variables to the likelihood of experiencing post-stroke depression. In particular, in the model adjusting for both individual compositional and background factors (model 2), the effect of age, sex, employment status, alcohol use, history

of suicidal behavior and history of stressful life events remained significant (Table 4).

Furthermore, stroke survivors aged ≤ 50 years were more likely to experience post-stroke depression (OR = 1.47; 95% CI: 1.16 – 1.85) than survivors who were 60 years old. Female stroke survivors are also more likely to experience post-stroke depression than male (OR = 1.37; 95% CI: 1.16 – 1.60). Stroke survivors who have retired from active services were more likely to experience depression compared to those who were employed at the time of study (OR = 1.23; 95% CI: 1.04 – 1.45). Respondents who ever used alcohol were 21% more likely to experience post stroke depression compared to non-users. Independent of stroke survivors with no past history of stressful life event, those with history of more than one stressful life events were 38% more likely to experience post-stroke depression.

DISCUSSION

The present study used multi-level modelling to assess predictors of post-stroke depression among stroke survivors in south-west Nigeria. Prevalence of post-stroke depression was higher than the global statistics (30%) reported elsewhere (Ayerbe *et al.*, 2011). Though the results of the present report are relatively higher than that of a study from Lagos, Nigeria (Aiyejusunle, Aina, Oladui, & Okafor, 2009), it is strongly supported by other hospital based studies in Nigeria and other African countries (Ali, Chidi, & Timothy, 2016; Sarfo *et al.*, 2017). For instance, in a study conducted in Maiduguri, Borno State, Nigeria by Ali, Chidi, and Timothy (2016) found the prevalence of post-stroke depression to be 52.9% while Sarfo *et al.* (2017) got the prevalence of 42.5% among a sample of stroke survivors in Ghana.

Post-stroke depression was more prevalent among female stroke survivors than male. Women generally have been reported to experience higher burden of depression than men (Mental Health Foundation, 2000). A further justification for our study is substantiated by reports from a previous similar study conducted in Lagos, Nigeria where women were reported to experience higher prevalence of post-stroke depression (61.5%) than men (Oladiji *et al.*, 2009). This is consistent with findings from a related study on burden and factors associated with post-stroke depression in East Central Nigeria (Ibenebe *et al.*, 2017). In particular, Ibenebe *et al.* (2017) found the prevalence of post-stroke depression to be 45.45% among the female stroke survivors in east central Nigeria.

History of stressful life events is a significant predictor of post-stroke depression in this study. In the present study, stressful life events consisted of marital failure, job loss, business failure, major illness or injury, and death of spouse among others. Stroke survivors that had previous experience of more than one stressful life events were more likely to experience post-stroke depression. Although, experience of any one of the stressful life events does not significantly influence development of post-stroke depression. Stress has generally be linked to development of depression (Kendler *et al.*, 1999). This result is similar to results from other similar studies in Nigeria that examined Post-stroke depression in relation to some characteristics of the vulnerable patients in socio-cultural context (Ibeneme, Nwosu, Ibeneme, Bakare, Fortwengel, & Limaye, 2017). The study found that stroke survivors with experience of stressful life events like job loss/business failure, marital separation and presence of complications are more vulnerable to experience post-stroke depression.

In conclusion, prevalence of post-stroke depression in south-west Nigeria is high. There are evidences that both individual and background characteristics are important in studying post-stroke depression in stroke survivors. Post stroke depression was common in younger and female survivors. Stroke survivors who consume alcohol and those with history of stressful life event are at higher risk of post stroke depression in this sample. Interventions focusing on women, alcohol users, and people with history of stressful life events that had survived a stroke may reduce the burden of post stroke depression and suicide possibilities among them

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