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FREQUENCY OF RISK FACTORS FOR STROKE IN YOUNG PAKISTANI POPULATION

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ABSTRACT

Background and Objective:

There is paucity of data regarding risk factors of stroke in young Pakistanis. The objective of this study was to identify the frequency of risk factors for ischemic stroke in the young Pakistani population.

Methods:

This was a retrospective Cross sectional study conducted at Aziz Fatima Hospital Neurology outpatient's department between January 2022 to April 2022. All patients presenting with an ischemic stroke within the past month and age between 20 and 49 years were included. Data was collected from patient notes using a table which listed the patient's demographic information and risk factors. All the patients had appropriate investigations on site to look for cardiac and vessel abnormalities along with relevant blood tests. The results were then assessed using univariate analysis to divide patients according to age, gender and prevalence of risk factors.

Results:

A total of 53 patient's data was collected. The mean age was 39 years. The commonest risk factor was hypertension (58%). The other important risk factors were diabetes mellitus (34%), dyslipidemia (26%), ischemic heart disease (22%), smoking (21%), large vessel occlusion (7%), atrial fibrillation (5%) and vasculitis (4%). Positive family history of stroke was found in 26%.

Conclusion:

Hypertension was the commonest risk factor for young age group under 50 years, followed by diabetes mellitus. Our younger population also had a higher frequency of causes like dyslipidemia, ischemic heart disease and smoking.

Keywords: Stroke, Young, Risk factors

INTRODUCTION

Stroke is defined as 'rapid development of a neurological deficit secondary to a disturbance of cerebral function, which can last more than twenty-four hours and has no apparent cause other than that of vascular origin.[1] It can usually present with a sudden weakness or sensory impairment of the face, arm, or leg, usually on one side of the body. Less common presentations include speech and visual disturbances or impaired co-ordination. It is a major health issue, since it is the second commonest cause of mortality and disability worldwide with an estimated global cost of USD 721 billion.[2] It can have devastating consequences on patients and their careers, especially if it occurs in the younger working age population. Stroke can be broadly divided into ischemic strokes, which make up the majority of cases and haemorrhagic strokes. The peak age of ischemic stroke occurrence is 55–65 years. Whilst older age group patients make up the majority of cases, younger age group patients i.e. under 50 years, make up an important cohort since they need a thorough workup due to the varied causes of stroke which need to be looked at apart from the conventional ones.[3,4]

Traditionally modifiable vascular risk factors have been associated with stroke occurring in the older age group whereas non-modifiable risk factors, like congenital and autoimmune disorders, are associated with increased risk of stroke in the young, as is well evident by previous researches. The presence of traditional modifiable vascular risk factors in young adults presenting with an acute ischemic stroke was debatable, however, the outlook regarding this seems to be changing due to a change in lifestyle choices globally which put younger people at increased risk of developing vascular risk factors.[5] Although there has been an increased awareness over the past decade regarding the importance of addressing modifiable lifestyle-related risk factors for prevention of stroke in the young age group, the focus of research has been mainly concentrated in developed western countries. In recent years, as a result of economic development in developing countries there has been a noticeable shift from poverty related illness towards chronic atherosclerotic diseases.[6] There is a lack of data regarding the impact of these diseases on the increased risk of stroke in the younger age group, especially in Pakistan, where there have been no large studies conducted looking the frequency of various risk factors for stroke in the young population.

We have therefore conducted a study of young patients presenting with a diagnosis of acute ischemic stroke to the Neurology department at Aziz Fatima Hospital with the aim of identifying the commonest risk factors for stroke in young patients amongst the local population. This will aid in the earlier screening and better management of risk factors for this population cohort, thus reducing the overall morbidity and mortality rate in our local population.

METHODS

This was a retrospective cross-sectional study which used temporal sampling methods to assess patients over a time period of four months, from January 2022 to April 2022. It included all young patients who presented with an acute ischemic stroke to the outpatient Neurology clinic at Aziz Fatima Hospital, Faisalabad, a tertiary Neurosciences Centre and the main teaching site of Aziz Fatima Medical and Dental College. The research proposal was submitted to Aziz Fatima Medical and Dental College research and ethics committee who approved the study (Ref: IEC/202-22). The patients included were within age range of 20 to 49 years with no previous history of neurological deficits and had an ischemic stroke confirmed by magnetic resonance imaging studies of the brain (with diffusion weighted imaging and ADC mapping). Younger stroke patients i.e. less than 20 years age and patients above 50 years of age or patients with head trauma and brain injury were excluded from this study. Patients with incomplete data were also excluded from the study. Data was collected using the patient's clinical notes, including previous discharge summaries and investigation reports with the aid of a table which listed the patient's age, gender, diagnosis, presence of a family history of stroke, vascular risk factors, presence of cardiac abnormalities e.g atrial fibrillation or patent foramen ovale, carotid/cerebral vessel abnormalities and results of a vasculitis screen. All the patients had an on-site echocardiogram and carotid/transcranial Doppler imaging performed by an experienced cardiologist and sonologist respectively. CT angiography was performed, where necessary, for vessel imaging abnormalities at Aziz Fatima hospital and all the blood test results were taken from Aziz Fatima hospital laboratory.

The Operational Definitions used were a resting blood pressure of >140/90 on two separate occasions for hypertension.[7] Diabetes mellitus was taken as Hba1c >6.5 or two-hour plasma glucose (2-h PG) >200 mg/dL during a 75-g oral glucose tolerance test.[8] Obesity was defined as BMI greater than 25kg/m^2.[9] Dyslipidemia was defined as total Serum cholesterol >200mg/dl, Triglycerides > 150mg/dl, low-density lipoprotein (LDL) >130 mg/dl and high-density lipoprotein (HDL) <40 mg/dl.[10] Smoking history was considered positive if greater than one pack year.[11] Ischemic heart disease was labeled when history of angina, ECG changes consistent with ischemia or echocardiogram showing evidence of ischemic wall damage were present. Large vessel occlusion was used for carotid and cerebral vessel stenosis of >50% on Carotid transcranial doppler studies.

Statistical analysis was done on SPSS 26 version. Continous variables were presented as mean ± age. Categorical variable were presented as frequencies and percentages. Proportions were compared by chi cquare test.

RESULTS

A total of 53 patients' data was collected. From the total population, 52.8% were male and 47.2% were female patients whilst mean + SD of age was 39.17+7.66 years. Table 1 shows the basic information of study population. Figure 1 depicts the

types of stroke classified according to vascular territories affected, the most common being a left middle cerebral artery infarction followed by a right middle cerebral infarction in our patients.

Table 1: Basic Characteristics of study population (n=53)

Variable	Categories	Frequency	Percentage
Gender	Male	28	52.8
	Female	25	47.2
Family History	Negative	39	73.6
	Positive	14	26.4
Age in years	20-29	7	13.2
	30-39	13	24.5
	40-49	33	62.3

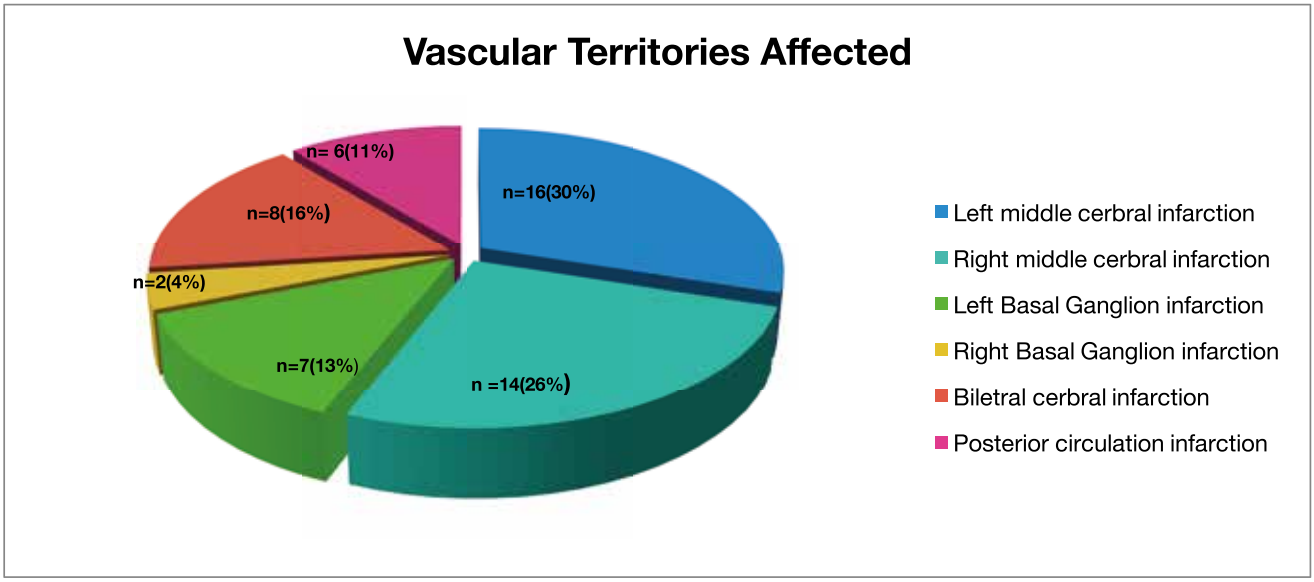

Figure 1: Stroke classification according to vascular territories affected (n=53)

Risk factors for stroke in our study population are presented in Figure 2. Upon analysis of the risk factors among the various age groups we noticed that the commonest risk factor for the youngest age group ranging from 20 to 29 years was again hypertension similar to all other age groups and smoking was seen in a higher percentage of cases in this age group. None of the stroke patient from this youngest age group had diabetes mellitus, however it was present amongst the other two age groups ranging from 30 to 39 and 40 to 49 years as shown in Table 2. During the analysis, we also noticed an interesting and rare finding in that the data showed an equal percentage i.e 14.1 % of stroke patients within the 20 to 29-year age group had vascular occlusion and ischemic heart diseases.

Table 2: Sorting Of Risk Factors for Stroke among Age Groups of Study Population (n=53)

Age n(%)	Family History n(%)	Dyslipidaemia n(%)	HTN n(%)	DM n(%)	AF n(%)	IHD n(%)	Smoking n(%)	LVO n(%)	Vasculits n(%)
20-29 7(13.2)	3(42.9)	00	3(42.9)	00	00	1(14.3)	3(42.9)	1(14.3)	00
30-39 13(24)	5(38.5)	1(7.7)	8(61.5)	1(7.7)	1(7.7)	2(15.4)	3(23.0)	1(7.7)	00
40-49 33(62)	6(18.2)	13(39.4)	2(60.6)	17(51.5)	2(6.1)	9(27.3)	4(12.1)	2(6.1)	2(6.1)

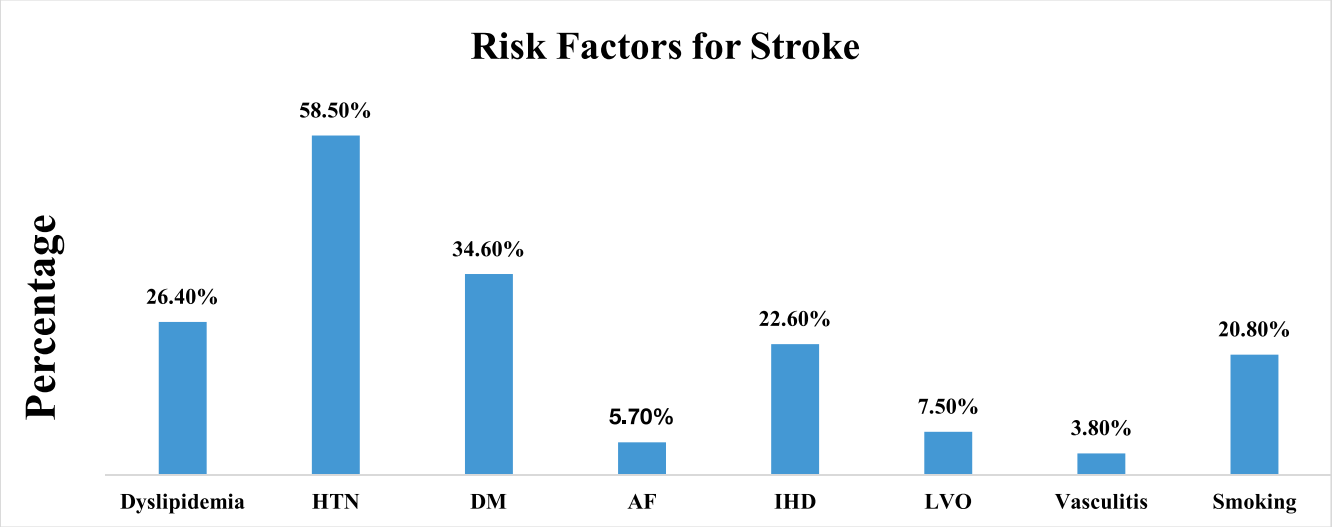

Figure 2: Risk factors for stroke among study population (n=53

DISCUSSION

Ischemic stroke is the most prevalent neurological disorder globally with a high rate of morbidity and mortality.[11] In our study, we noticed that the left middle cerebral artery followed by the right middle cerebral artery was most commonly affected in our stroke patients. The results from our study are supported by another Pakistani study conducted at Islamabad by Zafar et al, who evaluated their patients based on internationally recognized Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification and reported similar results with involvement of the left and right middle cerbral arteries as the most commonly affected territories in their stroke patients.[12]

The most frequent risk factors in stroke patients from our total study population of adults with acute ischemic stroke under 50 years were hypertension followed in descending order by diabetes mellitus, dyslipidemia and smoking. There were also a significant number of young patients included in our study who had a positive history of ischemic heart disease. A recent Pakistani study by Iqbal at el conducted at the Combined Military Hospital, Lahore, which evaluated young stroke patient risk factors had results similar to ours with the similar traditional modifiable vascular risk factors identified in the majority of patients included in the study and a recent cross-sectional study of stroke patients presenting to the neurology departments across various hospitals in the province of Sindh, Pakistan showed similar results.[13,14] The results seen in our study are also in agreement with another previous study conducted by Von Sarnowski et al which showed smoking, physical inactivity, arterial hypertension, dyslipidemia and obesity as the common modifiable vascular risk factors in a European cohort of young

patients aged 15 to 49 years who had presented with an acute ischemic stroke.[15]

Hypertension seems to be an area of growing concern due to its increasing frequency observed in stroke patients within studies of our local population as well as other populations including the CARDIA Study by the American Heart Association which showed that diastolic BP ≥90 mm/ Hg at age 40 was directly associated with a greater stroke risk. A local Pakistani population epidemiological study conducted in Rawalpindi also highlighted the significantly higher frequency of hypertension in the Pakistan population as compared to other risk factors. [16,17]

We also observed that large vascular occlusion was seen in 6.1% and 7.7 % of 40 to 49 years and 30 to 39 years age groups respectively. Iqbal et al in their study conducted in Lahore also reported this cause in 11.25% of young stroke patients which reflects the increasing perils of diet and lifestyle changes in the young Pakistani population.[13] Wasay et al. study also reported large vessel disease in young patients of South Asian Countries.[18] We noticed the surprising and unexpected result that amongst the youngest age group i.e 20-29 years, there was a significant yet equal number of patients with large vessel occlusion, ischemic heart disease at 14 % each respectively. Large vascular occlusion is an important finding in this age group which could partially be explained by presence of high vascular risk burden in population under 50 years of age.[14,19] Brouwer, et al study from Netherlands has reported that young patients from 18 to 49 years had a significantly better clinical outcome as compared to patients with ≥50 years of age with a lower risk of death or symptomatic intracranial bleeding as well, if diagnosed earlier and with timely management as well as reporting that large vessel occlusion is a common cause in young stroke patients of 18 to 49 years.[20] This study, however, was unable to identify the underlying cause of stroke in one-third of young cases, despite extensive diagnostic work-up, indicating the need for more research on risk factors and causes of stroke in young age group patients. The amount to which these vascular risk factors contribute as the cause of stroke, particularly for those <40 years of age is still debatable.4 Broad based studies would need to explore various causes in further detail.

There were 26.4% patients in our total study population who had a strongly positive family history of vascular risk factors. Importantly, half of the youngest patient of stroke of 20-29 this age group had strong family history of stroke ,which is important since the genetic variations in several stroke risk related genes are also related to various vascular traits.[21] Positive family history in young adults should be considered as a red flag so that these young age adults can be counselled about the need for being more cautious for their health and adopt prevention strategies the development of modifiable risk factors later in life thus saving them from the devastating consequences of ischemic stroke. Our findings suggest the need for earlier screening of risk factors, especially hypertension, and to plan nationwide strategies for prevention and adoption of more effective and affordable interventions to reduces modifiable risk factors specially particularly in Asian populations where incidence as well as prevalence of stroke is higher as compared to western countries.[22]

Smoking history seen in 20.8% was another important risk factor reflecting the lifestyle choices in our young population. This was also reflected in a recent study from Baltimore, USA which showed a strong relationship between the number of cigarettes smoked daily to the occurrence of ischemic stroke amongst young men.[23] Ideally complete cessation of smoking is the goal but even smoking fewer cigarettes may reduce the risk of ischemic stroke in young men.

Amongst the stroke patients in our study 18.9% were found to be obese. The link between obesity and stroke has been identified in larger multicenter trials.[24,25] This has important implications due to the obesity epidemic worldwide and increasing incidence of early-onset ischemic strokes. The outcome of our study results and the larger trials suggest that waist and hip circumference should be routinely measured for in health checkups for young individuals, to provide more precise estimations of stroke risk.

Atrial fibrillation is an important risk factor for ischemic stroke resulting in a fivefold increased stroke risk and a twofold increased mortality. The importance of early detection and treatment with anticoagulation for prevention of stroke has been highlighted in multiple trials worldwide and although it was seen in only 5.7% of the patients in our study it still remains an important risk factor for stroke in all age groups so earlier screening should be employed to reduce the risk of recurrent strokes.[26] Iqbal et al study from pakistan is in agreement with our results and reported AF in 7.5 % of their stroke patients of similar age group.[13] Zafar et al study found AF as the commonest cause of stroke in

Pakistani population residing in Islamabad.[12] Descripancy with our results concerning AF may be because of age group differences since this aforementioned study included patients ≥ 18 years but did not set an upper limit of age hence leading to enrollment of older patients , where as we only reviewed patients younger than 50 years age in our study.

Vasculitides of the cerebral vessels whilst considered important causes of stroke in the young, were seen in only 3.8% patients in our study.[27] Iqbal et al and his colleagues found vasculitis as a risk factor in 6.25% of their stroke patients.[13] This could be due to a low prevalence of these conditions in our population; however, larger trials would be needed to assess this in greater detail.

Stroke prevention results in greater quality-weighted life-year gain in younger patients than in elderly patients, but has received less attention. Future studies should target on finding novel environmental and intrinsic risk factors and their interactions predisposing to stroke and affecting its long-term outcome in these patients.

There were some limitations to our study which included a smaller study group and non-availability of detailed screening blood tests for patients with no identifiable risk factors or a strong family history, due to a lack of resources. We hope that future studies will be able to improve upon this.

CONCLUSION

Hypertension was the commonest risk factor for young age group under 50 years. Diabetes mellitus is also common in stroke patient with age 29 to 49 years, however none of our patients between age 20-29 years had diabetes mellitus. Our younger population also had a higher frequency of causes like dyslipidemia. ischemic heart disease and smoking. This mirrors what other studies assessing risk factors in young stroke patients have seen and physicians can address this issue by introducing earlier screening tests for vascular risk factors in the younger age group, along with encouraging young people into adopting healthier lifestyle choices.

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Faizan Aslam; Concept, data analysis, manuscript writing, manuscript revision
Atif Maqsood; Concept, data collection, data analysis, manuscript writing,
Adeel Rauf; Data collection, manuscript writing, manuscript revision
Kashif Nawaz; Data collection, data analysis, manuscript writing
Azam Aslam; Data collection, data analysis, manuscript writing

The authors have approved the final version of the article, and agrees to be accountable for all aspects of the work.