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Study of Risk Factors in Stroke in Tertiary Level Hospital of Pokhara: A Cross-Sectional Study

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Abstract— Background*: Stroke is defined as an "acute neurologic dysfunction of vascular origin with sudden (within seconds) or at least rapid (within hours) occurrence of symptoms and signs corresponding to the involvement of focal areas in the brain. The study aims to study the various risk factors in stroke.* ***Materials and Methods****: This was a hospital-based cross-sectional study conducted on 200 patients having the problems of stroke in Gandaki Medical College and Teaching Hospital, Pokhara from August 2020 to September 2021. Data of all the patients were collected and analyzed using the appropriate statistical tool.* ***Results****: A total of 200 patients with stroke were recruited; patients each had an ischemic and hemorrhagic stroke. Demographic, as well as clinical characteristics were recorded and data were analyzed by using statistical software like SPSS.* ***Conclusion****: There was a statistically significant association of risk factors of stroke and age in our study having a p-value <0.005. There was a statistically significant association between hypertension and stroke p=0.002.*

Keywords— *Stroke, risk, hemorrhagic, hypertension, thrombosis.*

I. INTRODUCTION

Stroke is defined as an "acute neurologic dysfunction of vascular origin with sudden (within seconds) or at least rapid (within hours) occurrence of symptoms and signs corresponding to the involvement of focal areas in the brain"[1]. It is a sudden onset of a very non- convulsive focal neurological defect that can last for 1 day. Stroke is the 3rd leading cause accounting for 10% of all death in the world[2].The cerebrovascular accident is a worldwide health problem. It is the third most common cause of death in the developing world and hence is an important cause of morbidity, mortality, and disability in developed as well as developing countries. Although there are substantial differences in frequencies from place to place, cerebral thrombosis is usually the most frequent form of stroke encountered in clinical studies followed by cerebral hemorrhage, subarachnoid hemorrhage, and cerebral embolism. Stroke management differs from patient to patient depending on the type of stroke, associated risk factors, and presence of complications[3].The management of hemorrhagic stroke differs from that of ischemic stroke, though the etiological factors are the same. The advent of investigative facilities like CT scan, MRI, digital subtraction angiography, etc., has brought into focus the discrepancies between clinical and radiological diagnosis. Though a good clinician is most often accurate in differentiating ischemic from hemorrhagic stroke, sometimes misdiagnosis may result in therapeutic disasters in this era of consumer activism, there is a crying need to prevent such errors of diagnosis[4]. It is a major global health issue that prematurely claims millions of otherwise healthy and productive lives each year. The WHO predicts that the total stroke burden will increase from approximately 38 million Disability Adjusted Life Years (DALYs) in 1991 to 51 million (DALYs) in 2020[5].

Strokes are rare in younger people and become increasingly common with older age but at the age of 45 years, the chances of having a stroke in the next 20 years are 1 in 30[6]. There has been a definite increase in the prevalence and incidence of stroke disorder in India over the last 30 years[7].

Stroke represented 1.2% of total deaths in India[8]. The average annual incidence rate of stroke in India currently is 145 per 100,000 populations, which is higher than the western nations and Indians may also be genetically prone for stroke due to the high prevalence of metabolic syndrome[9]. Ischemic and hemorrhagic stroke accounts for approximately 85% and 15%, respectively[10]. Stroke is a clinical culmination of many complex processes and interacting pathways, none of which is individually necessary or sufficient to cause the outcome. There is considerable evidence from twin studies and numerous epidemiologic studies have documented that stroke has a significant genetic component[11]. Studies looking at sibling risk and/or offspring showed significant risk in first-degree relatives of stroke patients, with odds ratios that average 1.76[12]. Family studies have shown an association of hemorrhagic stroke and a positive family history of hemorrhagic stroke, indicating an underlying genetic etiology[13].

The cause of most common strokes is multifactorial and involves both genetic variants, environmental triggers such as smoking or diet, and most likely results from that of additive or multiplicative effect of a wide spectrum of pathogenic alleles (a gene dose effect), each of which conferring a small degree of risk but the identification of individual causative

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mutations remains problematic[14]. Many common risk factors for stroke like diabetes and arterial hypertension are partly inherited; so many genetic loci contribute more or less to the stroke phenotype[15].

Risk factors for hemorrhagic stroke have become evident, including heavy alcohol intake and anticoagulant treatment. Less frequent and convincingly proven risk factors are cocaine use and low serum cholesterol[16].

Many candidate genes for hypertension have been suggested including genes for rennin angiotensin-converting enzyme, aldosterone, calmodulin, ion ATPases, phospholipase, kallikrein, endothelin, and androgenic receptors. Genome-wide linkage surveys have found linkage for blood-pressure loci on almost all chromosomes[17].

Several genetic polymorphisms have been also associated with an increased risk for apparently sporadic hemorrhagic stroke. The influence of *APOE* genotype on sporadic cerebral amyloid angiopathy-related –hemorrhagic stroke has been studied intensively, with contradicting results like in ischemic stroke. It is now accepted that the *APOE* E2 allele predisposes to rupture of βA4 laden blood vessels, thus increasing the chance of sporadic cerebral amyloid angiopathy - related-hemorrhagic stroke[18].

Atherosclerosis is a well-known risk factor for stroke and the genetic variants of the low-density lipoprotein receptor have already been highly informative for the genetics of atherosclerosis in vascular disease[19]. Ischemic stroke can be caused by many monogenic disorders and in such cases, stroke is frequently part of a multisystem disorder[20]. The ischemic stroke itself consists of many different phenotypes which may each have different genetic profiles[21].

A genome-wide linkage study on Icelandic individuals with stroke has indicated that a gene on chromosome 5 may contribute significantly to the risk of stroke[22]. In many of the studies, the risk persisted with hypertension, hyperlipidemia, diabetes, and smoking. These studies support the notion that stroke, as with all common diseases, occurs at the interface between genes and the environment. However, the significant genetic component to stroke risk is not fully explained by the genetic components driving the known medical risk factors[23].

To relieve the burden of stroke, we need to understand the mechanisms that will form the basis of improved prevention and treatment. In the post-genomic era, multiple genes have been termed low-penetrance genes and various studies have focused on different variants of these genes known as polymorphisms. Three strategies are being used to find stroke genes: positional cloning applied to rare monogenic forms of stroke, candidate gene association studies of common stroke, and positional cloning applied to common stroke[24].

There may be inter-individual variation in the studied subjects. Extensive effort has been expended to identify the association between single nucleotide polymorphisms (SNPs) in functional candidate genes and stroke[25]. However, the candidate gene approach is limited by how much is the underlying mechanism of the disease being investigated. In the present study, we have employed targeted candidate gene analysis to look for the association of genetic variants with the risk of stroke and their clinical subtypes. Candidate genes were chosen a priori based on assumed biological relevance.

Cerebrovascular accident is a worldwide health problem. It is the third most common cause of death in the developing world and hence is an important cause of morbidity, mortality, and disability in developed as well as developing countries. Although there are substantial differences in frequency from place to place, cerebral thrombosis is usually the most frequent form of stroke encountered in clinical studies followed by cerebral hemorrhage, subarachnoid hemorrhage, and Cerebral Embolism.

Stroke management differs from patient to patient depending on the type of stroke, associated risk factors, and presence of complications. The management of Hemorrhagic stroke differs from that of Ischaemic stroke, though the aetiological factors are the same. The advent of investigative facilities like CT scan, MRI, Digital subtraction angiography, etc., has brought into focus the discrepancies between clinical and radiological diagnosis. Though a good clinician is most often accurate in Differentiating ischaemic from hemorrhagic stroke, sometimes misdiagnosis may result in therapeutic disasters. In this era of Consumer activism, there is a crying need to prevent such errors of diagnosis[26-30]. Very limited information is available on the genetic basis of stroke especially in hemorrhagic stroke of Nepali population. In the present study we explored the possible risk factors of Nepali population.

II. METHODS

Subjects

The study population consisted of 200 both ischemic and hemorrhagic stroke patients. Based on inclusion/exclusion criteria, patients were recruited from the Neurology outpatient and inpatient of Gandaki Medical College Hospital. Also, question regarding the language they speak, the food they eat, determined the ethnicity. The study was ethically approved by institutional ethics committee.

Research Design

Hospital based cross-section observational study.

Type of Design

Hospital based cross-section observational study.

Research Question

To observe the risk factor according to age

To see the risk factor according to sex

Inclusion criteria:

1. Age above 35 years
2. Brain CT-scan indicative of cerebral infarction or intra-cerebral hemorrhage
3. MRI indicative of cerebral infraction or intra-cerebral hemorrhage

Exclusion criteria: The patients with following disorders were excluded

1. Patients in whom the cerebral hemorrhage secondary to trauma or previous coagulation disorders

Study Duration

The study was conducted from July 2020 to August 2021

Study Population

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Study population was any patients fulfilling the inclusion criteria with clinical features of stroke in Gandaki Medical College, Pokhara, Nepal.

Sampling Method

The sampling technique that was employed was non-probability convenience technique.

Sampling Technique: The participants that are required for the research are 200. As per the study of literature of prevalence of hypertension in stroke patients was 47.2%

$n= Z^2p*(1-p)/d^2$

$n= (1.962x47.2x52.8/7.08)^2$

n= 191.01

= 192 where, n = the desired samples men

z = the standard normal deviate usually set at 1.96 (or more)

p = Prevalence at 2.0 in previous study

Q-1.0-P

d= Absolute error or precision (15%)

i.e. 15% of 47.2 which is 7.08

For convenience 200 samples were taken into consideration.

Tools and technique

Data management and statistical analysis statistical methods

The data obtained by history, clinical examination and on investigations as per case entered in Microsoft excel. Demographic as well as clinical characteristics were recorded and data were analyzed by using statistical software like SPSS 15.

III. RESULTS

In the present case-control study, we selected 200 patients having hemorrhage and the same number had ischemic stroke. The risk factors of stroke such as age, gender, smoking, tobacco, alcohol intake, hypertension (systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg, history of hypertension or on antihypertensive drugs), diabetes (fasting blood sugar > 106 mg/dl, 2 hr postprandial blood sugar > 200 mg/dl, or on oral hypoglycemics/insulin), dyslipidemia (defined as a history of an abnormal lipid profile that required either dietary or pharmacological intervention, or an abnormal lipid profile) were recorded. History of heart disease such as atrial fibrillation, rheumatic heart disease or coronary artery disease, family history of hypertension, diabetes mellitus and stroke in first degree relatives were enquired.

3.1 Distribution of patients according to sex

The majority of the stroke patients were male i.e. 120 (60%) in the study group while the rest were females i.e. 40 %.

TABLE 1: Distribution of patients according to sex

N=200

	(n)	Percentage (%)
Male	120	60
Females	80	40

3.2 Distribution of patients according to age group

The persons are found to be highest in the age group of 30-39 i.e., 40, whereas the least number is found in the age group of 90-99.

TABLE 2: Distribution of cases according to age

N=200

Age in years	No. of patients	Percentage (%)
20-29	33	16.5
30-39	40	20.0
40-49	35	17.5
50-59	32	16.0
60-69	25	12.5
70-79	20	10.0
80-89	14	7.0
90-99	1	0.5

3.3 Age and gender of study groups

Mean age of stroke patients with healthy controls were compared using an independent t-test. The mean age of healthy controls was 55.25 years (SD±10.65) while ischemic stroke patients had mean age of 53.84 years (SD±12.14) and hemorrhagic stroke had 56.82 years (SD±10.35). The two-sided P value obtained on comparing mean ages of stroke patients with healthy controls was not significant (Ischemic stroke, P=0.32; hemorrhagic stroke, P=0.22). In healthy control group, there were 120 male and 80 female.

3.4 Demographic and risk factors:

109 persons visiting the hospital had clinical features related to stroke. Most patients were suffering from hemiparesis i.e. 84(77.06%) whereas 3(2.75%) persons were suffering from headache and vomiting.

TABLE 3: Distribution of clinical features

N=109

Clinical Features	(n)	Percentage (%)
Hemiparesis / hemiplegia	84	77.06
7th nerve palsy	42	38.5
Speech disorder	35	32.11
Comatose	19	17.43
Convulsions	4	3.66
Headache & Vomiting	3	2.75

3.5 Distribution of Stroke subtypes

Among 109 patients, most of them i.e. 69.72% had the cerebral infarction as subtype of stroke while only 2.75% were categorized under subarachnoid hemorrhage subtype.

TABLE 4: Distribution of Stroke subtypes

N=109

Stroke Subtypes	(n)	Percentage
Cerebral infarction	76	69.72
Intracerebral hemorrhage	16	14.67
Subarachnoid hemorrhage	3	2.75
Undetermined	14	12.84

3.6 Demographic and clinical characteristics of study subjects

Among the patient group, most of them i.e. 37.5% were hypertensive, 7.5% were diabetic and Ischemic Heart Disease being the least i.e. 0.5%. Hypertension was found to be the main cause of stroke. In the patient group, 5% were smokers, 9.4% chewed tobacco and 50% alcohol consumption patients showed more risk of stroke.

3.7 Stroke outcome at 30 days

Out of the total, nearly half of them i.e. 47.71% had stable conditions at 30 days while 28.85% had improved outcomes.

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TABLE 5: Distribution of Risk Factors in Stroke

N=200

Risk Factors	(n)	Percentage (%)
Hypertension	75	37.5
Dyslipidemia	32	16.0
H/O Stroke or Transient Ischemic Attack (TIA)	24	12.0
H/O hypertension	28	14.0
Diabetes mellitus	15	7.5
Valvular heart disease	25	12.5
Ischemic Heart Disease	1	0.5

TABLE 6: Stroke Outcome at 30 days

N=109

Outcomes	(n)	Percentage (%)
Stable	52	47.71%
Deteriorated	31	28.44%
Improved	26	23.85%

IV. DISCUSSION

Stroke is a common neurological disease and a leading cause of severe disability and death. Stroke is believed to be a multi-factorial disorder or complex trait for which it is not possible to demonstrate classical patterns of inheritance; however, twin, family and animal model studies have consistently suggested a genetic influence on stroke risk and prognosis[89].

Diagnosed hemorrhagic cases on CT scan and MR angiography were done among the patients who were normal tensive or had lobar hemorrhages. Therefore, other causes of hemorrhagic stroke such as arteriovenous malformation, aneurysm, and tumor bleeding were unlikely. Deep brain hemorrhage is mainly due to hypertension and is more common in Asian countries whereas lobar hemorrhagic stroke in the elderly is due to cerebral amyloid angiopathy and may have a different pathophysiological basis.

However, according to some studies, the frequency and contribution of hypertension to Intra-Cerebral Hemorrhage (ICH) were similar in patients with lobar hemorrhage compared with deep hemispheric, cerebellar, or pontine hemorrhage[90-93]. Patients with documented Cerebral Amyloid Angiopathy (CAA) may also have hypertensive angiopathy in 30% of patients. Hypertension may increase the tendency of hypertension-related hemorrhage and vice versa[94].

Hypertension was found to be the most important risk factor for ICH. In this study, Hypertension was detected in 80% of cases which correlated well with other studies. Probably other risk factors like smoking 60% and alcoholism (50%) were also responsible to the occurrence of ICH in males. In addition to hypertension, the male community is more prone to indulging in smoking and alcohol consumption when compared to females in developing countries like Nepal. Excessive intake of alcohol might result in increased Very Low Density Lipoprotein (VLDL) and Low Density Lipoprotein (LDL) content resulting in accelerated atherosclerosis. Diabetes mellitus was noted in 12% of cases in Archana Verma et al., 95.14% in Sk Mohapatra et al.,[96] and 8.57%o in Akbari et al.[97], and 22% in the present study. Clinical features like headache in 68%, vomiting in 58%, and convulsions in 16% of cases were important presenting features, which enabled a clinical diagnosis of ICH in this study. The onset of stroke was also taken into consideration. The diagnosis of ICH was considered with sudden onset of illness. In 200 cases, the onset is sudden i.e. 74%. Hemiplegia (80 cases) 80% was the most common presentation in the present study. Headache was noted as the most common presenting symptom and Hemiplegia was the most initial neurological sign in this study.

In the present study, a clinical diagnosis of ICH was made in 148 cases (74%) and the remaining 52 cases (26%) were considered to be Ischemic strokes. However, a CT scan showed ICH in all 200 cases. Thus, there is a discrepancy of 26% under-diagnosis. This significant number of misdiagnosis/under-diagnosis and therapeutic problems associated with misdiagnosis/under-diagnosis strongly favors and recommends the routine use of a CT Scan Brain for establishing the final diagnosis in all suspected cases of Cerebrovascular Accidents (CVAs). Size of Haematoma, site of hemorrhage, and Associated Mass Effect on CT scan were the important prognostic factors observed in this study. The site of hemorrhage also plays a vital role in predicting the outcome in patients with Intracerebral Haemorrhage. Mortality was lower in patients with capsule-ganglionic hematoma (21.4%). The level of sensorium at the time of onset is the most important prognostic factor of the final outcome. In the present study, most patients presented with coma, fewer patients presented with altered sensorium, and two Patient was conscious at the time of admission.

Amit Kumar et.al[98] dealt with 100 patients of stroke who were admitted to B. R. D. Medical College, Gorakhpur, India. Each patient was analyzed in detail about clinical presentation and the investigations were aimed to establish the pathologic type of stroke and estimation of risk factors. Stroke incidence was more in males (Male: Female= 1.43:1). Maximum incidence of stroke was in the 6th decade (32%) followed by the 7th decade (30%). Among modifiable risk factors, a history of hypertension was the commonest (51%) followed by smoking (36% of patients) exclusively, found in males. Hemiparesis was the most common presentation (95%) followed by altered sensorium (55%). Chest X-ray was abnormal in 16% of patients, abnormal ECG was found in 27% of patients and abnormal lipid values were found in 54 patients. They concluded that apart from control of hypertension and diabetes, abnormal lipid profile remains an important modifiable risk factor for stroke.

V. CONCLUSION

The majority of the stroke patients were male i.e. 120 (60%) in the study group and hypertension was found to be the main cause of stroke. 55.40% of the ischemic stroke patients were under the large vessel disease subgroup. In the patient group 5% were smokers, 9.4% chewed tobacco and 50% alcohol consumption patients showed more risk of stroke. Family H/o stroke was present in 15.54% of the total patients. History of TIA/stroke was observed in 11.65% of the total study subjects showed a higher (twentyfold) risk in lobar.

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