

Predictive Strength of Risk Factors of Stroke

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Abstract

The objective is to identify the risk factors for Stroke and to estimate their relative importance in a large nationally representative sample of 277 patients randomly selected public sector hospitals of Rawalpindi that we checked through modeling that which factors can contribute more significantly as compared to others in developing Stroke in this nationally representative sample. A hospital based case-control study of 277 patients with 78% cases (163 Ischemic and 52 Hemorrhagic) and 22% controls are carried out during the six months period of February 2008 to July 2008. Data is collected from Military Hospital Rawalpindi (MH) and Rawalpindi General Hospital (RGH) through well-designed and structured questionnaire. Data is classified and analyzed as socio-demographic and clinical risk factors. The analysis is descriptive as well as analytical. Multiple Logistic Regression Model and Probability of predicted risk of disease were used to get the degree of association between risk factors and Stroke. Odds Ratio (OR) and 95% Confidence Intervals (CI) are computed. The study shows that the incidence of stroke is due to three socio-demographic risk factors age (OR=1.045, p=0.000), home environment (OR=1.870, p=0.048) and living style (OR=1.731, p=0.003) and six clinical risk factors Hypertension (OR=59.570, p=0.000), Diabetes Mellitus (OR=5.163, p=0.001), Cholesterol Level (OR=12.113, p=0.000), Smoking (OR=5.137, p=0.002), Heart Diseases (OR=11.660, p=0.000) and Central Nervous System Infections (OR=7.580, p=0.009). The study concludes that Hypertension, Cholesterol Level and Heart Diseases are found to be the strongest significant risk factors in both genders to develop Stroke.

Keywords

Stroke, Risk factors, Logistic regression, Odds ratio.

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1. Introduction

Stroke or Brain Attack or Cerebrovascular Accident (CVA) is a clinical group of concurrent symptoms of a disease to assert a range of disorders which consequences in focal Cerebral Ischemia (Herekar and Hilal, 2008). The clinical definition of Stroke, carefully planned by the World Health Organization (WHO) as rapidly developed clinical signs of focal disturbance of Cerebral Function, lasting for more than 24 hours with the interruption of death, with no obvious cause of Vascular Origin (Brust, 2007). A despot time limit of 24-hours make prominent Stroke from Transient Ischemic Attack (TIA), which has the same definition but in TIA all symptoms resolve within 24 hours (Herekar and Hilal, 2008; Park, 2001).

Symptoms of Stroke depend on the type (clot or bleed) and which area of the brain is affected. Both type of Stroke include almost same symptoms including sudden severe headache with no known cause, paralyze or weakness of face, arm and leg, especially on one side of the body, difficulty in speaking, swallowing and understanding, difficulty in seeing from one or both eyes, difficulty in walking and feeling confused, loss of stability of body or mind, feeling nausea or vomiting and painful or stiff neck (National Stroke Association, 2008)

The aims of the study are; (1) to assess the predictive strength of known clinical features and socio demographic aspects of patients suffering from Stroke disease in Pakistani population by using the statistical analysis, (2) to develop a socio-demographic and clinical prediction model to discriminate between with and without significant Stroke disease, by using observed predictive strength of these risk factors, (3) to find the strength of association with which risk factors are associated with the disease, (4) to study risk factors for different groups such as male, female and postmenopausal female, (5) to use the model for prediction purposes.

2. Methodology

Data set is categorized as socio-demographic risk factors and clinical risk factors and then analyzed. Statistical Package for Social Sciences (SPSS Inc.) Version 15.0 is used to perform all statistical analysis. The risk factors are thoroughly analyzed on overall patients and on bifurcated groups of males, females and postmenopausal females. Relevant descriptive statistics, count and percentages are calculated for risk factors by Cross Tabulation. Mean and standard deviation is calculated for quantitative variable age. Bivariate and Multivariate Analysis is

performed to analyze whether the variables are related to Stroke. Separate Bivariate and Multivariate Analysis are carried out for overall patients and for each group of patients. In Bivariate Analysis, Pearson Chi-square, Phi and Cramer's Coefficient, Contingency Coefficient and Kendall's tau b is used to check the type of association i.e. positive or negative association of risk factors with Stroke by comparing α (level of significance), which is set at 10%, with p-value. In Multivariate Analysis, Multiple Logistic Models by Forward Stepwise Likelihood Ratio Method is applied and obtained the significant risk factors. The risk factors with insignificant effect are excluded from the Multiple Logistic Regression Models. All p-values are two tailed ($\alpha = 0.05$). Odds Ratio is also computed. Probability of predicted risk of disease is used to get the degree of association between risk factor and Stroke.

3. Results

Out of 277 patients, 78% are cases and 22% are controls. The overall age ranged is between 14 to 95 years. There are 61% males and 39% females and among 108 females 70% are postmenopausal females.

The maximum number of Stroke patients lies in the higher age group (51 year & above) in both male and female. Among 215 cases patients having Ischemic Stroke were 76% and Hemorrhagic Stroke were 24%. 52% presented with right sided weakness and 40% presented with left sided weakness, 79% had headache, 43% were vomiting and 59 27% developed fits. 58% were unable to speak properly, 35% had coma and 26% were having neck stiffness.

Bivariate Analyses for overall patients revealed that among socio-demographic variables that are statistically significant is age (0.000), employment status (0.089), social status (0.051), home environment (0.055) and living style (0.029) and have positive association with the development of Stroke. Among clinical variables that are statistically significant were Hypertension (0.000), Diabetes Mellitus (0.000), High Cholesterol Level (0.006), Smoking (0.003), Heart Disease (0.000), Central Nervous System Infections (0.044), Chronic Liver Disease (0.055) and Urinary Incontinence (0.059).

The variables that are statistically significant on bifurcated groups of male, females patients in Bivariate Analysis indicates that age, Hypertension, Diabetes Mellitus and High Cholesterol Level are found to be most important and

positively associated with the development of Stroke. For female patients the hormonal status is found to be significantly positively associated with Stroke, and an important risk factor for females.

3.1 Results of Multiple Logistic Regression

The p-values of three socio-demographic risk factors; age, home environment and living style, six clinical risk factors; Hypertension, Diabetes Mellitus, Cholesterol Level, Smoking, Heart Disease, Central Nervous System Infections are found to be significant. The Odds Ratios for the variables along with coefficients are given in Table 1.

Interpretation of Socio-Demographic Risk Factors

The first factor among socio-demographic risk factors was age. Age was taken as numeric variable. The coefficient of age has positive value 0.044 with Odds Ratio (OR) 1.045, which indicates that with the increase of one year in the age the risk of developing Stroke is increased 1.045 times or 4.5% provided all other factors kept constant. Second significant factor of first category is home environment and taken as categorical variable with positive value 0.626. Peaceful environment in the home was taken as base group against 'Disturbed Environment'. The OR is showing that the person belongs to some type of conflicting and disturbed home environment has 1.870 times more chances of having Stroke than a person having peaceful environment keeping all the others factors constant. Last (third) factor is living style shows that the persons who have normal or sedentary life styles has 1.731 times more chance of having Stroke than the active persons. So, the factor normal and sedentary lifestyle has positive statistically significant association with Stroke.

In male patients model age and living style, in female's patients model only age and in postmenopausal female patients model education and home environment were found to be significant risk factors among social and demographic factors. Above-mentioned variables have positive association with Stroke except education. Education has negative coefficient that means as the education level goes up, the prevalence of Stroke goes down.

Interpretation of Clinical Risk Factors

The first major and most significant risk factor among all clinical risk factors in overall patients, in male group and in female group is Hypertension. The coefficient of Hypertension is 4.087, which is positive. The OR is 59.570. It indicates high significance with Stroke. It also shows that Hypertensive patient

with higher code has 59 times more chance of developing Stroke than Non-hypertensive patient.

The significant factor Diabetes Mellitus is taken as a categorical variable. Its coefficient is positive. The factor Diabetes increases the Odds of suffering from Stroke is 5.163. Third statistically significant risk factor is Cholesterol and it has positive significance in developing Stroke. Smoking appeared to be fourth significant risk factor for Stroke with positive coefficient 1.637. Therefore, smokers have (higher code) 5.137 times more chance of having Stroke than non-smoke keeping all the others factors constant. Fifth significant factor is Heart Diseases. Therefore, patients with some Heart Disease have 11 times more chance of having Stroke than patients who do not have any Heart Disease. Sixth significant factor is Central Nervous System Infections with coefficient 2.205 and OR = 7.580. So, the factor has positive association with Stroke and is statistically significant.

In predictive male patients and female patients model almost same risk factors were significant except Central Nervous System Infections and Smoking, respectively. In the predictive model for postmenopausal female Hypertension, Diabetes Mellitus and Heart Disease were also found significant among clinical risk factors.

The final fitted Logistic Regression Model for overall observations of socio-demographic risk factors is (4.1) and for overall observations of clinical risk factors is (4.2) as under;

$$\hat{y} = p(\text{Str}) = \frac{1}{1 + e^{-Z}}$$

where,

$$Z = -3.024 + 0.044(\text{AGE}) + 0.626(\text{HE}) + 0.549(\text{LS}) \quad (4.1)$$

$$Z = -16.645 + 4.087(\text{HT}) + 1.641(\text{DM}) + 2.404(\text{CHOL}) + 1.637(\text{SMOK}) + 2.456(\text{HD}) + 2.025(\text{CNS}) \quad (4.2)$$

4. Discussion

Advanced age is the most important and uncontrollable factor of the number of new Stroke cases per year. The mean age of overall patients was 55.45 years \pm

18.55 years and for Stroke patients was 57.50 years \pm 14.83 years which is less than that observed in another study (69.9 years \pm 12.0 years) because the average life expectancy is rather less in Asian countries as compared to the Western countries (Sacco, 1998). The mean age of Stroke patients varies from 52-66 years in several local studies (Iqbal et al., 2003; Khan and Vohra, 2007 and Khealani et al., 2008) and not much greater than West 76-80 years (Khan and Vohra, 2007). Our study demonstrates that (31%) Stroke patients were of young ages 14-50 years which is higher than 26%; 15-45 years, 28%; under 55 years (Khan and Shah, 2000 and Syed et al., 2003) but less than 34% and 42% (Naseem et al., 2003 and Vohra et al., 2000). The mean age of male and females was 55.23 years and 55.79 years, respectively, which is again less reported as 68.6 years and 72.9 years, respectively (Appelros et al., 2009). In our study, peak age of Stroke patients was 51-95 years, which is similar to the other study (Khan and Vohra, 2007). Significance of age through Bivariate and Multivariate Analysis is also verified by some other Western studies (Sturgeon et al., 2007 and Wolinsky et al., 1998).

Stroke is generally more exists in males than in females throughout the world but females were more rigorously effected (Appelros et al., 2009). In our study, male-to-female ratio is 1.6:1 that is slightly greater than (1.5:1) (Iqbal et al., 2003; Khawaja and Shakoor, 1993 and Khealani et al., 2008) and quite resemble with the figure (1.6:1) (Imran and Raza, 2003) and but less than (1.7:1) and (2.5:1) (Khan et al., 2006 and Putaala et al., 2009). The male to female ratio in various local studies is about 1.5:1 (Khealani et al., 2008). Higher ratio in male patients is either due to the older age or presence of other risk factor like Diabetes Mellitus and Smoking etc. (Khan et al., 2006). In present findings, Stroke on the left hemisphere (right sided weakness) showed significance in Stroke disability in accordance with Western study (Naess et al., 2006 and Putala et al., 2009) and reported that left Cerebral Infarction is more frequent than right Cerebral Hemisphere Infarction among adults.

Physical inactivity is a changeable risk factor for total Stroke, Ischemic and Hemorrhagic Stroke. Physical activity also takes part in to reduce the risk of Stroke and minimized the Stroke risk up to 64% for active and fit persons as compared to inactive and unfit persons (Lee et al., 2003 and Wendel-Vos et al., 2004). An inverse relationship exists between physical activity and risk of Stroke independent of excessive alcohol intake and pre-existing Stroke or Ischemic Heart Disease (IHD) and moderate physical activity significantly minimize the risk of stroke in men (Shaper and Wannamethee, 1992).

The first major and most significant modifiable risk factor among all clinical risk factors in this study is Hypertension (HT) and found in (92%) patients. Male to female ratio is approximately same in the study. The significance of Hypertension as a risk factor in Stroke achieves a permanent acceptance (Khan et al., 2006). Hypertension maximized the occurrence of Stroke; however, the relationship between Hypertension and Stroke is dominant factor in those having Stroke at 90 years or less than 90 years (Arakawa et al., 2005). It is single independent risk factor of Stroke that is confirmed by many local South Asian studies (Herekar and Hilal, 2008; Iqbal et al., 2003; Khan et al., 2006; Khawaja and Shakoor, 1993; Khan and Vohra, 2007 and Naseem et al., 2003) and Western studies (Wolinsky et al., 1998; Arakawa et al., 2005 and You et al., 1997). The rate of occurrence of having a Stroke is increased four to six times and 40-90% of subjects have Hypertension before to the event. Age adjusted relative risk of Stroke among those having Hypertension was 3.1 for men and 2.9 for women. Occurrence of Hypertension was found in 92% samples in our study but this percentage was being observed higher than all local studies but nearly approximated to one local study (82%) (Iqbal et al., 2003).

Diabetes Mellitus (DM) was the second most important and modifiable risk factor present in 60% of patients in this study (Herekar and Hilal, 2008; Iqbal et al., 2003). Significance of Diabetes in Stroke was also verified by several Western studies (Wolinsky et al., 1998; You et al., 1997; Abbott et al., 1987; Davis et al., 1999; Arboix et al., 2005 and Janghorbani et al., 2007). The percentage of DM was found to be higher in our set up (18 - 42.5%) as compared to Western societies (10 - 26%) (Wolinsky et al., 1998). Diabetes Mellitus is extensively valid risk factor for Stroke as a whole and specifically for Ischemic Stroke (Iqbal et al., 2003). Ischemic Stroke occurring often in Diabetic individuals verses Non-diabetics (Arboix et al., 2009). Diabetics have 3 times more risk of developing Stroke than normal population and risk is greater for men at earlier age as compared to women. Ischemic Stroke is more common than Hemorrhagic Stroke in Diabetics individuals (Iqbal et al., 2003) Diabetes can affect Stroke in different aspects which is in subtype, in age, in speed of recovery and in deaths (Jorgensen et al., 1994).

Hypercholesterolemia was third most common and controllable risk factor in this study (National health Survey narrated that 12% population more than 15 years of age is suffering from Hypercholesterolemia (Khealani et al., 2008). Hyperlipidemia causes more Ischemic Strokes as compared to Hemorrhagic Stroke (Iqbal et al.,

2003). Higher Total Cholesterol (TC) and lower HDL Cholesterol Levels were attributed to increased risk of Ischemic Stroke (Tirschwell et al., 2004). A study by Kurth et al. (2007) describes the significance of cholesterol in developing Stroke in female subjects. Although our findings also showing the affirmative role of Cholesterol in posing the Stroke but the findings described by another study of Bowman et al. (2003) was denial our findings.

Chances of Stroke increased two times in smokers than non-smokers. Prevalence of tobacco smoking is estimated 36% for males and 9% for females in Pakistan (Ahmed et al., 2008). After five to ten years of smoke quitting, chances of stroke occurrence was same in smokers and non-smokers (Khan and Vohra, 2008). In our findings, smoking in male person shows significance in developing Stroke (Kurth et al., 2003; Robbins et al., 1994). Number of smokers was higher among the Stroke group than control group in the present study. Smoking may be regarded as a causal agent of stroke-associated morbidity and mortality (Robbins et al., 1994).

Risk of Stroke increased with the combination of Cardiac Impairment and Hypertension. Heart Diseases maximized the relative risk of stroke by 2 to 4 fold. Heart Diseases were less frequent 11% to 46.5% in our studies than Western series 35%-72% (Khan and Vohra, 2007). In our study, significant risk factor Heart Diseases was matched with the other findings (You et al., 1997).

Stroke can be a complication of a Central Nervous System (CNS) Infections or difficulty of an Immunization. Risk for Cerebrovascular Ischemia in all age groups increased with infection. Recent infection, primarily of bacterial origin, might be attributed for Cerebrovascular Ischemia in older as well as in younger patients. Central Nervous System (CNS) Infections show significance in our findings that was in accordance to other study (Grau et al., 1995).

5. Conclusion

Study focuses the socio-demographic risk factors as well as clinical risk factors and emphasize that we should not neglect the socio-demographic factors because many clinical factors produce from these factors. Present study demonstrates that Hypertension, Cholesterol Level and Heart Diseases are found to be the strongest significant risk factors in both genders to develop Stroke. By adopting preventive measure and adequate control on these factors, risk of Stroke can be reduced.

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Table 1: Significant Predictors of Stroke

Variables	B	Odds Ratio	95% CI for exp (B)	
Socio-Demographic Risk Factors				
AGE	.044	1.045	1.024	1.006
HE	.626	1.870	1.006	3.447
LS	.549	1.731	1.205	2.487
Clinical Risk Factors				
HT	4.087	59.570	16.722	212.209
DM	1.641	5.163	1.901	14.019
CHOL	2.404	12.413	4.232	34.673
SMOK	1.637	5.137	1.860	14.186
HD	2.456	11.660	3.383	40.188
CNS	2.025	7.580	1.668	34.453

Table 2: Significant Predictors of Stroke (Male Group)

Variables	B	Odds Ratio	95% CI for exp (B)	
Socio-Demographic Risk Factors				
AGE	.035	1.035	1.008	1.063
LS	.723	2.060	1.283	3.307
Clinical Risk Factors				
HT	4.886	32.414	17.787	185.775
DM	1.923	6.844	1.540	30.412
CHOL	3.165	23.680	4.638	120.910
SMOK	2.434	11.402	2.382	54.576
HD	2.849	17.272	2.710	110.088

Table 3: Significant Predictors of Stroke (Female Group)

Variables	B	Odds Ratio	95% CI for exp (B)	
Socio-Demographic Risk Factors				
AGE	.059	1.061	1.027	1.095
Clinical Risk Factors				
HT	3.494	32.926	5.152	210.414
DM	2.316	10.133	1.944	52.834
CHOL	2.128	8.394	1.769	39.839
HD	2.050	7.771	1.311	46.077
CN	3.012	20.335	1.752	236.032