A CROSS-SECTIONAL STUDY OF SUBTYPES OF ISCHEMIC STROKE AND ITS ASSOCIATED FACTORS AT A TERTIARY CARE HOSPITAL; PESHAWAR, KHYBER PUKHTUNKHWA, PAKISTAN

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ABSTRACT

Objective: To establish the frequency of subtypes of ischemic stroke according to Bamford classification and to determine the associated risk factors.

Material & Methods: This was a cross-sectional study conducted at the Stroke Unit of Rehman Medical Institute (RMI) Peshawar from January 2019 to June 2019. All patients admitted in the Stroke unit with acute ischemic stroke were included after taking informed consent. Their stroke subtype and factors associated with stroke were noted. For age, mean±SD were calculated and for gender, stroke territory, HTN, DM, AF, IHD, and dyslipidemia, frequencies and percentages were calculated. Data was collected on a pre-designed pro forma and analyzed using SPSS version 22.

Results: Ninety-three patients were included. 55.9% (n=52) were males. Mean age was 63.77±12.5 years. Majority patients 45.2%, n=42 had Partial Anterior Circulation Stroke (PACS) followed by Total Anterior Circulation Stroke (TACS) that was seen in 25.8%, n=24 patients. Posterior Circulation Stroke (POCS), Multi territory and Lacunar Stroke (LACS) were observed in 15.1 %(n=14), 10.8% (n=10) and 3.2% (n=3) patients respectively. Hypertension (HTN) was the most common associated risk factor that was seen in 79.6% patients followed by Diabetes mellitus (DM) that was present in 49.5% (n=46) and structural heart disease was the third most common risk factor affecting 36.6%(n=34) of our study population. About 29% (n=27) had Ischemic heart disease (IHD) and 23.7% had dyslipidemia. Atrial fibrillation (AF) was observed in 18.7% (n=17), while 8.6% (n=8) of our study populations were tobacco smoker.

Conclusion: PACS was the most observed subtype of ischaemic stroke. HTN was the most common associated factor, followed by DM, IHD and structural heart disease.

Keywords: Stroke, Hypertension, Diabetes Mellitus, Echocardiography

INTRODUCTION

Ischaemic stroke is an episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction attributable to ischaemia, based on pathological, imaging, or other objective evidence of cerebral, spinal cord, or retinal focal ischaemic injury in a defined vascular distribution; or clinical evidence of cerebral, spinal cord, or retinal focal ischaemic injury based on symptoms persisting ≥24 hours or until death, and other etiologies excluded.[1]

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Stroke is ranked as the second leading cause of death worldwide with major mortality and neurological disability.[2]

Approximately 15 million people worldwide suffer from stroke annually of which 5.5 million die while the remaining are left with permanent disability.[3] In general, the trends in stroke incidence and mortality rates have decreased in recent decades in developed countries like United States, United Kingdom, and Canada.[4,5,6] The reason for this may be improvement in control of risk factors for stroke and acute stroke care may have led to an overall reduction in the percentage of stroke hospitalisations resulting in death in the United States.[4] The reverse is true for under developed country where early stroke case fatality is 25% higher than that seen in high-income countries in the past decade.[7-10]

In Asia the incidence of stroke is increasing and Pakistan is having major contribution in that.[10] The exact epidemiology of stroke in Pakistan is not known. In one study, the

incidence rate of stroke in Pakistan was calculated to be 250/100000 that was significantly higher than other countries like UK, China, Canada, US, Japan and France.[10] A study conducted at one of the hospitals in Karachi reported 519 cases of stroke in 22months.[11] In another retrospective study, frequency of stroke was found to be 6.4%.[12] In a population-based study carried out in KPK province, Pakistan in 2006 showed a high prevalence (4.8%) of stroke in that area.[13] No study in this regard has been done after that in KPK. Furthermore sub typing of stroke and factors associated with it have been studied less frequently.

Prevention and management of stroke requires an in-depth understanding of the stroke subtypes and its risk factors like age, gender, HTN, DM etc.[14,15.16] These factors differ by geographic region, and even by ethnicity within the same region.

This study was designed to establish the frequency of subtypes of ischemic stroke according to Oxfordshire or Bamford classification and to determine the associated risk factors.

MATERIALS AND METHODS

This is a cross-sectional study conducted at the Stroke Unit of Rehman Medical Institute (RMI) Peshawar, Khyber Pakhtunkhwa province, Pakistan from January 2019 to June 2019. All patients admitted to the Stroke unit with Ischemic Stroke were included by non-probability consecutive sampling technique.

Patients were enrolled after taking informed consent from the patient or their next of kin if patient was unable to give consent.

The Oxfordshire or Bamford classification of stroke was used to classify stroke. It relies extensively on clinical findings and classifies it on the basis of the brain territory involved into Total Anterior Circulation Stroke (TACS), Partial Anterior Circulation Stroke (PACS), Lacunar Stroke (LACS) or Posterior Circulation Stroke (POCS).[17]

Patient's demographic profile and history was taken. Detailed neurological examination was carried out in all patients by a consultant and vascular territory of infarct was identified clinically and stroke was classified according to Bamford classification, furthermore CT brain and/or MRI brain with Diffusion weighted images (DWI) were conducted for all patients to confirm the involved territory. To determine the factors associated with development of stroke, past history regarding DM, HTN, IHD, structural heart disease, smoking and illicit drug use was taken. HbA1c level of 6.5% or higher with either laboratory tested random blood sugar of 200mg/dL and higher or fasting blood sugar of 126 mg/dL and higher was considered diagnostic of diabetes as per guidelines.[18] Total cholesterol level was carried out and level > 180 mg/dL was considered as Dyslipidaemia.[19] Further, blood pressure readings > 140/90 mmHg were considered for the diagnosis of HTN.[20] ECG and 24hrs holter recording were done to look for AF and echocardiography was carried out to determine the type of structural heart disease.

Data was collected in pre designed Pro forma and entered in SPSS version 22 for analysis. For quantitative variables like age, mean±SD were calculated and for qualitative variables like gender, ethnicity, stroke territory, HTN, DM, AF, IHD, Structural heart disease, and dyslipidemia, frequencies and percentages were calculated.

RESULTS

A total of 93 patients were admitted in the study duration in the RMI Stroke Unit. The mean age of the patients was 63.77 ± 12.5 years with 55.9% (n=52) males and 44.1% (n= 41) were females. 82.8% (n=77) were Pakistani and rest 17.2% (n=16) belonged to Afghanistan.

According to Oxfordshire or Bamford classification, PACS was the most observed pattern of stroke in our study population. About 45.2% (n=42) patient had PACS followed by TACS that was observed in 25.8% (n=24) subjects. In these patients 15.1% (n=14) came with POCS and 10.8% (n=10) had multi territory infarct. Only 3.2% (n=3) patients had lacunar infarct (LACS).

In factors associated with the development of stroke, we found that HTN was the most common contributing factor accounting for 79.6% (n=74) of patients. Diabetes Mellitus was next to HTN that was observed in 49.5% (n=46) of subjects. Structural heart disease was found in 36.6% (n=34) followed by IHD, dyslipidemia and AF that were observed in 29.0% (n=27), 23.7% (n=22) and 18.3% (n=17) patients respectively. Only 8.6% (n=8) of our patients were smokers. Rare factors like illicit drug use, hyperhomocysteinemia and Polycythemia vera were identified in one patient each. The frequency of these factors are graphically presented in Figure 1.
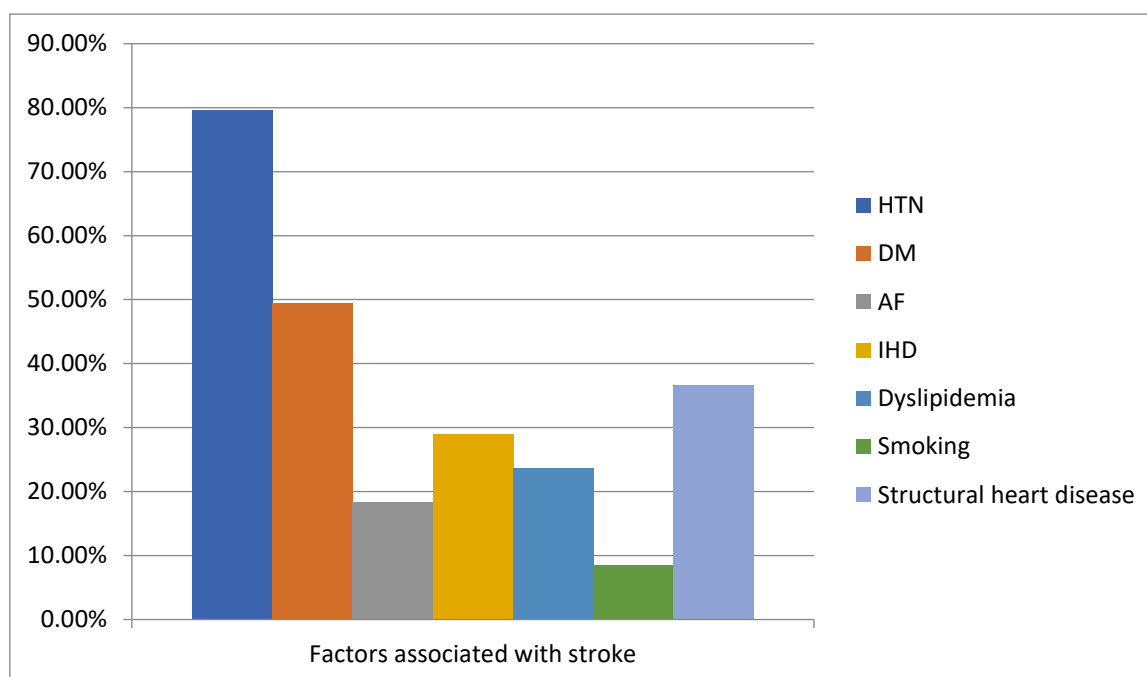
Figure 1: Frequency of factors associated with Stroke

We also looked for the different echocardiography findings in our patients. Regional wall motion abnormality (RWMA) was the most common finding on Echo accounting for 20.4% (n=19) of patients followed by mitral valve disease that was present in 11.8% (n=11) patients. Left ventricular dilatation and low Ejection fraction (EF) was noted in 2.2% (n=2) cases each. In 63.4% (n=59) patients had normal Echocardiography.

Furthermore we analysed each subtype of stroke individually. Details are given in table 1.

Mean age was higher in patients with multi territory and lacunar infarcts. Male gender predominated in all subtypes except TACS where 58.3% (n=14) were females. From LACS and multi territory subtype, majority belonged to Afghanistan while in other subtypes; patients from Pakistani origin were in higher number. HTN was the most common associated factors with all subtypes of stroke, the greatest frequency of hypertensive patients was seen in POCS subtype i.e. 85.7% (n=12) followed by PACS, multi territory and TACS. In LACS sub-type, 66.7% (n=2) had HTN and same number of patients were affected by diabetes in this subtype. Details of other factors are tabulated as under:

Table1: Factors associated with stroke subtypes

Factors		TACS (n = 24)	PACS (n = 42)	POCS (n = 14)	LACS (n = 03)	Multi territory (n = 10)
Age		59.45±12.70	64.14±13.36	64.64±11.24	69.33±5.13	69.70±9.03
Gender	Male	41.7%(n=10)	59.5%(n=25)	71.4%(n=10)	66.7%(n=2)	50.0%(n=5)
	Female	58.3%(n=14)	40.5%(n=17)	28.6%(n=4)	33.3%(n=1)	50.0%(n=5)
Country of origin	Pakistan	79.2%(n=19)	85.7%(n=36)	85.7%(n=12)	0.0% (n=0)	30.0%(n=3)
	Afghanistan	20.8%(n=5)	14.3%(n=6)	14.3%(n=2)	100%(n=3)	70.0%(n=7)
HTN		75%(n=18)	81.0%(n=34)	85.7%(n=12)	66.7%(n=2)	80.0%(n=8)
DM		33.3%(n=8)	52.4%(n=22)	50.0%(n=7)	66.7%(n=2)	70.0%(n=7)
AF		37.5%(n=9)	9.5%(n=4)	7.1%(n=1)	33.3%(n=1)	20.0%(n=2)

IHD	37.5%(n=9)	21.4%(n=9)	21.4%(n=3)	66.7%(n=2)	40.0%(n=4)
Dyslipidaemia	25.0%(n=6)	26.2%(n=11)	21.4%(n=3)	00.0%(n=0)	20%(n=2)
Smoking	4.2% (n=1)	4.8% (n=2)	14.3% (n=2)	33.3%(n=1)	20.0% (n=2)

We stratified age of each gender into different groups and found that females above 75yrs were the most affected. Males of age group between 66-75yrs had maximum frequency of stroke. Details regarding subtypes of stroke with age and gender stratification is given in table 2.

Table 2: Stroke subtypes in different age groups and gender

Gender	Age (yrs)	TACS (n = 24)	PACS (n = 42)	POCS (n = 14)	LACS (n = 03)	Multi territory (n = 10)
Female	25-35	00.0%(n=0)	100%(n=1)	00.0%(n=0)	00.0%(n=0)	00.0%(n=0)
	36-45	66%(n=4)	33%(n=2)	00.0%(n=0)	00.0%(n=0)	00.0%(n=0)
	46-55	37.5%(n=3)	62.5%(n=5)	00.0%(n=0)	00.0%(n=0)	00.0%(n=0)
	56-65	33%(n=3)	33%(n=3)	22%(n=2)	00.0%(n=0)	11%(n=1)
	66-75	25%(n=2)	50%(n=4)	12.5%(n=1)	00.0%(n=0)	12.5%(n=1)
	>75	20%(n=2)	30%(n=3)	10%(n=1)	10%(n=1)	30%(n=3)
Male	25-35	100%(n=1)	00.0%(n=0)	00.0%(n=0)	00.0%(n=0)	00.0%(n=0)
	36-45	00.0%(n=0)	50%(n=1)	50%(n=1)	00.0%(n=0)	00.0%(n=0)
	46-55	14.2%(n=1)	42.8%(n=3)	28.5%(n=2)	00.0%(n=0)	14.2%(n=1)
	56-65	25%(n=4)	56.2%(n=9)	18.7%(n=3)	00.0%(n=0)	00.0%(n=0)
	66-75	22.2%(n=4)	27.7%(n=5)	16.6%(n=3)	11.1%(n=2)	22.2%(n=4)
	>75	00.0%(n=0)	75%(n=6)	25%(n=2)	00.0%(n=0)	00.0%(n=0)

Discussion

Classification of the ischaemic stroke is essential for both clinical management and research. Age is the strongest determinant of stroke and the risk of stroke increases significantly above 55yrs.[2] The mean age of our patients was 63.77 ± 12.5 years. This finding is in concordant with the study carried out in Pakistan on 1180 patients of ischaemic stroke.[10] In 2009 a study from Karachi described the mean age of stroke patient as 56.47±15.8. The relatively higher age in our study is due to the increase in life expectancy of people over the ongoing years. A trail published in 2016 from Europe illustrated that mean age of ischaemic stroke was higher in white as compared to blacks i.e. 74.8±13.7 vs. 65.1±13.7. In our population, we noticed even younger age; it probably reflects the racial difference and provision of better health care facilities in West.

Overall, more strokes occur in women than men, because of the longer life span of women compared with men.[21, 22] A study performed in 8 different European countries found that the risk of stroke increased by 9% per year in men and 10% per year in women.[22] A study from Pakistan also showed female predominance in stroke patients.[10] The relationship of gender to stroke risk depends upon age. At young ages, women have as high or higher risk of stroke as compared to men but at older ages the risk is slightly higher for men.[23] Males were affected more as per our study because the mean age of our subjects were higher as compared to other studies.

Regarding stroke subtype, literature is deficient in terms of studies using Bamford classification in Pakistan. One study conducted in Karachi in 2006 showed that most observed pattern of stroke was PACS followed by TACS.[24] It is similar to our findings.

Hypertension is the most important modifiable risk factor for stroke, with a strong, direct, linear, and continuous relationship between blood pressure and stroke risk.[15, 23] 79.5% patients in our study were hypertensive. A UK stroke study showed that 83.9 % of UK black population and 72.9% of white population had hypertension.[25] A study from Pakistan described 68.2% of stroke population to be hypertensive.[10]

We found DM as the second most common factor accounting for 49.5% of stroke patients. It is relatively higher as compared to other studies done in Pakistan and in Europe where its frequency was found to be 17.8% and 18.3% in stroke patients respectively.[2,25] The reason for this difference may be the increasing prevalence of diabetes in KPK

province according to new statistics.[26] We did HbA1c level for all patients that is more reliable indicator of diabetes and pre-diabetes as compared to single blood sugar level.[18]

Heart diseases are the second cause of acute cerebrovascular events and are diagnosed in one third of patients with stroke.[27] Atrial fibrillation (AF) and Atrial flutter are the most important and modifiable risk factor, frequently associated with cardio embolic stroke. In our study 18.3% patients had AF at the time of presentation. This finding is similar to the other studies. Frequency of AF is documented as 12.7% in Africans in one analysis.[25] Dasti MA et al, study described 16.25% of the stroke patients with AF.[28] On the other hand comparatively increased frequency of AF has been observed in European as depicted in one study where 32.9% stroke patients had stroke, the reason may be that overall this race is more prone to have AF in old age and better diagnostic tests to detect AF.[23] IHD is also an important factors for stroke, there is an inverse correlation between ejection fraction of the left ventricle and the incidence of ischaemic stroke.[27] We noticed 29% of our study population suffering from IHD, it is relatively higher than the studies in national and international literature.[10,15,25]

In our stroke patients 36.6% of patient had valvular heart disease. This is very high as compared to the other studies. A data from Sagrat Cor Hospital of Barcelona Stroke Registry showed that 7.9% of stroke patients had valvular heart disease.[15] In Pakistan 1.67% stroke patients were noted to have valvular heart disease. The reason for this difference can be due to the comparatively high prevalence of rheumatic heart disease related valvular problems in the region of KPK province of Pakistan.[29]

The relationship between dyslipidemia and stroke risk is well established in terms of total cholesterol and LDL cholesterol.[23] Evidence for the influence of triglycerides on stroke risk is conflicting.[23] There is stronger association of serum cholesterol levels with ischaemic stroke involving large arteries.[23] 23.7% of our subjects had dyslipidemia, findings are similar to the study conducted on Spanish population that showed 22.3% stroke population below 65yrs had dyslipidemia.[15] In a study conducted in Bannu region of KPK, dyslipidemia accounted for 18% of patients with stroke.[30]

Smoking remains a major risk factor for stroke, nearly doubling the risk with a dose–response relationship between pack-years and stroke risk.[23] We found relatively less percentage of smokers in our study as compared to other studies.[15, 25] The reason for this difference can be explained on the fact that people in this region commonly use non smoked tobacco (Naswar) rather than cigarette.

This study is unique in a way that factors associated with each subtypes of stroke have not been studied before. This study also included patients from Afghanistan.

We present the 1st study of KPK region and patients from Afghanistan that elaborated the subtypes of stroke according to Oxfordshire or Bamford classification system and also described the association of multiple factors with each subtype.

Our study has some limitations. Firstly, it was the single hospital based study. Secondly, we presented only descriptive data, so we can't claim that our findings are statistically significant. Further studies in this regard are required to elaborate the statistical significance of factors associated with different subtypes of stroke.

Conclusion:

Since the burden of stroke is expected to increase significantly in future, there is the need for a better understanding of the factors associated with subtypes of stroke. Modifiable risk factors are the major causes of Stroke and can be optimally managed to reduce recurrence and complications.

Authors Contribution
MFK designed and led the project
WQ, MFK , DN did data collection/correction, manuscript writing & editing of the manuscript
WQ, MFK, MSI, SK, SN did data collection, statistical analysis & manuscript writing
DN, WQ did data correction, computer generation of the data bank
MFK, MSI, GF, SK, WQ, DN did the editing, review & final approval of the manuscript

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