



Is Stroke Tending towards the Young?

Jide Onyekwelu^{1*}, Chike H. Nwankwo² and I. C. A. Oyeka²

¹Obinwanne Hospital and Maternity, 19 Uba Street, Nkpor, Anambra State, Nigeria.
²Department of Statistics, Nnamdi Azikiwe University, Awka, Anambra State, Nigeria.

Authors' contributions

This work was carried out in collaboration between all authors. Author JO designed the study, managed the literature searches, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author CHN managed the analyses of the study and fine-tuned the first draft. Author ICAO conceived the idea and provided the title. All authors read and approved the final manuscript.

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ABSTRACT

Stroke is a devastating vascular disease of the brain that carries very poor prognosis. It is a disease of the elderly people but recent literature reports that it is occurring more in the young now than hitherto. Nigeria has a young population and if stroke were to occur more in the young now than hitherto, it will have a devastating effect on Nigeria's economy. This study is to determine whether stroke is occurring more in the young people now than in past decades. The findings will alert the health managers of the impending calamity in its eventuality.

Data on age and sex of stroke patients and year of stroke event were obtained from randomly selected referral hospitals in Southern Nigeria for the period 1973 to 2011. Proportion of stroke occurrence in the young was modelled. Z test was used to analyze the proportion of stroke that occurred classified by age and gender.

The proportion of stroke occurrence in the young has a downward trend from 1973 to 2011 that is best described by cubic polynomial model. Stroke is found to have an almost 50-50 sex distribution but 61% of those that have stroke at 45 years of age or less are found more likely to be females than males. This shows that more females than males are likely to have stroke at the young age of

*Corresponding author: E-mail: drjideonyekwelu@yahoo.com;

45 years or less. Stroke is found to be occurring less in the young people now than in the past four decades studied. It is recommended that a prospective study be undertaken over many decades to confirm or negate the observed decreasing trend of proportion of stroke occurrence in the young since 1973. Further study is also recommended to elucidate the factors associated with stroke occurrence in the young.

Keywords: Stroke; occurrence; young age; model; Southern Nigeria.

1. INTRODUCTION

Stroke, also known as cerebro-vascular accident, is defined as rapidly developing signs of focal or global disturbance of cerebral or intracranial neuronal function with symptoms lasting for more than 24 hours or leading to the death of the patient with no apparent cause other than that of vascular origin [1]. Young age is conventionally taken to be from 15 years to 45 years [2]. The prognosis of stroke disease is poor. Only about 3% of patients recover fully to resume their normal daily activities [3]. The rest die or live with permanent disabilities.

Hypertension and diabetes mellitus are known major factors associated with stroke [4]. These factors are diseases associated with the elderly. Hence stroke has been thought to be a disease of the elderly even though it also occurs in the young.

Mortality from stroke is 4.4 million every year worldwide [5]. According to World Health Organization (WHO), stroke is the third leading cause of mortality worldwide (after cancer and ischemic heart disease), accounting for approximately 4.6 million deaths annually [6]. It is a debilitating disease that carries a mortality rate of 34.59% in Ibadan, Nigeria [4], 38.5% in Lagos, Nigeria [7], 38.5% in Port Harcourt [8] and 27% in Gambia [9] within first month of occurrence. It is the commonest cause of neurological deaths [10]. A small percentage recovers fully leaving the rest with varying degrees of disability that makes them not capable of providing for themselves [3]. It is a disease of the old people [11] but it seems as if rate of occurrence in the young people aged less than or equal to 45 years is increasing in USA [12].

1.1 Justification for the Study

Peak age of incidence of stroke in Ibadan, Nigeria in 1973-1975 was in the 8th decade, 70-79 years, in males and 7th decade in females [4] and peak age of occurrence was found to be 60 – 69 years. In 2010, four decades later,

Damasceno et al. reported that in a prospective study they did on patients that had stroke between August 2005 and July 2006 in Maputo, Mozambique, the peak age of occurrence was 45 – 54 years [13].

Reinberg raised the alarm that stroke is tending towards the young in USA [14]. The number of people aged 15 to 44 hospitalized for stroke jumped by more than a third between 1995 and 2008 in USA [12]. This was attributed to obesity, diabetes, high blood pressure and other risk factors. There have been studies on stroke in Nigeria but very few have focused on the young and none has determined its trend over time.

Nigeria has a young population structure with the population estimated at about 174 million with 49.4% between 15 years and 54 years [15]. Nigerian population as at last census in 2006 was 140,003,542 [16]. If the trend were to change with stroke occurring more in the young, it means millions of Nigerians are at increasing risk of having the debilitating disease. It will have a devastating effect on the economy of a poorly managed resource country like Nigeria since it will affect the productive age group that constitutes the work force in the society.

If there is really a time trend, this study will be an opportunity to alert the ministry of health and health managers in Nigeria about the impending calamity.

1.2 Aim and Objectives

The aim of this study is to determine whether stroke is occurring more in the young people in Southern Nigeria now than in past decades. The objectives are:

To identify if there is a trend in the proportion of stroke that occurred in the young in Southern Nigeria and model it.

To check if gender is a predisposing factor in the occurrence of stroke in the young.

1.3 Ethical Issues

The identities of the patients whose folders were used for this study were not revealed. The ethical protocols of all the health facilities studied were fully followed. Each of the health facilities gave permission for the study to be conducted.

1.4 Ethical Approval

The authors have obtained all necessary ethical approval from suitable institutions and committees to conduct this study.

1.5 Limitations

There were no data in the medical records from 1973 to 2006 in the studied facilities. Data from published works were used to fill the gap. The other records were in doctor’s hand writing. So only medical doctors or experienced medical personnel could sieve the data from doctor’s handwritten case notes. Luckily the researcher is a medical doctor. He did the work of data collection in conjunction with records staff.

2. MATERIALS AND METHODS

This is a cross sectional exploratory study of stroke occurrence in the young from 1973 to 2011 in Southern Nigeria. Southern Nigeria has three geopolitical zones namely South-East, South-South and South-West geopolitical zones. Each zone has six tertiary hospitals that treat

stroke patients. Simple random sampling was used to select one hospital from each of the three geopolitical zones.

All the folders of patients diagnosed as stroke or cerebrovascular accident or hemiplegia were extracted from the medical records from 2011 to as far back as the records were able to show. Data on year of stroke occurrence, age and sex of patient were recorded. Secondary data from published medical articles were used to cover the period 1973 to 2006 for which records were not available in the studied hospitals.

Only folders of first strokes with year and sex clearly written were studied.

3. PRELIMINARY RESULTS

In column 1 of Table 1, “Year” indicates the year at the middle of the study period which is shown in brackets as period data were collected by the author. Year index is the number corresponding to the ith year. 1973 = 1, 1974 = 2, ..., 2011 = 39.

There are overlaps in third, fourth and fifth rows in Table 1. On the assumption of a uniform distribution of proportion of stroke occurrence within the short period data were collected by each of the authors for study, the proportion of stroke occurrence in a year will be the same for each of the years within the study period in each of the rows. Table 2 is therefore constructed to remove the overlaps.

Table 1. Year and percentage of stroke that occurred in the young

Year (Period data were collected by the author)	Year index i.e., ith year	Percentage of stroke that occurred in the young	Author
1974 (1973-1975)	2	25.47	Osuntokun et al. [4]
1988	16	27.9	Nwosu et al. [17]
1998 (1993-2003)	26	13.00	Chap-Jumbo [8]
2001 (2000 – 2002)	29	10.00	Amu et al. [18]
2002 (2000-2005)	30	11.10	Komolafe et al. [3]
2007	35	5.56	Data obtained from studied facilities
2008	36	16.67	Data obtained from studied facilities
2009	37	12.12	Data obtained from studied facilities
2010	38	8.62	Data obtained from studied facilities
2011	39	12.82	Data obtained from studied facilities

These data are as published by the authors. There are overlaps in the periods of collection.

Table 2. Year and percentage of stroke that occurred in the young without overlaps in the years

Year	Year index	Percentage of stroke that occurred in the young
1974 (1973 – 1975)	2	25.47
1988	16	27.90
1996 (1993 – 1999)	24	13.00
2001 (2000 – 2002)	29	10.00
2004 (2003 – 2005)	32	11.10
2007	35	5.56
2008	36	16.67
2009	37	12.12
2010	38	8.62
2011	39	12.82

Table 3. Gender distribution of stroke patients from data obtained from studied facilities from 2007 to 2011

Gender	Number	Percentage
Male	132	49.8
Female	133	50.2
Total	265	100.0

Table 4. Gender distribution of stroke patients that are ≤ 45 years from data obtained from studied facilities from 2007 to 2011

Gender	Number	Percentage
Male	12	38.3
Female	19	61.7
Total	31	100.0

3.1 Preliminary Treatment of Data

The scatter plot of the proportion of stroke occurrence in the young against the year of stroke occurrence is plotted as in Fig. 1.

By inspection of the scatter plot in Fig. 1, three possible models come to mind as possible candidates for modelling the stroke occurrence data. The models are a straight line (linear model), a curve with one turning point (quadratic model) and a curve with two turning points (cubic model). The linear model is not feasible since the proportion of stroke that occurs in the young can neither be zero nor infinity. That leaves the quadratic and cubic models for further exploration.

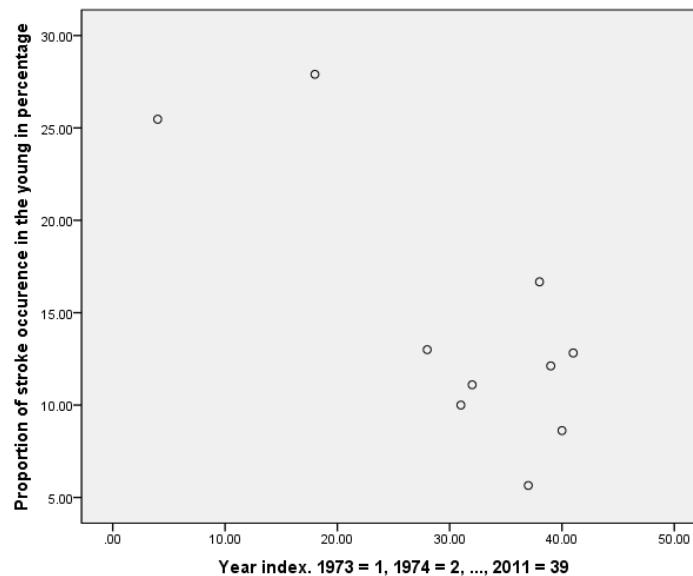


Fig. 1. Scatter diagram of proportion of stroke occurrence in the young against year of stroke occurrence from 1973 to 2011

3.2 The Quadratic Model

The quadratic model is expressed as

$$y_i = \beta_0 + \beta_1 \tilde{t}_i + \beta_{11} \tilde{t}_i^2 + \varepsilon_i \quad (i = 1, 2, \dots, n)$$

where $\tilde{t}_i = (t_i - \bar{t})$.

\bar{t} is the mean of time indexes and \tilde{t}_i are deviations of t_i from the mean of time indexes. The use of these deviations is to reduce the effect of multicollinearity usually associated with polynomial regression models.

ε_i is the error term assumed to be normally distributed with mean zero and constant variance.

The model is expressed in matrix form as

$$Y = t_q \beta_q + \varepsilon \tag{1}$$

Where $Y = \begin{bmatrix} y_1 \\ y_2 \\ \vdots \\ y_n \end{bmatrix}$ is an nx1 vector of proportion of stroke cases that occurred in the young.

$t_q = \begin{bmatrix} 1 & \tilde{t}_1 & \tilde{t}_1^2 \\ 1 & \tilde{t}_2 & \tilde{t}_2^2 \\ \vdots & \vdots & \vdots \\ 1 & \tilde{t}_n & \tilde{t}_n^2 \end{bmatrix}$ is an nx3 matrix of a column of 1's, the column of \tilde{t}_i and \tilde{t}_i^2 ,

(\tilde{t}_i^2 is the square of \tilde{t}_i), $i = 1, 2, \dots, n$.

$\beta_q = \begin{bmatrix} \beta_0 \\ \beta_1 \\ \beta_{11} \end{bmatrix}$ is a 3x1 vector of the constant term β_0 and the coefficients of \tilde{t}_i and \tilde{t}_i^2 in the model

and $\varepsilon = \begin{bmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \vdots \\ \varepsilon_n \end{bmatrix}$ is a nx1 vector of the error terms assumed to be normally distributed with mean 0 and constant variance.

The estimate of the model is

$$\hat{Y} = t_q \hat{\beta}_q \tag{2}$$

Where $\hat{\beta}_q$ is obtained by the least squares method as

$$\hat{\beta}_q = (t_q' t_q)^{-1} t_q' y \quad (t_q' \text{ is the transpose of } t_q) \tag{3}$$

3.3 The Cubic Model

The cubic model is similarly expressed as

$$y_i = \beta_0 + \beta_1 \tilde{t}_i + \beta_{11} \tilde{t}_i^2 + \beta_{111} \tilde{t}_i^3 + \varepsilon_i \quad (i = 1, 2, \dots, n)$$

where $\tilde{t}_i = (t_i - \bar{t})$

\bar{t} is the mean of time indexes

ε_i is the error term assumed to be normally distributed with mean zero and constant variance.

The model is expressed in matrix form as

$$Y = t_c \beta_c + \varepsilon \tag{4}$$

Where $Y = \begin{bmatrix} y_1 \\ y_2 \\ \vdots \\ y_n \end{bmatrix}$ is an nx1 vector of proportion of stroke cases that occurred in the young.

$t_c = \begin{bmatrix} 1 & \tilde{t}_1 & \tilde{t}_1^2 & \tilde{t}_1^3 \\ 1 & \tilde{t}_2 & \tilde{t}_2^2 & \tilde{t}_2^3 \\ \vdots & \vdots & \vdots & \vdots \\ 1 & \tilde{t}_n & \tilde{t}_n^2 & \tilde{t}_n^3 \end{bmatrix}$ is an nx4 matrix of a column of 1's, the columns of \tilde{t}_i , \tilde{t}_i^2 and \tilde{t}_i^3 , (\tilde{t}_i^2 is the square of \tilde{t}_i and \tilde{t}_i^3 is the cube of \tilde{t}_i), $i = 1, 2, \dots, n$.

$\beta_c = \begin{bmatrix} \beta_0 \\ \beta_1 \\ \beta_{11} \\ \beta_{111} \end{bmatrix}$ is a 4x1 vector of the constant term β_0 and the coefficients of \tilde{t}_i , \tilde{t}_i^2 and \tilde{t}_i^3 in the model

and $\varepsilon = \begin{bmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \vdots \\ \varepsilon_n \end{bmatrix}$ is a nx1 vector of the error terms assumed to be normally distributed with mean 0 and constant variance.

The estimate of the model is

$$\hat{Y} = t_c \hat{\beta}_c \tag{5}$$

Where $\hat{\beta}_c$ is obtained by the least squares method as

$$\hat{\beta}_c = (t_c' t_c)^{-1} t_c' y \quad (t_c' \text{ is the transpose of } t_c) \quad (6)$$

3.4 Methods of Data Analysis

In polynomial models, the independent variables that appear as various powers can be highly correlated. This introduces the problem of multicollinearity. Variance inflation factor (VIF) test is used to check for serious multicollinearity.

3.5 Variance Inflation Factor (VIF)

VIF measures how much the variances of the estimated regression coefficients are inflated as compared to when the independent variables are not linearly related. The formula is given by:

$$(VIF)_k = (1 - R_k^2)^{-1} \quad k = 1, 2, \dots, p-1 \quad [19] \quad (7)$$

R_k^2 = coefficients of determination when the kth independent variable is regressed on the p-2 other independent variables in the model.

Mean $(VIF)_k$ considerably greater than 1 indicates highly inflated variance.

Maximum $(VIF)_k$ greater than 10 indicates that multicollinearity may be unduly influencing the least squares estimates.

3.6 Choice of Model and Model Estimate

Data on Table 2 are used to generate the data on Table 5. The design matrix for t_q for application in equation 2 as well as design matrix

for t_c for equation 4 are generated from data in Table 5. The two models, quadratic and cubic, will be estimated and compared. The better model will be used to analyze the data.

Table 5. Proportion of stroke occurrence in the young in Southern Nigeria and time variables

y_i	t_i	\tilde{t}_i	\tilde{t}_i^2	\tilde{t}_i^3
25.47	2	-18	324	-5274
27.90	16	-4	16	-64
13.00	24	4	16	64
10.00	29	9	81	729
11.10	32	12	144	1728
5.65	35	15	225	3375
16.67	36	16	256	4096
12.12	37	17	298	4913
8.62	38	18	324	5832
12.82	39	19	361	6859

y_i = percentage of stroke that occurred in the young in the i th year.

t_i = year index

$$\tilde{t}_i = t_i - \bar{t} \quad \bar{t} = \frac{n(1+n)}{2n} \quad i = 1, 2, \dots, n.$$

n = number of years = 39

$\bar{t} = 20$

3.7 Estimation of Quadratic Model

For estimating equation 2, the first column of Table 5 makes up the y vector while the matrix t_q is made up of a column of 1's and columns of \tilde{t}_i and \tilde{t}_i^2 of Table 5 respectively. Hence, from equation 3, the least squares procedure yields the following parameter estimates as shown in Table 6.

Table 6. Coefficients of the quadratic model and their descriptive characteristics

Variable	b	Standard error	t-value	p-value
\tilde{t}_q	-0.484	0.146	-3.324	0.013
\tilde{t}_q^2	0.003	0.013	0.205	0.841
constant	18.033	3.078	5.859	0.001

The ANOVA table is as shown below.

Table 7. ANOVA Table of proportion of stroke that occurred in the young out of stroke that occurred in the studied tertiary hospitals in Southern Nigeria from 1973 to 2011 using the quadratic model

	Sum of squares	df	Mean square	F ratio	p-value
Regression	286.514	2	143.257	5.788	0.033
Residual	173.267	7	24.752		
Total	459.781	9			

The tested hypothesis here is $H_0: \beta_i's = 0$ versus $H_a: \text{Not all } \beta_i's = 0$. A p-value of 0.033 leads to a rejection of H_0 at $\alpha = 0.1$ indicating that the quadratic model is apt for fitting the data

The model is

$$\hat{y} = 18.033 - 0.484\bar{t}_q - 0.003\bar{t}_q^2 \quad (R^2 = 0.623; p = 0.033) \quad (8)$$

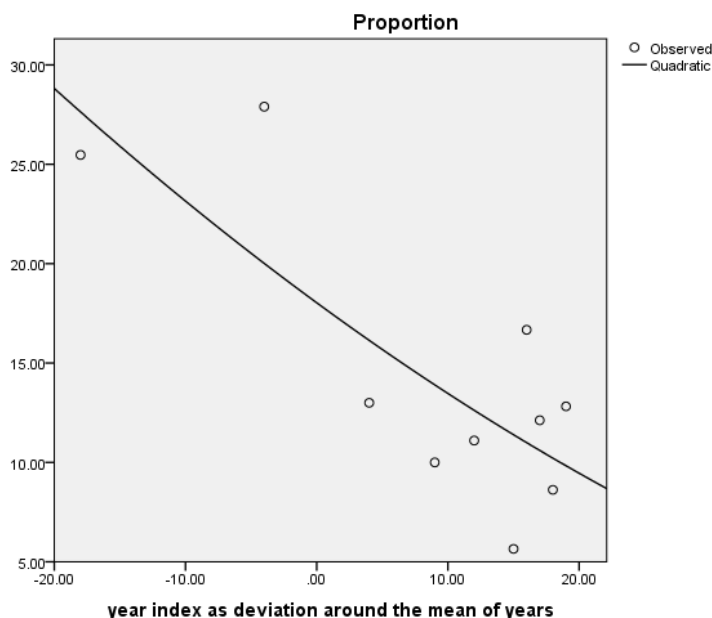


Fig. 2. Curve fitting for quadratic model

3.8 Estimation of Cubic Model

For estimating equation 4, the first column of Table 5 makes up the y vector while the matrix t_c is made up of a column of 1's and columns of

\bar{t}_i , \bar{t}_i^2 and \bar{t}_i^3 of Table 5 respectively. Hence, from equation 5, the least squares procedure yields the following parameter estimates as shown in Table 8.

Table 8. Coefficients of the third order polynomial model for rate of stroke occurrence in the young and their descriptive characteristics

Variables	b	Standard error	t-value	p-value
\bar{t}	-1.341	0.370	-3.625	0.011
\bar{t}^2	-0.007	-0.127	0-0.638	0.547
\bar{t}^3	0.003	0.001	2.430	0.051
Constant	21.112	2.679	7.882	0.000

The ANOVA table is as shown below

Table 9. ANOVA Table of proportion of occurrence of stroke that occurred in the young out of stroke that occurred in the studied tertiary hospitals in Southern Nigeria from 1973 to 2011 using the cubic model

	SS	df	MS	F	p-value
Regression	372.466	3	124.155	8.532	0.014
Residual	87.315	6	14.553		
Total	459.781	9			

The tested hypothesis here is $H_0: \beta_i's = 0$ versus $H_a: \text{Not all } \beta_i's = 0$. A p-value of 0.014 leads to a rejection of H_0 at $\alpha = 0.1$ indicating that the cubic model is apt for fitting the data.

The fitted model is:

$$\hat{y} = 21.112 - 1.341\bar{t} - 0.007\bar{t}^2 + 0.003\bar{t}^3 \quad (R^2 = 0.810; p = 0.014) \quad (9)$$

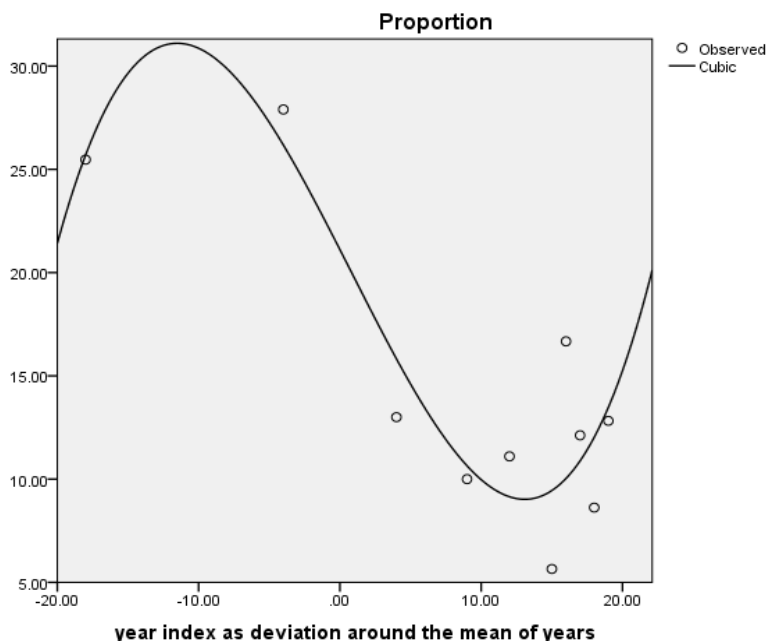


Fig. 3. Curve fitting for cubic model

The cubic model is more apt (p-value = 0.014) than the quadratic model (p-value = 0.033). The R^2 for cubic model (0.819) is higher than that of the quadratic model (0.623). Thus the variability in the proportion of stroke occurrence in the young out of the stroke that occurred in the Southern Nigeria from 1973 to 2011 is better reduced by the set of independent variables in the cubic model than that in the quadratic model. The cubic model is thus the model of choice. The quadratic term is not significant both in the quadratic and cubic models but by the hierarchical approach to fitting regression, the quadratic term will not be dropped since the cubic term which is higher in order is retained [20]. Equation (9) thus becomes the model for describing the proportion of stroke occurrence in the young in this study.

3.9 Stroke that Occurred in the Young Classified by Gender

When the proportion of occurrence of stroke in the young is classified by gender, there is an

apparently clear steep downwards relationship between proportion of occurrence of stroke in the young males and year of stroke occurrence. It is not so in females. The points are too few to make much sense if plotted, so it is left to be visually appreciated in tabular form as shown in Table 10.

The decline in proportion of stroke occurrence in the young is steeper in the young males than in the young females.

3.10 Proportion of Stroke that Occurred Classified by Age and Gender

Of the 265 patients that had stroke from the data obtained from patients' folders from 2007 to 2011, 31 were equal to or less than 45 years old and 19 out of that number are females. Table 11 shows the distribution of stroke data by age and gender. Test of difference in proportion of males and females that have stroke at age equal or less than 45 years is conducted.

Table 10. Proportion of stroke that occurred in the young in Southern Nigeria in decades classified by gender

Year index in decades*	Percentage of Stroke occurring in young males	Percentage of stroke occurring in young females	Percentage of stroke occurring in both young males and females
1	18.55	6.92	25.47**
2	Not available	Not available	27.9***
3	6.67	6.33	13****
4	4.53	5.26	9.79*****

*First decade = 1970s, 2nd = 1980s, 3rd = 1990s and 4th = 2000s.

**The data is from Osuntokun et al. [4].

***The data is from Nwosu et al. [17].

****The data from Chap-Jumbo [8].

***** The data are computed from data on patients' folders.

Table 11. Proportion of stroke that occurred classified by age and gender

Age in years	Males (%)	Females (%)	Total
≤45	12 (38.7)	19 (61.3)	31
>45	120 (51.3)	114 (48.7)	234
	132 (49.8)	133 (50.2)	265

Test of difference in proportion of stroke occurrence in males and females ≤ 45 years.

Null hypothesis, $H_0: P_1 = P_2$

Alternative hypothesis, $H_a: P_2 > P_1$

P_1 is proportion of stroke that occurs in the young males

P_2 is proportion of stroke that occurs in the young females

Decision rule, reject H_0 if z calculated $> z_{1-\alpha}$ else accept H_0 .

$$z_{1-\alpha} = 1.285, \alpha = 0.1$$

z calculated = 1.827 and it is greater than 1.285. Hence H_0 is rejected. Proportion of stroke that occurs in the young females is more than that that occurs in young males.

4. DISCUSSION

Studies in literature to compare with this study are scanty. This study has shown that stroke is not occurring more in the young aged 45 years and below since the proportion of stroke occurrence in the young has a downward trend for the period under study in Southern Nigeria. This downward trend is in agreement with the finding of Whisnant. He found out that stroke mortality in the USA declined from 1900 to 1950

[21]. He attributed the decline to decline in case fatality because of better case management, occurrence of less severe cases or decline in incidence of new cases. He also noted that the average annual incidence of stroke declined from 1950 to 1979. Better case management of predisposing factors to stroke occurrence such as hypertension, diabetes mellitus, kidney diseases, etc. can be a reason for the decline in proportion of stroke occurrence in the young. Improvement in healthcare delivery obviously reduces chances of people at risk developing stroke.

HIV is a factor in stroke occurrence mostly in young people. Stroke is known to occur at a lower mean age of less than 45 years in HIV patients than in the general population [22-26]. More females have HIV than males [27,28] especially in sub-Sahara Africa. Ukoha et al. reported that of the 27 stroke patients studied 4 had HIV and are all females [26] even though the sample size screened is small. In the present study, 265 stroke cases were studied from 2007 to 2011. Only 55 of the cases were screened for HIV. Of those screened, 4 tested positive to HIV and are made up of 3 males and 1 female. All the 4 cases are less than 45 years old. If more of young females have HIV than young males and stroke occurs more in young HIV patients, it explains the lack of steep downward trend in proportion of occurrence of stroke observed in young females. This study does not support this reasoning that HIV infection among females is the cause of this counterbalance probably because of the small number screened for HIV.

Ischemic stroke of unusual cause (ISUC) is frequent in young patients. Being 45 years or less is an independent predictor of ISUC [29]. Studies on this stroke subtype have not been

reported in Southern Nigeria to give a basis for comparison with the present study. It may contribute to the etiology of stroke in the young. Future studies will be able to elucidate that.

It can also be argued that more women are working as civil servants, entrepreneurs, business women, engaging in stressful life both in the home and work place more now than in decades past. Pregnancy and child delivery may also be added stressors since this age of ≤ 45 years falls within the child bearing age for women. Stress is a factor in stroke causation [30]. Since more women are living more stressful lives now than in past decades, the proportion of stroke in this population would consequently rise. This may also explain why the decline in young females is not as steep as that in young males. The downward trend is therefore more obvious in young males.

5. CONCLUSION

Stroke is not tending towards the young in Southern Nigeria. More young females have stroke than young males. The proportion of decrease in occurrence of stroke in the young in Southern Nigeria is more apparent in the males than in the females. Inasmuch as this conclusion is not intended to make health planners and stake holders to relax their plan to manage and contain stroke occurrence, especially in the young, they need not go into panic since the findings of George [12] may not be applicable to Southern Nigeria. If and when more studies are done to negate or support the findings of this study, then there will be added reasons for policy makers to act on.

6. RECOMMENDATIONS

It is recommended that a prospective study be undertaken over many decades to confirm or negate the observed decreasing trend in proportion of stroke occurrence in the young since 1973.

Further study is recommended to elucidate the factors associated with stroke occurrence in the young.

Further studies also need to be carried out to clearly establish sex distributions of stroke occurrence both in the young and elderly.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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