**Original Article** 

# **Integrated Care of Modifiable Risk**

Ischemic Stroke

# Factors in Patients with Ischemic Stroke can Improve the Reproductivity of State

1. Bushra Rehman 2. Aneela Qidwai 3. Shaista Ahmed 4. Tahir Hussain

1. Asstt. Prof. of Medicine, Hamdard University Hospital, Karachi 2,3. Asstt. Profs. of Medicine, Abbassi Shaheed Hospital, Karachi 4. Profs of Medicine, Abbassi Shaheed Hospital, Karachi

### **ABSTRACT**

**Objectives:** To identify modifiable risk factors in patient with ischemic stroke in tertiary care hospital of Karachi.

Study Design: Cross sectional study

**Place and Duration of Study:** This study was conducted in Medical Unit-I, II, III, Abbasi Shaheed Hospital Karachi from  $21^{st}$  September  $2006 - 21^{st}$  March 2007.

**Material and method:** All patients admitted during six months period, who met the inclusion criteria of recent ischemic stroke, were analyzed according to questionnaire for six selected variable i.e hypertension, diabetes mellitus, cigarette smoking, obesity, hyperlipidemia and cardiac disorder.

**Results:** Average age of patient was 65. 57 years. Hypertension involved in 76.6%, diabetes mellitus 53%, cigarette smoking in 31.7%, 13.3% patients were obese, hyperlipimedia found in 48.3% patients and cardiac disorder in 5% patients.

Combination of hypertension and smoking was found in 38.46%, combination of hypertension, diabetes and hyperlipidemia in 44.23% and combination of diabetes, obesity and hyperlipidemia in 17.31% patients.

**Conclusion:** Among the six risk factors analyzed, data revealed a significant effect of hypertension. Other contributing risk factors in order of frequency were diabetes, hyperlipidemia, smoking, obesity and cardiac disorders. Combinations of risk factors i.e hypertension and smoking, or combination of hypertension, diabetes and hyperlipidemia, or combination of diabetes, obesity and hyperlipidemia were the commonly occurring comorbidities in patients presented with ischemic stroke.

**Key words:** Ischemic stroke, hypertension, diabetes mellitus, cigarette smoking, hyperlipidemia, obesity, cardiac disorder.

#### INTRODUCTION

Stroke in the third most common cause of death in developed world<sup>1</sup>. There are approximately 5 million fatal and 15 million non fatal stroke occur each year and over 150 million survivor of stroke alive world wide today<sup>3</sup>.

Because of the morbidity and mortality associated with this grave condition, the primary focus of clinicians therefore is to identify and augment the record of the modifiable factors that can help in significant reduction of disease burden on health system. These include hypertension, diabetes, smoking, hyperlipidemia, obesity, myocardial infarction, atrial fibrillation and valvular heart diseases<sup>2</sup>. Good control or prevention of these factors leads to a progressive decline in the incidence of stroke<sup>1</sup>.

Hypertension is the most important contributing factor as risk of stroke increases by approximately 50% for every 5mm Hg increases in the diastolic pressure <sup>8</sup>. In a meta analysis lowering of blood pressure to level below 140/90mmHg is the simple and most important measure for decreasing the risk of stroke <sup>9,10</sup>.

Diabetes mellitus reached epidemic proportion in Pakistani population with a large number of patients had impaired fasting glucose and impaired glucose tolerance<sup>11</sup>.It independently carries a 3 fold increase in the incidence of stroke<sup>8</sup>.Perth community stroke study identified diabetes as a single most important risk factor for stroke.

Hyperlipidemia is another modifiable factor, patients with coronary artery disease and hyperlipidemia demonstrated 25-50% risk for stroke or TIA <sup>19.</sup>

The population attributed risk for stroke associated with smoking is about  $12\%^{.21}$ .

Obesity is the rising danger for stroke in high socioeconomic group but in our population central obesity is increasing which along with other factors contributes in syndrome X indirectly increases stroke risk.

Cardiac disorders attributed to the risk of stroke in young population<sup>26</sup>

The only approved treatment for acute ischemic stroke is intravenous tissue plasminogen activator which is given to less than 3% of population because of various reason<sup>6</sup>. The stroke or TIA work up must be completed quickly so that appropriate treatment and interventions can be initiated to reduce the risk of additional event<sup>1</sup>. Therefore, stroke prevention is the most important strategy for reducing the burden of this disorder in our developing society. It is found that better understanding and interaction with the risk factor has significantly

reduced the death rate from stroke in the United States<sup>4</sup>, same can be done in our society as greater than 70% of rural population are unaware that they have hypertension or diabetes or any lipid abnormality and do not come to medical notice until end organ damage had taken place<sup>7</sup>.

In this study we noticed prevalence of various factors involved in first ever ischemic stroke. Good control of these factors can minimize the risk of stroke recurrence and by increasing awareness can decrease the risk of first stroke in our population.

## MATERIALS AND METHODS

All the patients admitted to Medical Unit I, II and III of Abbasi Shaheed Hospital Karachi during September 2006 to March 2007 were included. Patients with the age above 18 years, presented with clinical signs and CTscan proven ischemic stroke were selected by non probability convinience technique. Patients who had focal neurological deficit ,hemiplegia, pareses, loss of sensation, aphasia, dysphasia, cranial nerve involvement or with sudden or altered level of consciousness with CT scan showing area of brain infraction were included.

Patients with hypertensive, uraemic or hepatic encephalopathy or who had traumatic or spontaneous brain haemorrhage, brain abcess or brain tumors were excluded from the study.

Patients with history of hypertension or who had sustained high blood pressure more than 140/90 during hospitalization were labeled as hypertensive. Patients with history of diabetes or who had fasting blood glucose more than 126mg/dl or random blood glucose of 200mg/dl on more than one occasion were labeled as diabetic. Patients who smoked more than 1 cigarette per day for 1 year were labeled as smoker. Patients who had BMI (body mass index) more than 30 labeled as obese. Patients with serum total cholesterol more than 200mg/dl, LDL(low density lipoprotein) more than 130mg/dl, HDL(high density lipoprotein) less than 32mg/dl and TG (triglyceride) more than 165mg/dl considered hyperlipidemic. Patients who either had history or presented with ECG or ECHO proven myocardial infarction, atrial fibrillation or valvular heart diseases were included in the study.

After taking informed consent, history and examination was done by doctor on duty and investigations were sent. All clinical and laboratory data as well the detail of treatment was entered in a proforma, specialty designed for the purpose.

## **RESULTS**

During study period, 120 patients with CT Scan proven ischemic stroke were evaluated.

Mean age was 65. 57 years (ranging from 50-70 Years). It is slightly higher in men (69.0) than in women (64.6). Age distribution showed that 15% of patients with

ischemic stroke belonged to the age group of 50-55 years, while 35.2% were between 55-65 years and 48.6% were above 65 years of age.

The profiles of six selected modifiable risk factors in patients with ischemic stroke were

analyzed. Hypertension as observed the most common risk factor that affects

92/120 (76.6%) patients out of whom 54 were male 38 were female, 34 were on regular

treatment, 46 were on irregular treatment and only 12 were on no treatment.

Diabetes mellitus was found in 64/120 (53.3%) patients. Although no patient had diabetes as

a lone risk factor, 46 patients presented with diabetes, hypertension and hyperlipidemia and

18 patients were diabetic, obese and hyperlipidemic.

In our study 58/120 patients (48.3%) were found to be hyperlipidemic. Out of them 32

had hypertriglyceridemia only and 26 patients presented with high LDL(low density

lipoprotein), low HDL(high density lipoprotein) and high TG (triglyceride) levels.

It was found in combination with diabetes and obesity as contributing factor.

Smoking was observed in 38/120(31.6%) patients. Out of them 36 were males and only 2

females. Among them 35 were active smokers and 3 were ex smokers.

In our study 16/120 patients (13.3%) were obese with the mean BMI (Body Mass Index) of

32.7. Out of them 12 women were obese with BMI(Body mass index) range between

29.5 - 34.0 and only 4 men found to be obese with BMI of 31.0 and 33.3 respectively.

Cardiac disorder noted in only 6/120 (5%) patients, 4 of them found to be in atrial

fibrillation, while 2 patients had myocardial infarction 4 days prior to stroke. All of them were males (Table 1).

Variable of gender was of compared with Comorbids by chi square test. Gender was

statistically non-significant with cardiac disease p-value 0.049. Regression analysis showed

that there is highly significant association between stroke and smoking keeping gender as

fixed factor(R=0.55) with p-value of 0.0001. Marginal significant association between stroke

and hypertension keeping gender as fixed fraction (R=0.23) with p-value 0.0001 and just

significant association between stroke and diabetes, obesity and hyperlipidemia keeping

gender as fixed fraction (R=0.71, R=0.17, R=0.87) p-value=0.001 (table 2).

Frequency of isolated and combined risk factors also determined.

Multiple risk factors found in 104 patients (fig 1). Hypertension, diabetes and hyperlipidemia in 46

(44.23%) patients together were the most common combination observed. Hypertension and smoking were the next common co-morbidities found in 40 (38.46%) patients. Only 18 (17.31%) patients were found to be diabetic, obese and hyperlipidemic (figure 1).

Isolated risk factors were found in 16 patients(fig 2). Hypertension was most common single risk factor seen in 10 patients, 4 patients had atrial fibrillation and 2 patients had myocardial infarction 3 days prior to stroke

Table No.1:

24024 110121		
Comorbids	Frequency	Percentage
Male	66	55%
Female	54	45%
Diabetes	64	53%
Obesity	16	13.3%
Hypertension	92	76.6%
Hyperlipidemia	58	48.3%
Smoking	38	31.7%
Cardiac diseases	6	5%
(myocardial infarction		
& atrial fibrillation)		

Table No.2:

Variable	Comorbids	<i>p</i> - values
Gender	Diabetes	0.0001
	Obesity	0.001
	Hypertension	0.0001
	Hyperlipidemia	0.0001
	Cardiac disease	0.049
	Smoking	0.0001

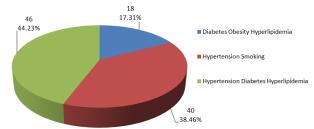


Figure 1: Combine Risk Factors

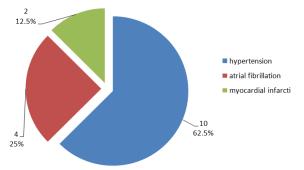


Figure 2: Isolated risk factors

#### **DISCUSSION**

Cerebro vascular accidents are the most devastating medical emergency in developing countries. Most of the studies conducted in developed world showed a declining pattern in contrast to the developing countries where the incidence of stroke is continuously inclining<sup>3</sup>. This study reports the frequency of hypertension, diabetes, hyperlipidemia, smoking, obesity and cardiac disorder in patients presented with cerebral ischemic stroke. An optimal management of risk factor for strokes is crucial to reduce the risk of recurrence and first ever stroke. One of the major public health issues for coming years will be to focus more on risk factors recognition and their prevention<sup>5</sup>.

Hypertension is probably the most important modifiable risk factor for stroke .It was mentioned in PROGRESS TRIAL<sup>6</sup> that there was steep and continuous association between hypertension and stroke, same as noticed in our study. Compliance of the drugs was the main issue 46 out of 120 patients were non-compliant to their medicine, 34 patients were compliant to their medicine but sedentary life style and lack of exercise might be the contributing factor. The prevalence of hypertension in Pakistan has been reported to be about 33% in the population over 45 years of age. The PMRC Pakistan health survey had reported hypertension as the number one chronic ailment in all four provinces. Thus the prevalence of around 10% of the entire population of Pakistan and 20% of the population over the age of 15 years and 30% over the age of 45 years is higher than in most parts of the world7. This is again emphasizes on good blood pressure control as highlighted in our study where compliance to medicine and sedentary life style are the main problem. It was noted that patients with first stroke, systolic blood pressure levels of >150mmHg during follow up were associated with increased risk of recurrent ischemic stroke<sup>12</sup> so good control with proper patient counseling is required to ensure compliance to drugs and proper follow up.

Second important risk factor was diabetes mellitus. It was noted to be one of the major factors responsible for the increased incidence of stroke in Pakistan<sup>14</sup>. Although no patient in our study had diabetes as a lone risk factor, in combination with hypertension, hyperlipidemia and obesity it takes major contribution in stroke occurrence.

Our Local data revealed significant combined effect of hypertension and diabetes mellitus<sup>13</sup> which was again supported by our study. It is also noted that Diabetes mellitus is associated with poor outcome of ischemic stroke both in term of mortality and morbidity during hospitalization<sup>14</sup> so good control of diabetes is required both for the primary and secondary prevention of stroke. The current consensus is that adequate control of diabetes is reasonable<sup>16</sup> because diabetes itself accelerates atherosclerosis along with hypertension and dyslipidemia as contributing factors for stroke<sup>17</sup>. This was similarly highlighted in our studied population where diabetes was found in 64/120 patients in different combinations (fig 1).

In our study a large proportion of patients found to be hyperlipidemic i.e 58/120 patients. Latest recommendation shows aggressive control of cholestrol with lipid lowering agents causes regression of atherosclerosis in saphenous venous grafts and can slow or reverse carotid artery atherosclerosis which reduces the emboli formation and significant decrease in stroke incidence <sup>18</sup> thus adequate early management of hyperlipidemia seems justified<sup>20</sup> and patients should be aware of this rising danger. Hyperlipidemia found in large number of patients in our study and can be control by life style modification and early use of statins.

Smoking is again a preventable risk factor in stroke. It increases stroke risk 2-4 folds<sup>8</sup> Current smoking contributes to approximately half of stroke events <sup>22</sup>. In present study 38 patients were smoker. Many of the smokers were also hypertensive which added to their risk of having stroke. There is clear evidence that quit smoking is highly beneficial for stroke prevention and after smoking cessation the risk of stroke decreases within 2-5 years<sup>22</sup>, <sup>23</sup>.

Obesity found in 16/120 patients. 12 were women and only 4 were men. Obesity seems to influence the risk of stroke through its association with other disorders like hypertension, diabetes mellitus and other cardio vascular risk factor<sup>24</sup>. Approximately 60% individual with obesity in the United States have metabolic syndrome and thrombo embolic disorders are more prevalent in obese<sup>25</sup>. It is noted that with each unit increase in body mass index there are 6% increase chance of stroke<sup>26</sup>. Sedantary life style, rich meals, lack of exercise and lack of awareness make obesity a rising danger for public health.

Many cardiac disorders were associated with an increased risk of stroke, among them atrial fibrillation is perhaps the most well recognized cardiac risk factor <sup>26</sup> but only 4 patients in our study were found to be in atrial fibrillation. One patient was a diagnosed case of mitral stenosis but it was unclear that either she was non compliant to anticoagulants or atrial fibrillation was not adequately controlled. Other important cardiac disorder is myocardial infarction. One of our patient had myocardial infarction 4 days prior to stroke, so early intervention and thrombolytic therapy in recommended to prevent cardiac embolism to brain circulation <sup>27</sup>.

Present study had included only six modifiable risk factors, other non modifiable risk factors like homocystein, protein C, protein S deficiency, hyperviscosity syndrome and others were not included. However even with this limitation, present study showed that hypertension, diabetes mellitus, hyperlipidemia, cigarette smoking, obesity and cardiac embolism are significant risk factors for ischemic stroke and offer hope that aggressive control, awareness about the risk factors and a proper clinical practice guideline for management of stroke will substantially

lower the risk of cerebral ischemic stroke in our country.

It is emphasized that government should establish stroke management and rehabilitation centre for stroke patients and private sector should come forward to help the efforts of government in this regard.

In present era of economic crisis, major portions of our resources must be spend towards stroke prevention by mean of having good control of modifiable risk factors and educating layman with the help of print and electronic media.

We need to organize large multi centric studies to know the exact prevalence of stroke risk factors in racial / ethinic sub groups as well as any regional differences that might exist, this helps in developing guidelines for the treatment and more specifically for the prevention of first ever stroke in our society.

#### CONCLUSION

Among the risk factors analyzed, data revealed a significant effect of hypertension, diabetes, smoking and hyperlipidemia as the commonest occurring comorbidities in patient with cerebral ischemic stroke. These finding serves to emphasize the tight control of blood pressure, early and prompt treatment of diabetes, exercise, diet modification, early start of statins in hyperlipidemia and obese, cessation of smoking, careful assessment and use of thrombolytic drugs in cardiac patients, present with first ever stroke.

# REFERENCES

- 1. Preventing recurrent cerebrovascular events in patients with stroke or transient ischemic attack the current data. J Am acad nurse practice 2011; 23(12):659-66.
- 2. Alam I, Haider I: Risk factors stratification in 100 patients of acute stroke. JPMA 2004;18.
- 3. WHO study on prevention of recurrences of MI and stroke(WHO premise). Bull world health Org 2005;83(11):820-9.
- 4. Lepllanue D, Vehier CM, Lucas C, Brodet R. stroke prevention, management of modifiable vascular risk factors. J Neurol 2002;249:507-17.
- 5. Integrated care improve risk factor modification one year after Stroke: initial results of ICARUSS model. J Neurol Neurosurg Psychiatry 2008;14.
- Progress collaborative group: Randomized trial of prandopril based blood pressure lowering regimen among 6105 individuals with previous stroke or transient ischemic attack. Lancet 2001;358: 1033-41.
- 7. Pakistan health education survey 1991-1992. Islamabad ministry of health, government of Pakistan 1993:115-22.
- 8. Pulsinelli WA. Cerebrovascular disease In: Benette JC, Plum F, editors. Cecil text book of medicine. 22<sup>nd</sup> ed. Philadelphia: WB Saunder; 2004.p.2070.

- Leonardi BI, Bath PM, Philips SJ, Sandereock PA, Blood pressure and clinical outcomes in the international stroke trial. Stroke 2002;33: 1315-1320.
- 10. Snow V, et al. The evidence base for tight blood pressure control in the management of type 2 diabetes mellitus. Ann Intern Med 2003;138:587.
- 11. Kielly DK, Wolf PA, Cupples LA, et al. Physical activity and stroke risk: the Framingham study, Am J Epidimiol1994;140:608-620.
- 12. Level of systolic blood pressure with in the normal range and risk of recurrent stroke. Jama 2011; 306 (19):2137-44.
- 13. Siddiqui AM, Ali A, Masruir S, Monga MA, Tauqeer A, Rehman KU. Clinical audit of patients with CVA in medical unit 1 jinnah hospital Lahore. Annals of King Edward Medical College 2001;7:79-82.
- 14. Functional outcome of ischemic stroke in diabetes. Ann King Edward Med Uni 2005;11(4):545-8.
- Straton IM, Alder AL, Neil AW, Methew DR, Mankey SE, Cull CA, et al. Association of glycemia with macro vascular and microvascular complication of type @ diabetes (UKPDS35) :prospective observational study. BMJ 2000; 321: 405-412.
- Masharani U. diabetes and hypoglycemia. Current medical diagnosis and treatment. 46<sup>th</sup> ed. New York: McGraw Hill; 2007.p.1226.
- 17. American Diabetic association: standard of medical care in diabetes. Diabetes care 2006;29:476.
- 18. Collin R, et al. Heart protection study collaborative group effect of cholesterol lowering with simvastatin on stroke and other major vascular events in 20536 peoples with cerebrovascular

- disease or other high risk conditions. Lancet 2004; 363:757.
- 19. Long term intervention with provastatin in ischemic diseases (lipid) study group . prevention of cardiovascular events and death with provastatin in patients with coronary heart disease and broad range of initial cholesterol levels. N Engl J Med 1998;339:1349-1357.
- Ischemic stroke in young adults of south Asia. J Pak Med Assoc 2002;32(9):417-22.
- 21. Wishnat JP. Modeling of risk factors for ischemic stroke: the Willis Lecture. Stroke 1997;28: 1840-1844.
- 22. Shinton R Beevers G. Metaanalysis of relation between cigarette smoking and stroke. BMJ 1989:298:789-94.
- Diaz MC, Matias GJ. Stroke in young people. Rev Neural 1996;24 (126):148-52.
- American medical association: assessment and management of adult obesity: A primer for physicians 2003.
- 25. Flier JS. Obesity. Harrisons principals of medicine. 16<sup>th</sup> ed. New York: McGraw Hill;2006.p.483.
- 26. Appelros P, Nyderick I, Seiger A, Teret A. predictor of severe stroke: Influence of prerexisting dementia and cardiac disorders. Stroke 2002; 33:2357-2362.
- 27. Clinical practice guidelines for the management of ischemic stroke in Pakistan. J Pak Med Assoc 2003;53(12):600-2.

# Address for Corresponding Author: Dr. Bushra Rehman

Assistant Professor of Medicine, Hamdard University Hospital Karachi