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EVALUATION OF STROKE PATIENTS' PRIME AND CONTRIBUTORY RISK FACTORS FOR RECURRENT STROKE: AN IDENTIFICATION OF NEWER AREAS OF PHARMACEUTICAL CARE NEEDS TO AVOID FURTHER STROKE EPISODES

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ABSTRACT

Background: The determination of patients' individual risk factors for transient ischaemic attack (TIA), stroke and recurrent stroke (RS) in hypertension with existing stroke is desirable in order to institute appropriate preventive measures and treatment monitoring approaches that will prevent recurrent stroke episodes. **Objectives:** The objectives of the study were to identify patient-focussed prime and contributory risk factors having the potential of causing recurrent stroke and to determine the number of such risk factors in individual patient. **Methods:** A total of 156 patients who have witnessed at least one episode of stroke were evaluated for prime risk factors for recurrent stroke. The most recent laboratory data were obtained from their folders during clinic visits and were used to evaluate individual's total cardiovascular and non-cardiovascular risk factors burden for recurrent stroke. **Results:** The mean and the standard deviation of the study population irrespective of gender was 61.2 ± 10.78 years. The incidence of stroke peaked in patients in their sixth decades of life (51-60 year). The mean ages and standard deviations for male and female patients were 61.7 ± 11.2 years and 59.8 ± 9.77 years respectively. The incidence of stroke related illness is 1.89 higher in male than female. Time interval between hypertension diagnosis and development of stroke in most patients 66(42.3%) was 5-10 years with few patients 26(16.7%) developing stroke after 15 years post hypertension diagnosis. In 77(48.7%) patients only hypertension exist without co-morbid disease conditions while 79(51.3%) had various co-morbid conditions such as diabetes 24(15.4%), chronic kidney disease 20(12.8%), obesity 11(7.1%) and so on. The stroke related illnesses were TIA 25(21.2%), ischaemic stroke 83(53.2%), haemorrhagic stroke 15(9.6%), and recurrent stroke 33(26.2%). The risk factors identified ranges from 1-7 with a cumulative value of 621 and a risk factor average of 3.98. About 75(48.1%) patients have 1-3 different types of risks while 81(51.9%) have total risk factors ≥4. prime risk factors identified in the study or considered high are smoking 15(9.6%), fasting blood sugar 14(19.7%), TIA 25(16.0%), uncontrolled blood pressure 133(85.3%). Other modifiable risk factors that may contribute to the development of recurrent strokes are low potassium level 11(8.3%), low packed cell volume 74(50.7%). **Conclusion:** Several vascular risk factors capable of triggering another stroke episode such as hypertension, hyperlipidaemia, current smoking, dyslipidaemia, low packed cell volume and some non-vascular risk factors including low potassium levels were still observed present in high proportions in most patients. This underscore the need to keenly monitor such individual's health and drug therapy and institute appropriate individualized patient education and care in order to limit or prevent further episode of stroke.

KEYWORDS: Hypertension, stroke, recurrent stroke, risk factors.

INTRODUCTION

Despite improved knowledge in the diagnosis of hypertension or other related illnesses, and many available drugs and non-drug options in their managements, many patients still come down with stroke and recurrent strokes episodes, transient ischaemic attacks as complication or progression of the disease.

Hypertension (HTN) one of the major causes of stroke is worldwide disease, which affect great proportion of populace and with high potential for several other complications that are similarly associated with high morbidity or mortality. The illness cause great health challenge and a great deal of cost to the society as it places tremendous burden on the health resources throughout the world. Poorly or uncontrolled hypertension is one of the prime factors responsible for

stroke in the populace.[1] Stroke often present with the symptoms and signs of focal and loss of cerebral functions[2] and is a frequent cause of major morbidity and mortality after ischemic heart disease and cancer.

Hypertension is often associated with many illnesses such as ischemic heart disease or Stroke, peripheral vascular disease or other cardiovascular diseases like heart failure, aortic aneurysm, diffuse atherosclerosis and pulmonary embolism since it is one of the major risk factors for these conditions.[3,4,5] Hypertension has long been identified as an important risk factor for brain infarction and haemorrhage[6] and may cause other structure and functional changes like left ventricular hypertrophy and hypertensive heart disease conditions.[7]

Cerebrovascular accident (**s**troke) is one of the cerebral complications of untreated or poorly managed hypertension, which manifest as loss of the brain functions, or disturbance in the blood supply to the brain leading to blockage, thrombosis, arterial embolism or haemorrhage[8]. Stroke affects limbs movement, speech understanding or its formulation as well as one side of the visual field,[9] and is often associated with permanent neurological damage, complications, and death.[9]

Many factors can cause stroke conditions like old age, high blood pressure, previous stroke or transient ischemic attack (TIA), diabetes, high cholesterol, tobacco smoking and atrial fibrillation increases the risks for developing stroke are well established as risk factors for stroke.[9] Ischemic stroke result from decrease in blood supply to part of the brain is decreased, leading to dysfunction of the brain tissue in that area.[10] Therefore the use of thrombolytic agents are important in ischaemic stroke but patients with haemorrhagic strokes may benefit from neurosurgery while the prevention of recurrence of stroke may involve the administration of antiplatelet drugs such as aspirin, clopidegrel or dipyridamole. The control or reduction of high blood pressure, and the use of statins as well as removal of other risk factors are primary preventive measures of recurrent stroke. Systemic hypo-perfusion due to general decrease in blood supply and venous thrombosis may all result into stroke.[11,12] Cryptogenic stroke which constitutes about 30-40% of all ischemic strokes have an unknown cause.[13]

Stroke causes major disability because the illness affects the brain stem and brain to produce symptoms relating to deficits in cranial nerves: which altered smell, taste, hearing, or vision (total or partial)/drooping of eyelid (ptosis) and weakness of ocular muscles, decreased reflexes: gag, swallow, pupil reactivity to light, decreased sensation and muscle weakness of the face, balance problems and nystagmus, altered breathing and heart rate, weakness in sternocleidomastoid muscle as well weakness in tongue.[14] The involvement of the cerebral cortex can further lead to aphasia, auditory comprehension while the reading and/or writing Broca's or Wernicke's area typically involved, dysarthria, apraxia, visual field defect, and memory deficits etc.[8] Alterations in walking gait, altered movement coordination, and vertigo and or disequilibrium are possible when cerebellum is affected.[8] Other symptoms like loss of consciousness, headache, and vomiting are observed in haemorrhagic stroke than in thrombosis because of the increased intracranial pressure from the leaking blood compressing the brain.[9]

Many lifestyle modifications are adopted to reduce stroke. Nutrition, specifically the Mediterranean-style diet, has the potential for decreasing the risk of having a stroke by more than half.[15] Excessive salt intake and fatty food are required to be modified since they can cause high blood pressure and consequently stroke.

MATERIALS AND METHOD

This cross-sectional descriptive study was conducted at the departments of Cardiology, Neurology and Nephrology units of the University of Maiduguri Teaching Hospital, Maiduguri, Borno, state, Nigeria. The hospital is located in the north eastern Nigeria dominated by the Kanuri, Babur, Bura and Shuwa Arab ethnical groups. Ethical clearance was sought for and granted by the relevant authority of the hospital. A total of 156 patients comprising 102 males and 54 females who experienced stroke were studied. The most recent laboratory data and other information such as pack cell volume and serum potassium, duration of diagnosis of hypertension, duration between diagnosis of hypertension to stroke episode, concomitant diseases and cardiovascular risk factors of stroke like cigarette smoking, alcohol consumption, fasting blood sugar, lipids level, and family history of stroke were obtained from patient and were evaluated to find the burden of individual risk factors that may trigger recurrent stroke episode. The data generated were analyzed using statistical package for social science (SPSS).

RESULTS

Cardiovascular and other risk factors having the potential of causing recurrent strokes were evaluated in 156 patients comprising 102 (65.4%) males and 54 (34.6%) females with age ranges 45-87 years who experienced episode(s) of stroke and transient ischaemic attack. The mean and the standard deviation of the study population irrespective of gender was 61.2 ± 10.78 years. The incidence of stroke peaked in patients in their sixth decades of life (51-60 year). The mean ages and standard deviations for male and female patients were 61.7 ± 11.2 years and 59.8 ± 9.77 years respectively. The incidence of stroke related illness is 1.89 higher in male than female (Table 1). Time interval between hypertension diagnosis and development of stroke in most patients 66(42.3%) was 5-10 years with few patients 26(16.7%) developing stroke after 15 years post hypertension diagnosis (Table 3). While 77(48.7%) patients have hypertension only without other co-morbid disease

conditions, about 79(51.3%) had various co-morbid conditions such as diabetes 24(15.4%), chronic kidney disease 20(12.8%), obesity 11(7.1%) and so on (Table 4). The distributions of stroke related illnesses were TIA 25(21.2%), ischaemic stroke 83(53.2%), haemorrhagic stroke 15(9.6%), and recurrent stroke 33(26.2%) (Table 5). Most patients 76(88.4%) with ischemic stroke were placed on low dose of acetylsalicylic acid as part of the medication to prevent recurrent stroke (Table 6).

The risk factors identified in the study ranges from 1-7 with a cumulative value of 621 and a risk factor average of 3.98. About 75(48.1%) patients have 1-3 different types of risks while 81(51.9%) have total risk factors ≥4 (Table 7).

Low HDL cholesterols were identified in a few proportion 2(1.3%) of patients evaluated but high LDL-cholesterols were observed in 31(23.8%)(Table 8). Triglycerides were high in 44(29.1%) cases. Other prime risk factors identified in the study or considered high are smoking 15(9.6%), fasting blood sugar 14(19.7%), TIA 25(16.0%), uncontrolled blood pressure 133(85.3%). Other modifiable risk factors that may contribute to the development of recurrent strokes are low potassium level 11(8.3%), low packed cell volume 74(50.7%), and alcohol consumption 46(29.5%). Family history of stroke was positive in 34(21.8%) patients.

Table 1: Age and gender distribution of patients.

Age	Male	Female	Total (%)
< 40 years	0	0	0 (0)
40-49 years	14	7	21(13.5)
50-59 years	40	12	52(33.3)
60-69 years	35	15	50(32.1)
70-79 years	18	7	25(16.0)
80-89 years	8	0	8(5.1)
TOTAL	115	41	156(100)

Table 2: Duration of Diagnosis of Hypertension.

Duration (Years)	Frequency	Percentage (%)
1.0-2.0	13	8.3
2.1-5.0	17	10.9
5.1-10.0	52	33.3
10.1-15.0	25	16.0
15.1-20.0	5	3.2
20.1-25.0	20	12.8
25.1-30.0	10	6.4
30.1-35.0	7	4.5
unknown	7	4.5
TOTAL	156	100

Table 3: Time Interval Between Hypertension Diagnosis and Stroke Episode.

Duration (Years)	Frequency	Percentage (%)
1.0-5.0	42	26.9
5.1-10.0	66	42.3
10.1-15.0	15	9.6
15.1-20.0	10	6.4
20.1-25.0	16	10.3
25.1-30.0	0	0
Unknown	7	4.5
TOTAL	156	100

Table 4: Comorbid diseases of patient who experienced stroke.

Co-morbid Diseases	Frequency	Percentage
Hypertension only	76	48.7
HTN with Diabetes	24	15.4
HTN with CKD	20	12.8
HTN with Obesity	11	7.1
HTN with Others	25	16.0

TOTAL	156	100

Table 5: Types of stroke episode.

Type of strokes	Male	Female	Total (%)
Ischaemic	59 (37.8%)	24 (15.4%)	83 (53.2%)
Haemorrhagic	11 (7.1%)	4 (2.6%)	15 (9.6%)
TIA	9 (5.3%)	16 (10.3%)	25 (16.0%)
Recurrent	23 (14.7%)	10 (6.4%)	33 (21.2%)
Total	102 (65.4%)	54 (34.6%)	156 (100%)

Table 6: Medication used by Hypertensive/stroke patients.

Drugs	Frequency	Percentage (%)
Captopril	22	25.6
Amilodipine	56	65.1
Vasoprin	76	88.4
Frusemide	33	38.4
Valsatan	10	11.6
Bendroflorothiazide	34	39.6
Atenolol	37	43
Hydralazine+amilod	16	18.6
Vitamin E	47	54.7
Spinorolactone	20	23.3
Lisinopril	45	52.3

Table 7a: Number of Risk Factors of patients.

No. of Risk Factors	No. of Patient(s)	Percentage (%)	Cumulative	Percentage (%)
1	1	0.6	1	0.16
2	24	15.2	48	7.73
3	50	32.1	150	24.2
4	28	18.0	112	18.0
5	22	14.1	110	17.7
6	17	10.9	102	16.4
7	14	9.0	98	15.8
Total	156	100	621	100

Table 7b: Risk factors classification.

Risk Factors description	No. of Patient(s)	Percentage (%)
Prime modifiable risk factors	395	63.6
Prime un-modifiable risk factors	136	21.9
contributory modifiable factors	90	14.5
TOTAL	621	100

Table 8: Laboratory Parameter/Risk assessment of patients with stroke.

S/No.	Parameter assessed	Status	Frequency	Percentage (%)
1.	HDL-C (n=156)	Low	2	1.3
		Normal	133	85.3
		High	21	13.5
2.	LDL-C (n=130)	Low	1	0.77
		Normal	98	75.4
		High	31	23.8
3.	Triglyceride (n=151)	Low	4	2.65
		Normal	103	68.2
		High	44	29.1
4.	Potassium level (n=133)	Low	11	8.3
		Normal	93	69.9

		High	29	21.8
5.	Packed Cell Volume (n=146)	Low	74	50.7
		Normal	60	41.1
		High	12	8.2
6.	Smoking status (n=156)	Non-smoker	116	74.4
		Ex-smoker	25	16.0
		Smoker	15	9.6
7.	Alcohol drinking (n=156)	consumer	46	29.5
		Non-consumer	110	70.5
8.	Family History of Stroke/TIA (n=156)	Positive	34	21.8
		Negative	122	78..2
9.	Blood Pressure (n=156)	Normotensive	3	1.9
		Pre-hypertensive	20	12.8
		Hypertensive	133	85.3
10.	Fasting Blood sugar (n=71)	Within normal	46	64.8
		Impaired	11	15.5
		Diabetic range	14	19.7
11.	TIA (n=156)	Experienced	25	16.0
		Not Experienced	131	84.0
12.	Haemorrhagic Stroke (n=156)	Experienced	15	9.6
		Not Experienced	141	90.4
13.	Ischaemic stroke (n=156)	Experienced	83	52.3
		Not Experienced	73	47.7
14.	Recurrent stroke (n=156)	Experienced	33	21.2
		Not Experienced	123	78.8
15.	Gender (n=156)	Being male	102	65.4
		Non-male	54	34.6

Key: HDL-C= High density lipoprotein cholesterol, LDL-C= Low density lipoprotein cholesterol, TIA= Transient Ischaemic attack.

DISCUSSION

Cardiovascular and other risk factors having the potential of triggering recurrent strokes in patients who have experienced first episodes of stroke were evaluated. A very high proportion of stroke occurred in patients who are within the age band of 50-70 years. The preponderance of stroke in both genders above 50 years in this study is consistent. The result further showed that peaked stroke prone age for male patients occurred in those who are in their sixth decade of life 50-59 years in males and 60-69 years in females. Although this is consistent with many studies.[16]

The female to male ratio for the development of stroke is 1:1.89. According to a report, life expectancy is longer for women and women are older than men at stroke onset.[16] The study by Mozaffarian and associates.[17] showed that stoke incidence is higher in men than women in those above 60 years. Although many males develop hypertension than females, but stroke episodes are reported to be slightly higher in the females than the males.[18] This is in contrast to the findings in this result. Many factors may have influenced this observed pattern. Although the estimated risks for hypertension (one of the prime causes of stroke) is estimated to be 90% for men compared with their female counterparts,[19] many other factors including socio-economic and environmental factors, variation in vascular risk factors such as PAD, DM, smoking, and alcohol consumptions, which affect more men than women.[20] may account for this observed differences between the two genders. In both genders, incidence rates were lower in those below 60 years compared to those above 60 years, and cases of stroke were not recorded in both genders in those below 40 years of age which contrast report of cases. However, the value recorded in those in their fifth decades of life alone is higher than the value reported in adult ≥18 years to 50 years in one study.[21]

As observed, most people with stroke have their hypertensive status diagnosed within 5-10 years. According to Buck and colleagues,[22] the 5 years risk for cardiovascular complications compared with the normotensive subjects of similar age is inversely related to the age of onset.

The duration of diagnosis of stroke episode in patients (Table 4) showed increased recent cases of stroke (1-5 years) and decreases thereafter because usually mortality increases with age. Although increase cardiovascular risk factors as well as non-compliance to medications can result into early development of complications like stroke, most patients must have poorly being monitored and/or educated on the disease. These results may have suggested that the episode of stroke is high associated with high mortality in the region judging with the low incidence with increasing age post diagnosis. The rising

trend may also be attributed to the problem of insurgence that existed during the period of the study during which both patients access to healthcare facilities and service delivery was poor in addition to the direct health negative consequences that insurgence can cause.

The duration between the diagnosis of hypertension and stroke episode showed that the time between diagnoses of hypertension to the time of first episode of stroke in most of the people studied is between 5-10 years. This pattern may be influenced by several interplay of factors including those of non-compliance to medications, variation in cardiovascular risk factors and several others patient specific characteristics such as their attitude and knowledge towards the disease. Although the higher the risk factor, the higher the chances of developing complications, the chronic nature of hypertension and the apparent symptomless nature of the disease may be perceived by most patients as having the illness under control particularly in those who have not been adequately educated on the disease matter. This result is however slightly higher than similar stroke episode reported by Buck and colleagues.[22]

The comorbid diseases in patients with stroke also showed that hypertension alone when untreated can lead to stroke in a large proportion of patients but other comorbid conditions like diabetic mellitus, chronic kidney disease, obesity, arthritis, cardiac arrhythmias, congestive heart failure and myocardial infarction either act as cardiovascular risk factors or may be a contributory factor towards the development of stroke. According to Whisnant [23], high blood pressure accounts for 35-50% of stroke. There is also a linear relationship between stroke and hypertension but treating hypertension will decrease incidence of stroke. Lowering blood pressure has been conclusively shown to prevent both ischemic and haemorrhagic strokes[24]. Some authors have similarly reported that blood pressure reduction of 10 mmHg systolic or 5 mmHg diastolic reduces the risk of stroke by about 40%[25]. Our result however indicated that attention should also be paid to other comorbid conditions of patients as well as educating them on the consequences of comorbid diseases. The proportion of hypertensive patients in this study is a little lower than the 52% of stroke patients with hypertension and lower than the 18% cases of hyperlipidaemia as well as the 46% cases of current smokers reported by Kisella and associates.[26]

Ischaemic stroke was the predominant form of stroke in this study accounting for more than half of the study group. This is lower than the 68.6% reported by Kisella and associates.[26] in those between 20-54 years.

The drug therapy management of patients with stroke or its primary cause is as shown in Table. The result shows that very high proportion (88%) of patients on low dose aspirin for the prevention of stroke recurrence. The agent is potent antiplatelet drug which prevents blood clotting thereby preventing the formation of emboli or thrombi that may potentially cause blockage of the cerebral blood vessel, and hence preventing stroke episode especially ischemic.[27] The agent also has cardio-protective properties in patients.

Many individuals with low potassium levels may be at risk of further stroke episode and therefore will require more attention.

The potassium status of most patients are within the normal range while in many patients their potassium status are below normal range with others having hyperkalaemia. Many researchers have reported that people with low potassium in their diets could be more likely to be at risk of developing stroke than individuals with adequate potassium intake and stroke episodes as well as mortality arising from it have been demonstrated to show positive association with low serum potassium levels [28]. Furthermore, high intake of potassium in diets is associated low risk of all stroke and ischaemic heart attack.[29]

The low PCV of some patient with stroke may be indicative of being at risk for further stroke episode. Close to half of the study population with stroke related illness are having low pack cell volume. Anaemia has been shown to have high risk of developing stroke or contributing to it.[30] The Framingham study[31] has shown that haematocrit level can make significant contribution to the risk of stroke and TIA. The study therefore, identified a high proportion of individuals with low PCV or who are anaemic requires interventions.

Hypercholesterolemia (dyslipidaemia) is one of the major cardiovascular risk factors in the development of stroke and recurrent stroke. In this study, a small proportion of the studied population have low level of high density lipoprotein, more than one-fifth have high levels of low dense lipoprotein cholesterol (LDLC) and a little below one-third have high levels of triglycerides. The trio of high levels of LDLC, low levels of HDLC and high levels of triglyceride can cause increase in stroke incidence and high total cholesterol levels have also been consistently associated with ischemic stroke.[32] All these group of patients therefore require immediate attention in order to limit or avoid recurrent stroke episode.

High level of blood glucose concentrations is another major factor to the development of stroke or recurrent stroke in patient who have had a previous episode. Although close to two-third of the population have normal blood glucose concentrations, about one-fifth of the patients are at the diabetic range while a good number of others have an impaired glucose concentration (Table 8). Diabetes mellitus increases the risk of stroke by 2 to 3 times. While intensive control of blood sugar has been shown to reduce micro-vascular complications such as nephropathy and retinopathy as well as reduce

macro-vascular complications such as stroke.[14] Aggressive control of blood pressure and blood sugar level is always advocated when the two disease conditions co-exist since they both accelerate risks of complications or disease progression. Our results indicated that one-quarter of the study population may benefit from patients education as part of patients focused goals in pharmaceutical care, and well are requiring adequate therapy monitoring in order to prevent recurrent stroke. Blood pressure levels after a stroke episode is a major factor for stroke control. Some studies have shown that there is a direct relationship between stroke and hypertension.[33]

Both alcohol intake and cigarette smoking are modifiable risk factors that can lead to stroke and recurrent stroke episode. Alcohol use could predispose to ischemic stroke, and intra-cerebral and subarachnoid haemorrhage via multiple mechanisms such as hypertension, atrial fibrillation, rebound thrombocytosis and platelet aggregation and clotting disturbances.[34] Alcohol is responsible for 30% cases of hypertension leading to stroke in one study.

This present study identified a good number of patients who drinks or smoke cigarette prior to their stroke episode or still engaged in similar habits post-stroke episode. Both substances can cause addiction and therefore require patients' education through limit risk associated with them. Patients who are Current smokers have a 2 to 4 times increased risk of stroke compared with non-smokers or those who have quit for >10 years[35,36] as well as impact the effect of other stroke risk factors on stroke risk, particularly its synergistic effect with SBP.[37] Even second-hand smoke is viewed as a risk factor for stroke. Other studies have demonstrated that cigarette smoking is a risk factor for ischemic stroke and SAH.[35,36,38] Cigarette smoking increases blood pressure by increasing cardiac output.[39]

Several non-modifiable risk factors for stroke and recurrent stroke were also observed with several patients. For example, the family history of stroke in patients (Table 7) showed that more than one-fifth of the study population have positive family history of stroke. Family members may have a genetic tendency for stroke or share a lifestyle that contributes to stroke.[40] Having had a stroke in the past greatly increases one's risk of future strokes. Even though this factor is fixed, but the overall cardiovascular risk of these patients can be minimized when other modifiable risk factors are controlled.

The evaluation of the past medication history of these stroke patients showed a very high proportion have previously shown non-compliances to medication. Lowering blood pressure has been conclusively shown to prevent both ischemic and hemorrhagic strokes.[14] which can only happen if patients are compliant with medications. This high percentage as observed may be due to patient's attitude towards medication, knowledge and understanding of the disease or availability of the drugs. Even among patients (5.1%) who claimed to have shown good compliance history still develop stroke possibly as a result of resistant hypertension, unmodified lifestyle, or poor quality of drugs etc. There is need for pharmaceutical care in all patients regarding to improve compliances so as to prevent recurrent stroke.

The summary of cardiovascular risk factors is as shown in Table 8. The results showed that majority of patients have 3 risk factors while about 18 patients have as high as 8 risk factors. The assessed risk factors include age, gender, cigarette smoking, alcohol consumption, family history of stroke, high blood pressure, diabetes mellitus, and high level cholesterol. Patient with all the eight risk factors from the study is at greater risk of developing stroke than that with one.

CONCLUSION

Several vascular risk factors capable of triggering further stroke episodes such as hypertension, hyperlipidaemia, current smoking, low packed cell volume and some non-vascular risk factors including low potassium levels are still present in high proportions in most patients who have witnessed stroke episode. This underscore the need to keenly monitor such individual's health and drug therapy and institute appropriate individualize education and care in order to limit or prevent further episode of stroke.

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