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BIO SOCIAL RISK FACTORS OF ACUTE STROKE: A CASE CONTROL STUDY FROM TERTIARY CARE HOSPITAL OF UTTARAKHAND

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Abstract

Background & objectives: Stroke is third most common cause of death worldwide. It represents 1.2% of the total deaths in India. Various research findings from the state of Uttarakhand shows high prevalence of alcoholism, tobacco addiction, Hypertension etc. making the population prone for stroke. With the objective of identifying the risk factors for development of stroke present case - control study was carried out in a tertiary care hospital.

Methods: 200 diagnosed patients of stroke were included in the study. For each case, one control without clinical athero-thrombotic disease, matched for age, sex and geographical residence area was selected. Various risk factors like hypertension, diabetes, addiction habits, stress profile, etc were studied by standard procedures.

Results: *I*solated hypertension (OR=27.5), Stress (OR=10.5), History of Diabetes Mellitus with Hypertension(OR=6.51), Daily smoking(OR=3.01), were found as important risk factors .Result showed a very interesting pattern of risk factor prevalence in agewise analysis. Amongst younger age group (20-40 years) Stress (OR-7.33), Daily smoking (OR-4.45) and Hypertension (OR- 4.41) were found to be major risk factors. With the advancement of age during 40-60 years- stress (OR-24.2) remains the major risk factor while Hypertension (OR- 11.2), takes over the Daily smoking habit (OR- 2.62). With reaching elderly age(>60 years age) hypertension (OR- 19.14)becomes the stronger risk factor followed by habit of Daily smoking (OR-6.02).

Interpretation & conclusions.: Major risk factor in this set of population is Stress followed by Hypertension and smoking. Preventive strategies must investigate causes of stress and its management techniques as primordial and primary prevention besides other risk factors.

Introduction-

Stroke is one of the leading cause of morbidity and mortality and third most common cause of death worldwide. Stroke represents about 1.2% of the total deaths in the country, which includes not only deaths at age > 70 years (2.4%) [1], but also 8.8% of urban young population (<40years of age) [2] The most recent community based study on stroke conducted in Kolkata (2003 to 2004) reported the crude Prevalence Rate to be 471.58 per 100,000 persons which captured the stroke survivors and stroke-caused deaths with an Annual Incidence Rate (AIR) of 123.15 per 100, 000 persons per year[3]

With the greater interconnectedness, rural population is increasingly adopting urban lifestyles leading to a nearly equal prevalence of stroke in both the population[4]. Prospective epidemiological studies have identified diabetes mellitus, hypertension, tobacco use, and low hemoglobin[5-8], higher levels of cholesterol, triglycerides, and low high-density lipoprotein[9,] physical inactivity as the most important risk factors of stroke .In a significant percentage of stroke patients no definite cause can be identified. Uttarakhand is a newly formed hilly state of the country with predominant rural population; It lacks data on various risk factors for stroke. Excessive alcoholism / tobacco addiction[10], high prevalence of Hypertension[11-13], unemployment, hostile terrain and limited accessibility of health services to population make the population prone for several non-communicable diseases including stroke, which require systematic investigation for appropriate planning of stroke prevention and control in the state. Current research paper analyses the risk factors which could be significant in stroke patients.

Materials and Methods-

A hospital based **case - control** study was planned on 200 diagnosed patients of cerebro vascular accidents (stroke) attending outdoor clinics and indoor admissions of Himalayan Institute of Medical Sciences, Dehradun over the period of 1 year. The WHO's (World Health Organization) definition of Stroke as "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than due to vascular origin" was used for recruiting the patients for the study[14].

Cases: Total 200 patients of less than 70 years of age presenting with acute stroke were recruited. The patients were clinically examined in detail by a neurologist applying a preset protocol. Their cerebral scans (CT/MRI) of the stroke was obtained and examined. Stroke cases as diagnosed by neurologist were interviewed by Investigator and trained research fellow, based on the tailored pre-set questionnaire on demographic, anthropomorphic, risk factors &stress profile. Informed consent was taken from patient or patient's family member.

Controls: For each case, one control without clinical athero-thrombotic disease, matched for age (± 1 year), sex, and geographical residence area was selected. If a selected control did not respond, refused to participate or was ineligible because of any history of CVS cerebro vascular accidents/valvular lesions a second and then a third matched control was invited. Controls were selected from the clinically healthy attendants and personals accompanying the patients from the same area of residence.

Study Instrument – Study was conducted using Stroke questionnaire adapted to local needs. Instrument was pre-tested prior to finalization. It included following information on Age, sex, history of Hypertension, Cardiac disease, Diabetes, Cancer, stroke, drug compliance etc. Addiction information was obtained as per WHO alcohol, smoking and substance Involvement screening test WHO - assist v3.0 which was tailored to local needs. Stress levels were assessed by using questionnaire-bfec.kenyon.edu/Healthy Kenyon/stress_psymptoms.pdf assessed on 16/11/10 tailored to local needs. **Anthropometric Measurements** like Height (length was measured in patients who were not able to stand) and weight were measured as per standard WHO protocol[15]. Height/length was measured up to nearest 0.1 cm. Weight was recorded upto nearest 0.5 kg.

Random blood sugar and Blood cholesterol were assessed by standard procedures from the Institute lab, which has received NABL accreditation. Signs of ischemic heart disease & atrial fibrillation were assessed by resting electrocardiogram (ECG) according to the Minnesota code (1982)[16]

Data analysis is done by using descriptive statistics and presented as frequencies or mean values and standard deviations (SD). Differences between groups were examined with the χ^2 test for proportions. Risk factor analysis is done by calculation of Odds Ratio(OR) with 95% confidence interval . A p-value less than 0.05 was considered significant

Study was approved by Institutional Ethics Committee of Himalayan Institute Hospital Trust University (HIHT University).

Observations-

Total 200 stroke patients were recruited in the study, they were admitted to Himalayan Hospital from August 2012 to July 2013 i.e. over 12 months period. Similar number of age and sex matched controls were included in the study. Himalayan Hospital being the tertiary care center attached with the medical college has received most of the cases as referral patients. These patients got admitted in the hospital after an average time lag of seven days following the stroke.

Table –I presents the comparative data of bio-social factors amongst cases and controls in the study. Out of 200 cases males and females were in approximately 3:1 ratio. Mean age of cases and control was approximately same i.e. 58.43±14.1years. Average BMI was slightly higher amongst Controls (0.67±0.19 kg/m^2) and the prevalence of obesity (BMI ($\geq$ 25Kg/m^2) was also 9% higher amongst them.

Table-I Characteristics of the cases and controls		
Parameters	**Cases (N=200)**	**Controls (N= 200)**
Demographic factors		
Males	152(76%)	152(76%)
Females	48(24%)	48(24%)
Mean age (years)	58.43±14.1	57.09±8.7
Anthropometric Factors		
Average BMI (Kg/m^2)	26.24±3.71	26.91± 3.9
BMI ($\geq$ 25Kg/m^2)	103(51.5%)	121(60.5%)
Past History of Diseases		
History of Hypertension(HTN)	66(33.0%)	9(4.5%)
History of Diabetes Mellitus (DM)	6(3.0%)	12(6.0%)
History of Diabetes Mellitus(DM) with Hypertension(HTN)	47(23.5%)	0(0.0%)
Addiction Habits		
Daily Smoking	108(54%)	56(28%)
Daily intake of Alcohol	56(28%)	88(44%)
Blood Investigations		
Total Serum Cholesterol (>220mg/dl)	18(9.0%)	36(18.0%)
Random Blood Sugar ($\geq$140g/dl)	58(29.0%)	35(17.5%)
Stress profile		
Stress score (>70)	10(5.0%)	1(0.5%)

History of hypertension was almost 7 times more common amongst cases than controls. Whereas history of diabetes was twice more common amongst controls (Cases: Controls- 3%:6%).However when RBS was examined 29% cases & 17.5% controls were having RBS > 140mg/dl. History of diabetes along with Hypertension was reported in 23.5% cases, with none of the controls suffering from both the conditions together.

As far as addiction is concerned 54% were daily smokers amongst the cases in comparison to just half of them (28%) were daily smokers amongst controls. However many more (44%) controls were taking alcohol daily than cases (28%).

Study observation showed lower level of average Total serum cholesterol level (158 ±47.0 mg/dl) among cases than controls (175.8± 44.3 mg/dl), and almost half of the cases were having cholesterol level more than 220 mg/dl (9.0%) than controls (18.0%). Average random blood sugar was marginally higher amongst cases than controls. Higher percentage of the cases (29%) showed Random blood sugar ≥ 140g/dl than controls (17.5%).Only 10 cases have shown stress score level more than 70 i.e. needing certain de-stressing programme.

Table 2. Odd Risk of development of stroke				
Risk factors	Odds Ratio	95% CI	Chi value	P Value
Anthropometric Factors				
BMI (>/=25Kg/m2)	0.69	0.46 – 1.03	3.29	0.06
Addiction Habits				
Daily Smoking	3.01	1.99 – 4.57	27.95	<0.0001
Daily intake of Alcohol	0.49	0.32-0.75	11.1	<0.001
Past History of diseases				
History of isolated HTN	27.5	13.3 – 56.8	127.5	<0.0001
History of isolated DM	0.48	0.19– 0.96	0.33	0.93
History of Diabetes Mellitus(DM) with Hypertension(HTN)	6.51	3.09 – 13.7	29.9	<0.0001
Blood profile				
Random Blood Sugar (>140mg %)	1.92	1.19 – 3.09	7.41	0.008
Total Cholesterol (>/= 220mg/dl)	0.45	0.24 – 0.82	6.94	0.008
Stress profile				
Stress score (>70)	10.47	1.32 – 82.6	7.57	0.005

Table –II shows that History of isolate hypertension (OR=27.5, Stress score more than 70(OR=10.47), History of Diabetes Mellitus with Hypertension(OR=6.51), Daily smoking(OR=3.01), have come out as some important risk factors for development of stroke.

Table-III Agewise Bio-Social characteristics of the cases and controls						
Parameters	Cases (N=200)			Controls (N= 200)		
Age (years)	20 -40 (n=23) No.(%)	40 -60 (82) No.(%)	>60 (n=95) No.(%)	20-40 (n=27) No.(%)	40-60 (n=133) No.(%)	>60 (n=40) No.(%)
Anthropometric Factors						
BMI (≥ 25Kg/m^2)	14(60.8)	49(58.5)	40(42.1)	15(55.5)	79(59.4)	26(65)
Addiction Habits						
Daily Smoking	15(65.2)	46(56.1)	46(48.4)	8(29.6)	35(26.3)	7(17.5)
Daily intake of Alcohol	6(26.0)	21(25.6)	20(21.0)	4(14.8)	32(24.0)	7(17.5)
Past History of Diseases						
History of isolated Hypertension(HTN)	6(26.0)	33(40.2)	27(28.4)	2(7.4)	6(4.5)	1(2.5)
History of isolated Diabetes Mellitus (DM)	0.0	2(2.4)	4(4.2)	2(7.4)	8(6.0)	2(5.0)
History of Diabetes Mellitus(DM) With Hypertension(HTN)	2(8.7)	15(18.3)	30(31.6)	0.0	0.0	0.0
Blood Profile						
Total Serum Cholesterol (>220mg/dl)	3(13.0)	10(12.2)	5(5.3)	3(11.1)	22(16.5)	11(27.5)
Random Blood Sugar (≥140g/dl)	7(30.4)	25(30.5)	27(28.4)	4(14.8)	24(18.0)	7(17.5)
Stress profile						
Stress score (>70)	11(47.8)	34(41.5)	30(31.6)	3(11.1)	3(2.2)	0.0

Table –III Shows a contrasting relationship of obesity amongst cases and controls with age changes, decrease in obesity was found with increasing age amongst cases, while a reverse relationship was observed among controls. Addiction habits were also found to be decreasing with increasing age amongst cases where as no such clear cut pattern was observed amongst controls.

Prevalence of history of hypertension was highest amongst 40-60 year age group amongst cases, while it was highest in 20-40 year age group amongst controls. Prevalence of Total serum cholesterol more than 220 mg/dl was highest in 20-40 year age group of cases, while amongst control it was highest in more than 60 year age group. Random Blood Sugar (≥140g/dl) was reported in almost equal percentage from 20-40 and 40-60 years (30.5%) with slightly lesser percentage (28.4%) among > 60 years cases. Amongst control, highest prevalence of Random Blood Sugar (≥140g/dl) was observed amongst 40-60 years age group (18.0%)

Table-IV presents the agewise analysis of OR of various risk factors. In 20-40 years age group stress score >70(7.33), Daily smoking (OR-4.45) and History of Hypertension (OR- 4.41) were found to be the three important risk factors for development of stroke.In the 40-60 years age group stress score >70(OR-24.2) and History of Hypertension (OR- 11.2), and in >60 years age group History of Hypertension (OR- 19.14) and Daily smoking (OR-6.02) were found to be the important factors

Table-IV Age wise analysis of Odd's ratio and p values							
Risk Factors	**Odds Ratio (95% CI)**			**P value (Chi Value)**			
Age (yrs)	20 -40	40 -60	>60	20-40		40-60	>60
Anthropometric factors							
BMI (>/=25Kg/m2)	1.24 (0.40-3.8)	0.72 (0.42-1.2)	0.51 (0.2-1.1)	0.70 (0.14)		0.24 (1.38)	0.09 (2.85)
Addiction Habits							
Daily Smoking	4.45 (1.3-14.6)	2.62 (1.5-4.6)	6.02 (2.4-15.1)	0.011 (6.3)		0.0005 (11.82)	0.0001 (16.3)
Daily intake of Alcohol	2.02 (0.5-8.3)	0.89 (0.5-1.7)	0.59 (0.2-1.7)	0.26 (1.39)		0.72 (0.12)	0.33 (0.93)
Past History of Diseases							
History of HTN	4.41(1.07-3.1)	11.2 (4.4-28.3)	19.14 (1.3-1.9)	0.07 (2.90)		<0.0001 (35.7)	<0.0001 (14.08)
History of DM	-	0.33 0.13-1.63	0.97 (0.17-5.55)	-		0.13 (2.25)	0.64 (0.19)
Blood Investigations							
Total Serum Cholesterol(≥220mg/dl)	1.2 (0.34-11.4)	0.59 (0.26-1.31)	0.17 (0.05-0.53)	0.36 (0.98)		0.19 (1.66)	0.001 (10.8)
Random Blood Sugar (>140g/dl)	2.51 (0.63-10.0)	1.62 (0.85-3.06)	2.82 (1.09-7.2)	0.18 (1.7)		0.13 (2.25)	0.027 (4.87)
Stress Profile							
Stress>70	7.33 (1.71-31.3)	24.15 (7.13-81.7)	-		0.003 (8.3)	<0.000 (145.84)	-

Discussion-

To our knowledge, the present investigation is the first case- control study from the hilly states of the country that has evaluated risk factors for acute stroke in this population, which is considered to be still following traditional life style with better environmental conditions.

The selection of controls is usually the most difficult aspect of the case- control study design. To evaluate risk factors, community controls have always been considered a better choice[17] hence we had planned to select age ((± 1 year) and sex matched controls. However with all the possible efforts,

only 160 age ((± 1 year) and sex matched control could be selected. Rest 40 were sex matched but the age matching varied ± 5years.

In the present study median arrival time of the patient in the Himalayan Hospital was 13 hours, however in another study from a major urban centre, the median time to casualty arrival was 7.66 hours, with 25% of cases arriving within 3 hours and 49% of cases arriving within 6 hours. In this study, distance from hospital, contact with a local doctor, and low threat perceptions of symptoms were independent factors for delay in arrival[18] A rural-based study documented that the mean arrival time of stroke patients was 34±6 hours[19]. Poor recognition of early stroke symptoms and low perception of threat lead to delayed arrival of stroke subjects at hospitals

As the cases in the present study have been selected from the patients reporting to IPD of the medical college, 90% cases were the referral cases, which were already started with the treatment, 10% cases reported directly, hence Blood pressure is not included for the risk factor analysis. Blood cholesterol levels and Random blood sugar level although analysed as risk factors for the study but needs to be interpreted cautiously. Such limitations have also been reported by K Lipska et.al (2007) in their study from south India[20] .Considering various such limitations of the hospital based case control studies, Deepti Vibha & Kameshwar Prasad in their review article mentioned that risk factors with borderline association (odds ratio [OR], <3) are not considered to be established or important hence present article has focussed on risk factors with more than 3 odd's ratio[17]

In our study history of isolated hypertension(OR-27.5), Stress score more than 70(OR-10.5) , History of Diabetes Mellitus with Hypertension(OR-6.5) and Daily smoking(OR-3.1) have come out as some important risk factors for development of stroke. Similar findings have also been reported from two case control studies from India that included ischemic stroke in all age groups suggested that hypertension, diabetes mellitus and smoking are important risk factors for stroke as they are worldwide[21,22] . Many Other community- and hospital-based studies have identified hypertension as the most important risk factor similarly to the present study findings[23-27]

In a comparison of 201 consecutive patients with first onset stroke due to cerebral infarction aged 15–55 years and the same number of matched neighbourhood control subjects conducted as part of the Melbourne Risk Factor Study[29] hypertension, diabetes mellitus, current smoking, heart disease and long term heavy alcohol consumption were found to be major risk factors. Besides other factors, in the present study alcohol did not appear as a risk factor which was actually much more prevalent amongst controls, but this finding should be interpreted with caution, as many cases were already suffering from Hypertension and /or diabetes, so they might have received instructions for abstaining the alcohol.

In the present study average BMI and prevalence of obesity was lower amongst cases than controls (9% less), which could be attributed to higher co-morbid conditions like hypertension and /with diabetes mellitus amongst cases which might have led to various diet restrictions and life style changes. Hence obesity also did not appear as risk factor for stoke as reported in other studies. However in a multi-centric, hospital-based case-control study revealed low haemoglobin, rather than cholesterol level, as one of the important risk factors of ischemic stroke[23]. Considering the present findings it is important to further explore relationship of various nutrional factors with stroke.

Many of the studies have assessed the role of stress as risk factor[29], which has also come out to be important risk factor in the present study.

Present research has showed a very interesting pattern of risk factor transition in agewise analysis. Amongst younger age group (20-40 years) Stress (OR-7.33), Daily smoking (OR-4.45) and Hypertension (OR- 4.41) were found to be major risk factors. With the advancement of age during 40-60 years- stress (OR-24.2) remains the major risk factor while Hypertension (OR- 11.2), takes

over the Daily smoking habit (OR-2.62). With reaching elderly age(>60 years age) hypertension (OR-19.14)becomes the stronger risk factor followed by habit of Daily smoking (OR-6.02).So this analysis shows that with the advancement of age risk of stroke due to hypertension rises while stress remains major risk factor for four decades i.e. from 20-60 years.

Conclusion: Major risk factor in this set of population is Stress followed by Hypertension and smoking. It is important preventive strategies must look into causes of stress and its management techniques as primordial and primary prevention. Screening for diabetes and hypertension followed with appropriate management can also be important strategy for stroke prevention.

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