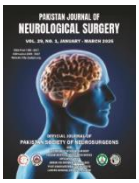

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Original Research

Determining the Occurrence, Predictors and Contributing Factors of Ischemic Versus Hemorrhagic Stroke Among Patients with Post Stroke Epilepsy; A Comparative Study

Aneeqa Saad[1], Sohaib Hassan[1], Fatima Nazir Siddiqui[2], Ashraf Mahmood[3]

[1]Department of Neurology, Nishtar Medical University, Multan

[2]Town Hospital, Mumtazabad, Multan

[3]Department of Neurosurgery Holy Family Hospital, RMU Rawalpindi – Pakistan

ABSTRACT

Objective: To assess the occurrence, and contributing factors of post-stroke epilepsy in stroke patients and to compare the frequency of ischemic versus hemorrhagic stroke in patients presenting at Nishtar Hospital, Multan.

Materials & Methods: The patients with stroke, fulfilling inclusion criteria admitted to the neurology department of Nishtar Hospital, Multan were recruited in the study. A detailed history of the current illness as well as a history especially related to seizures was questioned. CT scan brain of all the patients was done and type of type i.e., ischemic or hemorrhagic was determined. Patients were followed for 3-month intervals for the occurrence of epilepsy.

Results: out of a total of 136 patients with stroke, ischemic stroke was found in 107 (78.7%) patients and hemorrhagic stroke in 29 (21.3%). Most patients were males 80 (58.8%) while 56 (41.2%) were females. The mean age of the patients was 55.55±10.17 years and the mean BMI was 25.26±5.54 kg/m2. The frequency of obesity, hypertension, diabetes, and smoking was 21.3%, 48.5%, 44.9%, and 44.1% respectively. Seizure was observed in 35(25.7%) patients with stroke, commonly in hemorrhagic stroke (12/17, 70.58%).

Conclusion: Old age, hypertension, and smoking significantly increase stroke risk. Epilepsy can complicate stroke with a higher incidence of hemorrhagic stroke.

Keywords: Post-stroke epilepsy, Hemorrhagic Stroke, Predictors, Ischemic – Stroke.

Corresponding Author: Sohaib Hassan
Assistant Professor of Neurology, Nishtar Medical University, Multan
Email: hassannmc@gmail.com

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INTRODUCTION

"According to the International League Against

Epilepsy Epidemiology Commission epilepsy" Epilepsy can be defined as unprovoked seizures occurring with intervals.[1] According to a systematic analysis in 2016, 45.9 million people had active epilepsy, it's a common chronic brain disease with multiple causes i.e., genetic or developmental brain pathologies, infections of both central nervous system infections or severe systemic infections, head injury, metabolic disorders, and cerebrovascular accidents, etc.[2]

The WHO's Global Burden of Diseases study ranks epilepsy as the 2nd most common neurological disease across the globe in terms of disability secondary epilepsy is more common in old patients, in men, and low-income countries mainly due to differences in lifestyle and availability of health care facilities.[3] The estimated prevalence of epilepsy in Pakistan is 9.99 per 1000 accounting for 1/10th of the world burden of epilepsy. Stroke can be characterized by abruptly developed symptoms and signs of focal or global (coma) loss of cerebral functions lasting more than 24 hours.[4-5]

It can be ischemic, due to blockage of blood supply, or hemorrhagic due to rupture of blood vessels with the frequency of 85% and 10-15% respectively, and the leading cause of disability among patients globally affecting around 13.7 million people annually.[6] From these, about 5 million die, and another 5 million are left permanently disabled. This has a huge impact on individuals, families, and communities, particularly in the underdeveloped world.[7]

According to a WHO report, stroke is one of the leading causes of death in developing countries.[8] Though there are no studies on the overall incidence of stroke in Pakistan, in a regional study at KPK, the estimated annual incidence of stroke in Pakistan is 250/100,000 with a total of 350000 new cases every year, in a WHO report from 2002, the total mortality from stroke in Pakistan was found to be >75000. Stroke is a leading cause of secondary epilepsy, defined as the occurrence of two or more seizures after a cerebrovascular accident.[9]

In Sweden, the incidence of post-stroke epilepsy is 7.3%, 6.4% in ischemic and 12.4% in hemorrhagic stroke. The incidence of post-stroke epilepsy after a hemorrhagic stroke is 13.5%, in a study by Dziadkowiak et al, the incidence of post-stroke epilepsy was 6%.[10-12]

The risk factors for stroke vary in different age groups. These risk factors are divided into two main classes modifiable risk factors the factors are most important to address as their control can prevent the occurrence of stroke and thus decrease the disease burden of society.[11]

The current study aims to determine the frequency of post-stroke epilepsy in patients presenting with acute stroke both ischemic and hemorrhagic stroke at tertiary care hospitals so that the patients at increased risk of secondary epilepsy should be observed more closely and attendants should be counseled about this complication.

PATIENTS AND METHODS

Study Design & Setting

A Descriptive case series study was conducted at the Department of Neurology, Nishtar Medical University, Multan from 4 June 2024 to 24 October 2024 after taking IRB from Nishtar Medical University (Reference no:7108). A total of 136 cases were included.

Inclusion Criteria

Both male and female patients, of age ≥ 20 years and ≤ 80 years. All the patients have to find on a CT scan Brain (plain) consistent with stroke according to operational definitions.

Exclusion Criteria

All the patients with a stroke duration of ≤ three days with a history of seizures before the index event of stroke and Patients having a history of

head injury or CT brain plain suggestive of SOL and subarachnoid hemorrhage. Patients not giving consent of participation and having electrolyte disturbance (hyponatremia defined as serum sodium less than 135mEq/L, hypocalcemia defined as serum calcium less than 8mg/dl, hypomagnesemia defined as serum magnesium less than 1.7mg/dl), hypoglycemia (defined as blood glucose less than 70mg/dl), renal dysfunction (defined as serum creatinine greater than 1.3mg/dl) and liver diseases as per medical record were also excluded from study.

Ethical Approval

IRB is provided as per requirement from Nishtar Medical University (Reference no:7108).

Data Collection

Data was collected using the non-probability, consecutive sampling technique. All the patients with stroke, fulfilling inclusion criteria admitted to the neurology department of Nishtar Hospital, Multan were recruited in the study after briefing the details of the study, to caretakers of patients and obtaining informed consent. Baseline data like age, gender, BMI, Blood glucose, and blood pressure were noted on a specialized Performa. A detailed history of the current illness as well as a history especially related to seizures was questioned. CT scan brain of all the patients was done and type of type i.e., ischemic or hemorrhagic was determined. A required lab test was done to exclude other possibilities of seizure in these patients, as per exclusion criteria. Patients were followed for 3-month intervals for the occurrence of epilepsy.

Data Analysis

Data was entered and analyzed by the SPSS version. 23. Descriptive statistics was used to calculate the mean and standard deviation for the age and duration of hospital stay. Frequencies and percentages of categorical variables e.g., gender, presence of diabetes and hypertension, smoking, epilepsy, and type of stroke were calculated. Effect modifiers like age, gender, diabetes, hypertension, obesity, smoking, and type of stroke were controlled by stratification and a post-stratification chi-square test was used to see their effect on the frequency of epilepsy. A P-value less than 0.05 was considered significant.

RESULTS

In this study, 136 consecutive stroke patients admitted to the neurology department of Nishtar Hospital, Multan, were enrolled. Most patients were males, 80 (58.8%), while 56 (41.2%) were females. The mean age of the stroke patients was 55.55±10.17 years. The mean age of male patients was 55.92±9.18 years, while that of female patients was 55.01±11.50 years, almost the same in both genders.

Age and Gender Distribution

Table 1: Age & Gender details of patients.

Demographic data		No of Patients (n)	Percentages (%)
Gender	Male	80	58.8%
	Female	56	41.2%
Age groups	20-40	4	2.9%
	41-60	99	72.8%
	61-80	33	24.3%
Total		**136**	**100.0%**

The mean BMI of the participants was 25.26±5.54 kg/m^2, of males was 25.26±5.45 kg/$m^{2,}$ and of female patients was 25.25±5.72 kg/m^2. 16(20%) male patients were obese and 13 (23.2%) female patients were obese, obesity is slightly more common in female stroke patients as mentioned in Table 1.

Ischemic stroke was observed in 107 (78.7%) patients and hemorrhagic stroke in 29 (21.3%) patients. Among male patients, 16(20%) had

hemorrhage and 80% (64) had ischemic stroke. In female stroke patients, the distribution of ischemic and hemorrhagic stroke was 43(76.8%) and 13 (23.2%) respectively as shown in Figure 1.

The frequency of hypertension was 48.5% (66), in male 52.5% (42/80) and in female were 42.9% (24/56). Diabetes was observed in 61 (44.9%) participants of the study, with male and female distributions of 30/80 (37.5%) and 31/56 (55.4%) respectively, showing diabetes was a more frequent cause of stroke in female patients, the intervals between stroke and occurrences of epilepsy is given in Figure 2.

Smoking was observed in 60(44.1%) patients of stroke, with mark difference among male and female patients i.e., 51/80 (63.7%) and 9/56(16.1%) respectively.

Table 2 shows the relationship between demographic data and stroke. Seizure was commonly observed in hemorrhagic stroke (12/17, 70.58%). The mean interval between stroke and epilepsy occurrence was 6.5 ± 7.6 hours. The seizure was observed in 35(25.7%) patients with stroke, among whom 18 were male (18/80, 22.5%) and 17 were female (17/56, 30.6%).

Type of Stroke & Gender Representation

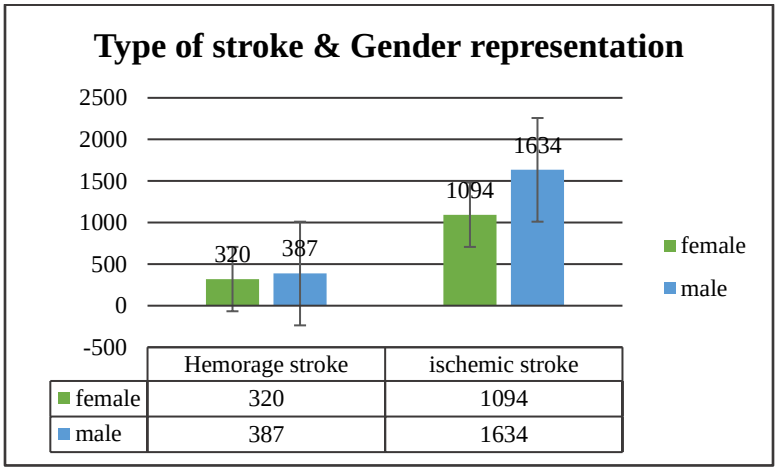

Figure 1: Type of stroke and gender representation of patients.

Stroke Interval and Occurrence of Epilepsy

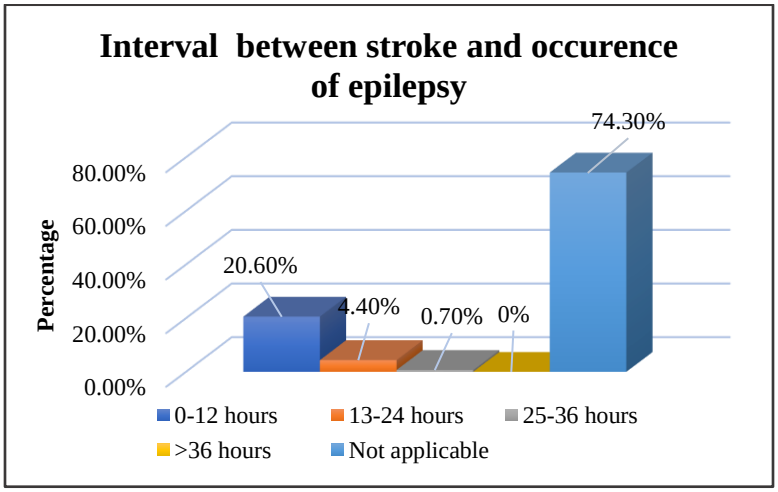

Figure 2: Interval between stroke and occurrence of epilepsy.

Table 2: Relationship between Demographic data and stroke & post-stroke epilepsy.

Effect modifier		Stroke		P-value	Post-stroke epilepsy		P-Value
		Ischemic	hemorrhage		Yes	No	
Age groups (Years)	20-40	2(1.4%)	2(1.4%)	0.024	1(0.7%)	3(2.2%)	0.973
	41-60	74(54.4%)	25(18.3%)		25(18.3%)	74(54.4%)	
	60-80	31(22.7%)	2(1.4%)		9(6.6%)	24(17.6%)	
Gender	Male	64(47.0%)	16(11.7%)	0.652	18(13.2%)	62(0.4%)	0.302
	Female	43(31.6%)	13(9.5%)		17(12.5%)	39(28.6%)	
Obesity	Yes	24(17.6%)	5(3.6%)	0.545	7(5.1%)	22(16.1%)	0.824
	No	83(61.0%)	24(17.6%)		28(20.5%)	79(58.0%)	
Hypertension	Yes	59(43.3%)	7 (5.1%)	0.003	17(12.5%)	49(36.0%)	0.995
	No	48(35.2%)	22(16.1%)		18(13.2%)	52(38.2%)	

Diabetes	Yes	51(37.5%)	10(7.3%)	0.206	18(13.2%)	43(31.6%)	0.364
	No	56(41.1%)	19(13.9%)		17(12.5%)	58(42.6%)	
Smoking	Yes	55(40.4%)	5(3.6%)	0.001	16(11.7%)	44(0.3%)	0.825
	No	52(38.2%)	24(17.6%)		19(13.9%)	57(41.9%)	

Table 3: Interval between stroke and occurrence of epilepsy.

The interval between stroke and occurrence of epilepsy (in hours)	**Stroke**		**P-value**	**Post-stroke epilepsy**		
	Ischemic	**Hemorrhage**		**Yes**	**Not applicable**	**P-Value**
0-12 hours	20(14.7%)	8(5.8%)		28(20.5%)	0(00%)	
13-24 hours	3(2.2%)	3(2.2%)		6(4.4%)	0(00%)	
24-36 hours	0(00%)	1(0.7%)	0.033	1(0.7%)	0(00%)	0.000
>36 hours	0(00%)	0(00)		0(00%)	0(00%)	
Not applicable	84(61.7%)	17(12.5%)		28(20.5%)	0(00%)	

DISCUSSION

Seizures are a significant cause of disability, commonly associated with genetic factors, abnormal labor (e.g., birth asphyxia), CNS infections, metabolic disorders (e.g., hypocalcemia and renal failure), stroke, and head trauma.[13-14] Post-stroke epilepsy (PSE) contributes to a notable percentage of newly diagnosed epilepsy cases, with some studies showing a considerably higher risk of developing epilepsy post-stroke compared to the general population.[15] Our study aimed to determine the frequency of PSE in a local population and its relationship with stroke type, adding to the growing body of research on this topic.

Our study included 136 stroke patients, with a higher proportion of male patients (58.8%). This is consistent with findings from Karachi, where stroke was more prevalent in males, and similar to Rawlings et al, who also reported a higher incidence of cerebrovascular accidents in males.[16] The mean age of stroke patients in our study was 55.55 ± 10.17 years, which is lower than the mean age reported in Karachi (68 ± 6.97 years) and the Thai Stroke Registry (65 years).[17]

In our study, hypertension was observed in 48.5% of patients, which is higher than the 21.77% prevalence in Khyber Pakhtunkhwa (KPK).[18] Similarly, diabetes and smoking were more frequent in our study population, with 44.9% and 44.1%, respectively, compared to the KPK study results of 5.9% and 6.64%.[19] The mean BMI in our study was 25.26 ± 5.54, which is higher than the 22.75 kg/m^2 observed in the KPK cohort.[19] Studies from Lahore also reported higher mean BMI and obesity rates, but the prevalence of smoking, hypertension, and diabetes was slightly lower in those studies compared to ours.[20-21]

In terms of post-stroke seizures, 25.7% of our stroke patients experienced seizures, with a notably higher incidence of hemorrhagic stroke 70.58%. This is in line with the findings of Obata and colleagues, who also found seizures to be more common in hemorrhagic strokes, although their overall incidence was lower than ours.[22] Similarly, studies by Owolabi (11%) [23], Kissani (6%)[24] and Dziadkowiak (7.3%),[25] report varying incidences of post-stroke epilepsy, with hemorrhagic strokes being more strongly associated with PSE, consistent with our findings. The study used a non-probability consecutive sampling technique, which may introduce selection bias and limit the generalizability of the results. Additionally, the study's short follow-up period of three months may not fully capture the long-term occurrence of post-stroke epilepsy, which could potentially lead to underreporting of later seizures. Results regarding the frequency and characteristics of post-stroke seizures generally align with those from previous studies, though

some regional differences in prevalence were observed. These variations highlight the complexity of post-stroke epilepsy and underscore the need for continued research in diverse populations.

CONCLUSION

Stroke is a major cause of mortality and morbidity in old age, with common risk factors being hypertension, diabetes, and smoking. Epilepsy can complicate stroke with a higher incidence of hemorrhagic stroke. Further studies are required to determine the predictors of epilepsy in stroke patients.

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Additional Information

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Other Relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.
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AUTHORS CONTRIBUTIONS

Sr.#	Author's Full Name	Intellectual Contribution to Paper in Terms of:
1.	Aneeqa Saad	1. Study design, methodology, and Literature review and referencing.
2.	Sohaib Hassan	2. Paper writeup and editing and quality insurer.
3.	Fatima Nazir Siddiqui	3. Data collection & calculations and analysis of data & interpretation of results.
4.	Ashraf Mahmood	4. Editing and referencing.