

Clinical and Brain Computed Tomographic Profile of Stroke Patients in a Tertiary Hospital, North Central Nigeria

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Abstract

Background: Stroke is a common neurological disorder associated with high morbidity and mortality worldwide. **Aim:** The study set out to characterize the clinico-radiologic pattern of stroke patients as well as to determine the correlation between the clinical and computed tomographic (CT) scan findings in a tertiary hospital in Makurdi, North central Nigeria. **Method:** This was a retrospective study of 145 patients with clinically suspected stroke, who underwent CT imaging at the Benue State University Teaching Hospital, Makurdi Nigeria between December 2020 and June 2022. Data were analyzed using Statistical Package for Social Sciences (SPSS) version 26. **Results:** Of the 145 clinically diagnosed cases of stroke, 122 (84.1%) were confirmed on CT. 7 (4.8%) were stroke mimics and 16 (11.0%) were normal. There were 65 (53.3%) males and 57 (46.7%) females with a male: female ratio of 1.1:1. The mean age at presentation was 58.7 ± 12.87 years with age range of 69 - 78 years being affected most. Few cases of stroke were seen below the age of fifty years. Ischaemic stroke was the commonest 77 (63.1%) followed by primary intracerebral haemorrhage (ICH) 38 (31.4%) then sub arachnoid haemorrhage (SAH) 5 (4.1%). Most infarcts were below 10 cm^2 , while for ICH volume those below 10 cm^3 and above 100 cm^3 occurred in equal proportion. Hypertension was the main risk factor for stroke with respective frequency of 31 (21.4%) and 94 (64.8%) in isolation or associated with other risk factors like Diabetes mellitus (DM), hyperlipidemia, alcohol, and smoking among others. There was significant correlation between clinical and radiological diagnosis of stroke ($p < 0.05$). **Conclusion:** The result showed slight male preponderance with majority of suspected stroke confirmed by CT; these were mostly of ischaemic type.

There was significant correlation between clinical and radiologic diagnosis of stroke while hypertension was the main risk factor identified.

Keywords

Stroke, Risk Factors, Computed Tomography, Neuroimaging, Makurdi

1. Introduction

Stroke is a common emergency and a major global public health problem due to its significant economic, social and medical implications [1]. It is defined by the World Health Organisation (WHO) as “neurological deficit which could be focal or global (with coma) of cerebrovascular cause that persists beyond 24 hours or is interrupted by death within 24 hours” [2]. The updated definition by American Heart Association (AHA)/American Stroke Association (ASA) suggests the need for objective evidence of haemorrhage or infarction in the central nervous system irrespective of duration of clinical symptom possibly by using neuroimaging modality like Computed Tomography. Stroke occurs when ischaemia or haemorrhage interrupts or reduces the supply of blood to the brain. When this happens, the brain does not receive enough oxygen or nutrients, leading to initial ischaemia and subsequent infarction if prolonged or haematoma formation [3].

Stroke can be classified into two major categories, namely ischaemic and haemorrhagic. It has been established that the proportion of ischaemic and haemorrhagic stroke in low-and-middle-income countries (LMICs) especially sub-Saharan Africa were about 70% and 30% respectively; whereas in high-income countries (HICs), it is about 90% and 10% respectively. Of recent however, changing pattern of stroke is recorded in Africa in which increasing frequency of hemorrhagic stroke is been reported [4]. Hemorrhagic stroke is known to be associated with higher mortality rates while ischaemic stroke has higher morbidity-like disability [5] [6].

The goal of imaging in a patient with acute stroke is to exclude hemorrhage, differentiate between irreversibly affected brain tissue and reversibly impaired tissue (umbra versus penumbra). It can also identify stenosis or occlusion of major extra- and intracranial arteries and exclude stroke mimics [7]. Brain neuroimaging is essential to determine patients who will benefit from thrombolytic therapy aside from other criteria like time of symptom onset [8] [9] [10] [11].

Rapid and accurate stroke diagnosis is important for commencement of appropriate acute stroke care so as to reduce stroke complications; which ultimately could determine outcome [12] [13]. Computed Tomography (CT) has the advantage of being rapid in image acquisition, and availability in many centers. It is the gold standard in acute stroke care units to help exclude brain hemorrhage [14]. Hemorrhage on magnetic resonance images can be quite confusing [15].

On CT; about 60% of infarcts are seen within 3 - 6 hours and virtually all are seen in 24 hours. CT has sensitivity of 64% and is 85% specific in stroke diagnosis [15]. Early signs of ischaemic stroke seen on CT include hypodense areas within the brain parenchyma, increases in density of the middle cerebral artery called dense MCA sign, obliteration of the lentiform nucleus, loss of definition of the gray-white interface in the lateral margin of the insula cortex called insula ribbon sign and brain swelling manifested as sulcal effacement [16].

Incidence, clinical and radiological characteristics and outcome of stroke may differ between countries, geographical regions, and ethnic groups [17]. In this study, we therefore set out to characterize the clinical and brain CT scan pattern of stroke patients as well as to determine the correlation between the clinical and radiologic findings in a tertiary hospital in Makurdi, North central Nigeria. This will be invaluable for physicians in instituting preventive approaches to mitigate stroke as well as public health policymakers.

2. Materials and Methods

2.1. Study Design and Setting

This was a retrospective cross-sectional hospital-based study conducted as collaboration between the Departments of Radiology and Internal Medicine of the Benue state University Teaching Hospital (BSUTH) Makurdi, Nigeria between December 2020 and June 2022. Patients were included in the study if they had clinical diagnosis of stroke with subsequent radiologic confirmation and managed at BSUTH. Excluded were clinically suspected cases of stroke mimics and patients below 18 years. The teaching hospital is a major referral center for acute stroke care and CT scan in the north central geopolitical zone of Nigeria.

2.2. Ethical Consideration

Ethical clearance for this study was obtained from the institutional Research Review Board. Confidentiality of the data obtained was maintained all through the study.

2.3. Data Collection

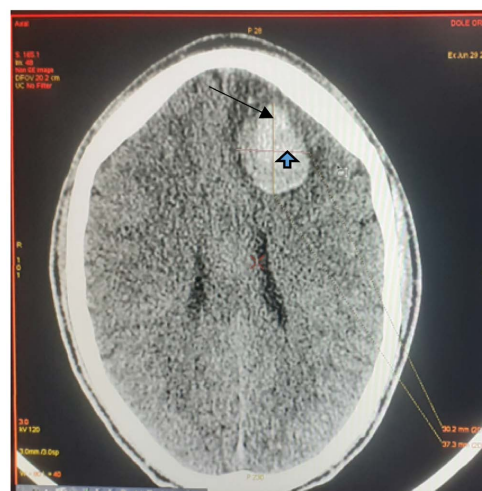
Demographic data including age, sex, tribe, marital status, religion and the level of education were obtained from the case notes of the patients. Also obtained were the clinical diagnosis, dominant handedness, and stroke hemisphere, duration of symptoms before presentation to the hospital, major stroke symptoms and stroke risk factors. Hypertension was classified based on staging by International Society of Hypertension (ISH) [18].

The brain CT examinations were performed by qualified CT Radiographers using standard departmental protocol for brain investigations on 32 Slices Philips Brilliance CT. The procedure was explained to the patients where possible. Then they were placed supine into the gantry with their head going in first stabilized by the head holder. Scanogram was taken and then subsequently conti-

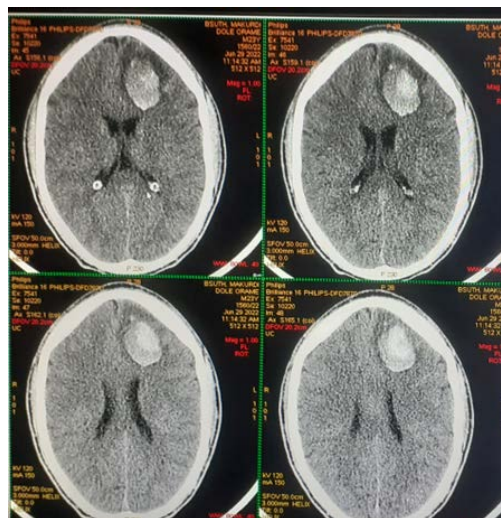
nuous axial native images of 5 mm thickness were obtained without contrast administration from the base of the skull to the vertex. If the native image appeared normal or showed area of infarction or mass lesion, intravenous contrast (IV) was administered. But in those with haemorrhages, no IV contrast was given.

CT images of these patients from December 2020 to June 2022 were reviewed for presence or absence of hemorrhage and CT features of presence or absence of infarction including the early signs. Also, the site of hemorrhage or infarction was also recorded.

To obtain the volume of bleed, slices showing the hemorrhage were individually assessed. The slice with the largest area of hematoma was chosen. Volume was obtained using the formular $ABC/2$ expressed in cm^3 where A is the widest transverse diameter of the bleed, B is the highest vertical diameter and C is the total number of slides with the largest haematoma [19]. [In **Figure 1(a)**, values



(a)



(b)

Figure 1. (a): Vertical (arrow) and transverse (arrow head) measurement of haematoma volume; (b): Sample of some of the slides showing same bleed in (a) above.

A (widest transverse diameter of the bleed corresponds to arrow head) B (the highest vertical diameter corresponds to straight arrow), and C (sum total of slides with bleed from the vertex to the base of skull, **Figure 1(b)**)). For the sum of the slice thickness (C), one was excluded if the hematoma area was smaller than 25% of the larger obtained place. Half of the slice thickness was taking into consideration if the measured area were between 25% and 75% when compared to the largest one.

In ischaemic strokes, area of the infarcted region was obtained. The slice with the largest area of ischaemia was obtained for the measurements. Similarly, measure A corresponds to the greatest diameter of infarction; B to the largest perpendicular diameter to A. The infarcted area was a product of A and B in cm^2 .

2.4. Statistical Analysis

Data analysis was done using Statistical Package for Social Sciences (SPSS) software (version 26.0) for windows. Results were presented as mean \pm standard deviation, percentages, tables and graphs as appropriate. Chi-square was used to determine the relationship between categorical variables. Spearman's correlation was used to determine the correlation between clinical diagnosis and CT findings. p values less than or equal to 0.05 were considered statistically significant.

3. Result

Profile of Patients

A total of one hundred and forty-five patients clinically diagnosed with stroke in our institution underwent brain CT for radiological investigation. One hundred and twenty-two (84.1%) had stroke as confirmed by brain CT. Seven (4.8%) were stroke mimics comprising subdural haematoma, brain atrophy and brain tumour while sixteen (11.0%) brain CT were normal (**Table 1**). Sixty-five (53.3%) of the 122 confirmed stroke patients were males and 57 (46.7%) females with a male: female ratio of 1.1:1, however this was not statistically significant ($p = 0.207$) (**Figure 2**). The mean age at presentation was 58.7 ± 12.87 years with range 17 - 96 year. The age group, 69 - 78 years had the highest frequency of stroke at presentation with 42 (34.4%) cases, followed by 79 - 88 years and 59 - 68 years having 33 (27.0%) and 25 (20.5%) cases respectively. Stroke was noted to be very low below fifty years (**Table 2**).

Out of the 122 confirmed cases of stroke on brain CT, ischaemic stroke was most frequent with 77 (63.1%); primary intracerebral haemorrhage (ICH) 38 (31.4%) and subarachnoid hemorrhage (SAH), 5 (4.1%). When ICH and SAH is combined, haemorrhagic stroke had a frequency of 43 (35.5%). Most infarcted areas were less than 10 cm^2 while bleeds below 10 cm^3 and above 100 cm^3 occurred in equal proportion (**Table 3**). Primary intracerebral haemorrhage was more common among younger age group; however, this was not statically significant ($p = 0.390$) (**Table 4**). Similarly, the individual strokes types comprising

Table 1. CT findings and risk factors in stroke.

CT FINDINGS	frequency	%	p-value
Intracranial haemorrhage	38	26.2	
Ischaemic	77	53.1	
SAH	5	3.4	
mixed	2	1.5	
Subdural haemorrhage	2	1.5	
Senile atrophy	4	2.7	
Brain tumour	1	0.6	
Normal	16	11.0	
Total	145	100.0	
RISK FACTORS			
Hypertension	31	21.4	0.000
Alcohol	2	1.4	
Previous stroke	2	1.4	
TIA	1	0.7	
OTHERS + Hypertension	94	64.8	
OTHERS – Hypertension	13	9.0	
SCD	1	0.7	
Nil	1	0.7	
Total	145	100	

Table 2. Age group and frequency of stroke.

Age groups (years)	True stroke (%)	Mimics (%)	Normal (%)	Total
29 - 38	1 (0.9)	0	0	1
39 - 48	1 (0.9)	0	0	1
49 - 58	7 (5.7)	0	0	7
59 - 68	25 (20.5)	1	5	31
69 - 78	42 (34.4)	0	4	46
79 - 88	33 (27.0)	3	5	41
89 - 98	6 (4.9)	1	2	9
99 - 108	5 (4.1)	2	0	7
>108	2 (1.6)	0	0	2
Total	122	7	16	145

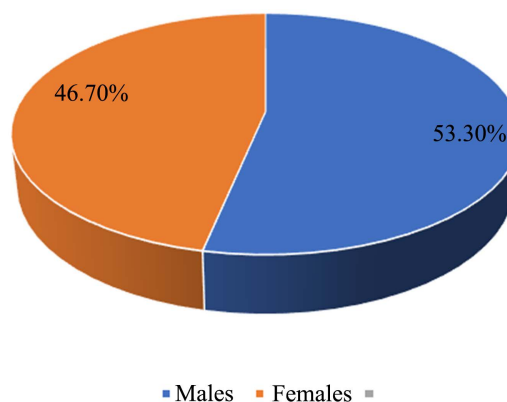


Figure 2. Sex distribution of stroke patients.

Table 3. Size and volume estimation of ischaemic and Intracerebral haemorrhage.

Size/vol. (cm ² /cm ³)	Ischaemic size cm ² (%)	Haemorrhagic cm ³ (%)
<10	31 (21.4%)	6 (4.1%)
11 - 20	8 (5.5%)	-
21 - 30	7 (4.8%)	1 (0.7%)
31 - 40	3 (2.1%)	-
51 - 60	1 (0.7%)	-
71 - 80	1 (0.7%)	1 (0.7%)
>100	2 (1.4%)	6 (4.1%)

NB: Fifty-three images of the stroke patients on study were erroneously deleted on the CT hard drive for haemorrhagic volume and infarct size estimation.

Table 4. Age and Intracerebral haemorrhage volume.

Volume (cm ³)	<10	21 - 30	81 - 90	>100	Total
Age (years)					
59 - 68	3	0	0	3	6
69 - 78	2	1	0	0	3
79 - 88	1	0	1	2	4
89 - 98	0	0	0	1	1

of ischaemic, primary intracerebral haemorrhage (ICH) and subarachnoid haemorrhage (SAH) also followed the same age pattern at presentation with age groups 69 - 78 years recording highest followed by age groups 79 - 88 years and 59 - 68 years but there was no statistical correction ($p = 0.351$).

Hypertension was the major risk factor for stroke occurring respectively with a frequency of 31 (21.4%) and 94 (64.8%) in isolation and when combined with other risk factors including DM, alcohol, smoking, obesity, hypercholesteremia amongst others and this was statistically significant ($p = 0.000$) (**Table 1**).

Most cases of stroke in the study came in with stage 1 hypertension seen in 43 (35.2%) commonly of the age group 69 - 78 years (**Table 5**). Of this group, males were 24 (55.8%) and females 19 (44.2%) (**Table 5**). Extremely high BP was associated with ICH whereas ischaemic stroke and SAH were common in stage 1 and stage 2 hypertension respectively (**Table 5**).

Patients with tertiary education presented earlier than others. Most are within hours 6 (33.4%) and before one week 33 (33.6%) of the onset of symptoms. The less educated and those with no formal education presented late, this was however statistically not significant ($p = 0.844$) as in (**Figure 3**). Majority of the stroke patients, 117 (95.9%) of the 122 were right-handed. All the subtypes of stroke were common in them. No case of SAH was recorded in individuals who were left-handed but this was not statistically significant ($p = 0.011$) (**Table 6**)

Table 5. Age, sex and stroke types with stages of hypertension.

Stage of hypertension	Normal	Pre-hypertension	Stage 1	Stage 2	Extremely high	Isolated BP	Total
Age group (years)							
29 - 38	1	0	0	0	0	0	1
39 - 48	0	0	0	0	1	0	1
49 - 58	2	0	2	0	1	2	7
59 - 68	0	1	6	8	9	2	26
69 - 78	1	5	12	13	8	3	42
79 - 88	0	4	16	16	4	2	32
89 - 98	1	0	3	1	0	1	6
99 - 108	0	1	3	0	0	1	5
>108	0	0	1	0	0	1	2
Total	5	11	43	28	23	12	122
Sex							
Male	4	5	24	11	15	6	64
Female	1	6	19	17	8	6	57
Total	5	11	43	28	23	12	122
Stroke type							
ICH	1	3	10	7	13	3	37
Ischaemic	4	7	33	17	9	8	78
SAH	0	1	1	2	1	0	5
H.Trans.	0	0	0	1	0	1	2
Total	5	11	43	28	23	12	122

Key: H. Trans.: Haemorrhagic Transformation.

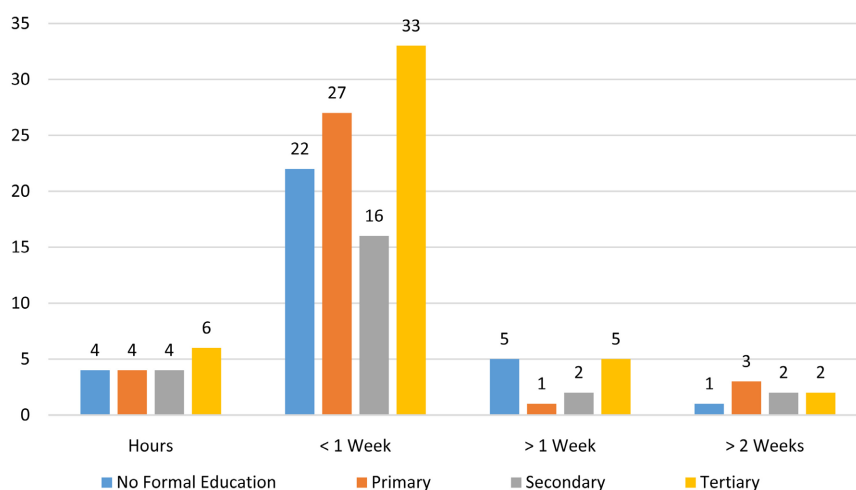


Figure 3. Level of education and time of presentation.

Table 6. Handedness and occupation with stroke types.

STROKE TYPE	Haemorrhagic (%)	Ischaemic (%)	SAH (%)	Mixed (%)	Total
Handedness					
Right	36 (94.7%)	75 (97.4%)	5 (100%)	1 (50%)	117
Left	2 (5.3%)	2 (2.6%)	0	1 (50%)	5
Total	38	77	5	2	122
Occupation					
Farmers	19	32	3	1	64
Drivers	0	2	0	0	2
C/S	8	21	1	0	29
Spiritual leaders	2	0	1	0	3
Students	0	1	0	0	1
Traders	7	13	0	1	21
Others	0	2	0	0	2
Total	36	71	5	16	122

Key: C/S: Civil servants, SAH: Subarachnoid haemorrhage.

Regarding occupation, most of the stroke patients were farmers accounting for 64 (52.0%). Twenty-nine (33.6%) were civil servants and 21 (18.9%) were traders. Only 1 (0.8%) was a student. Both haemorrhagic and ischaemic strokes were noted to be high in the farmers group followed by civil servants and then traders (**Table 6**).

On clinical diagnostic accuracy, there was significant correlation between the clinical and imaging diagnosis of stroke regarding the hemisphere and type ($p = 0.000$ and 0.001) respectively. Sixty-one (42.1%) and 79 (54.5%) cases diagnosed

clinically for right and left respectively of the 122 cases; CT demonstrated 47 (38.0%) and 62 (50.0%) cases on right and left respectively. Similarly, there were 43 (29.7%) clinically diagnosed cases of haemorrhagic, 92 (63.4%) of ischaemic and 5 (3.4%) cases of SAH. On CT, 38 (31.1%), 77 (63.1%) and 5 (4.0%) was obtained for haemorrhagic, ischaemic and SAH respectively (**Table 7**).

4. Discussion

One hundred and twenty-two patients (84.1%) out of 145 who were clinically diagnosed of having had a stroke had brain CT scan confirmation in this study. Acute stroke is an emergency in which treatment decisions are made after carefully considering clinical information and assessing available imaging result to determine whether it is an infarction or a haemorrhage. It will also assist in excluding stroke mimics like subdural haematoma, cerebral abscess and brain tumour etc. [20]. This emphasizes the usefulness of the updated stroke definition that suggested the need for neuroimaging confirmation in stroke diagnosis [3].

Table 7. Correlation between clinical and imaging diagnosis of stroke.

	CLINICAL DIAGNOSIS	IMAGING DIAGNOSIS	p-value
STROKE SIDE			
Right (%)	61 (42.4%)	47 (32.6%)	0.000
Left (%)	79 (54.8%)	62 (43.1%)	
Not sure	4 (2.8%)	-	
H. Trans.	-	15 (10.4%)	
Normal	-	20 (13.9%)	
Total	145	100.0	
STROKE TYPE			
Haemorrhagic (%)	43 (29.9%)	38 (26.2%)	0.001
Ischaemic (%)	92 (63.9%)	77 (53.1%)	
SAH (%)	5 (3.4%)	5 (3.4%)	
Not sure	5 (2.8%)	-	
H. Trans	-	2 (1.5%)	
Subdural haemorrhage		2 (1.5%)	
Senile atrophy		4 (2.7%)	
Brain tumour		1 (0.6%)	
Normal	-	16 (11.0%)	
	145	100.0	

Key: H. Trans.: Haemorrhagic Transformation.

The mean age of the subjects was 58.7 years. Onubiyi *et al.* [21] in the south south region of the country on the pattern of CT findings on stroke patients obtained the mean age of 58.3 years. A study by Obajami *et al.* on one thousand one hundred and seventy-two (1172) stroke patients in Ghana, had a mean age of 55.7 years. Naik *et al.* [22] in their prospective study of CT stroke profile of 150 patients in Eastern Nepal, had a mean age of 58.3 years. The mean ages of the aforementioned studies are not much different from this study.

In this study, males predominated slightly accounting for 53.3% of the study population while females were 46.7% giving a male to female ratio of 1.1:1. This corroborated with similar studies done by Naik *et al.* [22] and that done in the USA by Turtzo *et al.* [23] and El Zein *et al.* [24] which also showed male preponderance in their studies. Similarly, Onubiyi *et al.* [25] obtained male predominance in their cohorts in the southern region of this country with a M: F ratio of 1.1:1. Generally stroke incidence has been reported to be higher in males as compared to premenopausal females [26]. This difference may be due to the effect of the sex steroid hormones. However, once women pass menopause, their rates of stroke are far greater than male rates [27].

Stroke in the young, patients below 50 years of age was found to be uncommon in our study as the risk of stroke occurrence increases with advancing age [28] [29] [30]. Only 1.8% patients in this study were under the age of 48 years. A positive correlation was seen in this study between increasing age and incidence of stroke. This corresponds to the middle age group with higher prevalence of risk factors for cerebrovascular accidents [28]. Previous studies have demonstrated this. Sacco *et al.* [29] reported that age is the single most important risk factor for stroke. Njoku *et al.* [30] in Sokoto, corroborated this, observing that stroke is most commonly seen in those above 40 years which was in agreement with the current study.

We also found that cerebral infarction constituted 63.1% of all cases examined with a CT scan, while haemorrhagic stroke comprising of ICH and SAH constituted 35.2%. This finding is in agreement with previous studies that reported a higher prevalence of ischemic than hemorrhagic stroke in Sokoto north western Nigeria by Garba *et al.* [31], South western Nigeria by Eze *et al.* [32] and South south Nigeria by Onubiyi *et al.* [21]. On the other hand haemorrhagic stroke made up of more than 60% of all stroke in two studies in Ghana [33] and Tanzania. [34] Obajimi *et al.* [22] reported a higher incidence of ICH of up to 52.9% among Ghanaians. Our study also revealed a small proportion of stroke mimics such as extraparenchymal haemorrhages and brain tumours which can only be definitively diagnosed by CT. These findings suggest that the recommendation that CT imaging be carried out in all cases of suspected stroke should be adhered to [35].

Hypertension was the main risk factor encountered in our study accounting for 69.4% of ischaemic stroke and 30.6% of haemorrhagic stroke. This was followed by DM as the second commonest risk factor which accounted for 79.6% and 20.4% of ischaemic and haemorrhagic strokes respectively. This finding is in

agreement with the study by Sagui *et al.* [36] in Dakar Senegal which also showed Hypertension and DM to be the main and the second risk factors associated with strokes in that region. Globally, hypertension is the most prevalent risk factor for stroke [4] [37] [38]. There is robust evidence that screening and treatment of hypertension is beneficial and reduces the risk of stroke and its associated morbidity and mortality [39].

In our study, brain infarction was commonly found in the frontal lobe (%) followed by the parietal lobe (%) while ICH was mostly found in the basal ganglia (%) followed by the parietal lobe (%). These findings were close to the work of Ijeh-Terila *et al.* [40] who reported ischaemic infarct to be located more in the parietal lobe and ICH stroke occurring in the basal ganglia. In ICH bleeding occurs directly into the brain parenchyma which is thought to be due to leakage from small intracerebral arteries damaged by chronic hypertension and has a predilection for the thalamus, basal ganglia, cerebellum, and brainstem in that order [20].

About 50.0% of the patients had CT confirmed left hemispheric stroke (LHS) while 38.0% was located on the right hemisphere with a left sided preponderance. A previous study had reported a LHS of 60.1% [41]. LHS may present clinically with right sided limb weakness, impaired sensation, expressive or receptive aphasia and visual problems. On the other hand, a right-sided hemispheric stroke (RHS) could present with hemi-spatial neglect which is characterized by reduced attention or spatial awareness of the body and environment on the hemiplegic/hemiparetic side. However, LHS was found to determine functional recovery and post-stroke complications related to walking ability and language deficit which could ultimately hamper rehabilitative effort [42].

On the correlation of clinical assessment with brain CT finding; there were 42.1% and 54.5% cases diagnosed clinically to occur on the right and left respectively which on imaging 38.0% and 50.0% was obtained on right and left respectively. Similarly there were 29.7% clinically diagnosed cases of haemorrhagic, 63.4% of ischaemic and 3.4% cases of SAH. On CT, 31.1%, 63.1% and 4.0% was obtained for haemorrhagic, ischemic and SAH respectively. There was a fairly acceptable correlation between clinical diagnosis in terms of side of lesion and stroke subtype. A previous study had reported poor reliability in clinical diagnosis as compared to CT scan [43]. Brain CT scan is reliable and will help to confirm stroke diagnosis, determine stroke subtype as well as accurately help identify stroke chameleons presenting with uncommon clinical features.

This study also revealed that patient's educational level affected their time of presentation from onset of symptom and possible health seeking behavior as more proportion of those with tertiary education presented within hours in 33.4% and before one week in 33.6% after the onset of symptoms. Factors noted to contribute to poor stroke outcomes in LIMCs include the challenge of late presentation and poor health seeking behavior of the populace [44] [45]. A study that evaluated the time of presentation of stroke patients for CT imaging at University College Hospital Ibadan found that none of their patients met the

time criteria for thrombolytic therapy among those with ischemic stroke presenting for neuroimaging. They suggested the need to increase awareness regarding early recognition, presentation and diagnosis of stroke for timely intervention [46].

5. Conclusion

We found slight male preponderance with majority having ischaemic stroke on the left hemisphere. There was significant correlation between the clinical and radiologic diagnosis. Generally, most patients presented late after symptom onset which appeared to be mitigated by higher level of educational attainment. We also emphasize the need for both thorough neurologic assessment and early brain CT scan in making diagnosis and instituting appropriate stroke therapy.

6. Limitations

Our study is a retrospective hospital-based study and hence the possibility of missing and incomplete data cannot be ruled out. Also, it may not be a true representative of stroke cases in the community as only those who presented to our facility were recruited. However, it has highlighted the correlation between the clinical and radiologic characteristics of stroke patients presenting in our hospital.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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