

Risk Factors for Stroke in Rural Population of Telangana State of India, an Unmatched Case Control Study

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Abstract	Context Stroke tops the list of causes for acquired disability among adults and is the second leading cause of death worldwide. Evidence from developed countries indicate significant decline in stroke incidence and mortality, attributable to prevention of risk factors in general population. There is limited evidence on risk factors for stroke in rural India.
	Aims This study aims to ascertain the risk factors for stroke in rural Telangana and provide a guide to health care providers in adopting treatment and prevention strategies.
	Settings and Design The study was conducted in the Moinabad mandal of Ranga Reddy District, Telangana state of India. This is a population based unmatched case–control study.
	Methods and Materials All the houses of Moinabad were approached by a door-to-door survey to identify cases. A total of 288 persons were enrolled in the study which included 144 cases and 144 controls.
	Statistical Analysis To derive age and gender adjusted odds ratios of various risk factors, binary logistic regression analysis was performed.
	Results The estimated crude prevalence of stroke in Moinabad mandal is 257 per lakh population. Modifiable risk factors identified were, total cholesterol, systolic blood pressure, alcohol consumption, smoking, diastolic blood pressure, low high-density lipoprotein cholesterol, and central obesity as measured by waist circumference.
Keywords	Nonmodifiable risk factors identified were male gender and higher age group.
► case-control study	Conclusion The high prevalence of stroke in rural Telangana makes it an important
► risk factors	public health challenge for the state. The identified risk factors need to be addressed
► stroke	at population level.

Key Messages

The health care providers including the National Program for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS) program officers should prioritize the identified risk factor for control of stroke in rural Telangana. The order of priority is high total cholesterol, systolic blood pressure,

alcohol consumption, smoking, diastolic blood pressure, low high-density lipoprotein (HDL) cholesterol, diabetes, and central obesity as measured by waist circumference.

Introduction

Stroke, or cerebrovascular accident, forms an important contributor to the global burden of diseases, leading the list of causes for adult acquired disabilities and death

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across the world.^{1,2} A consequence of rapid epidemiological transition in India over past decades is a phenomenal rise in the occurrence of cardiovascular diseases including stroke. Recent estimate of stroke prevalence ranged widely among rural and urban population in India and has considerable regional differences.^{3,4} During the past decade four urban centers adopted WHO (World Health Organization) steps guidelines and undertook stroke surveillance studies to arrive at an estimate of stroke burden in their cities. There is insufficient information on stroke burden in rural India, where 70% of our population resides. Data from rural surveys on neurological disorders (including stroke) do not elucidate the actual stroke burden in this population. To our knowledge, there are only three studies that have examined this problem in rural India. One is from Kuthar valley Kashmir,⁵ the second is the Trivandrum stroke study⁶ which compared rural and urban population in Kerala, and the third examined stroke mortality in Gadchiroli district, Maharashtra.7 Studies focusing on cardiovascular risk factors in rural districts of erstwhile combined state of Andhra Pradesh (AP) and Karnataka reveal high prevalence of risk factors with more than 90% of adults having at least one modifiable cardiovascular risk factor and more than 15% at risk for MI or stroke in 10 years.^{8,9} Data from Trivandrum Stroke Registry also showed 90% of strokes had at least one modifiable risk factor, higher prevalence of risk factors, and 28-day poststroke mortality in rural subjects.⁶ Evaluation of local risk factors for stroke helps in developing policies specific to respective populations and achieve long-term gains in stroke control.

Need for the Study

Evidence from developed countries indicates significant fall in stroke burden attributable to secondary prevention strategies and prevention of risk factors (such as smoking) in the general population. Rural Andhra Pradesh data diverges from WHO Premise study which reveals a large urban to rural gap in knowledge of cardiovascular risk factors and use of medication for stroke prevention with less than 25% rural subjects using prescribed medication.⁹ The erstwhile combined state of Andhra Pradesh is now re-carved into states of Telangana and Andhra Pradesh. The proposed study will ascertain the risk factors for stroke in rural Telangana population and provide a guide to health care providers in adopting treatment and prevention strategies.

Methodology

Study Design

The study design applied is community-based unmatched case-referent study.

Study Setting and Time Frame

The population of Moinabad mandal of Ranga Reddy District, Telangana, India was studied, between July 2016 and December 2017. Moinabad mandal, has a population of approximately 56,000, residing in nearly 13,000 households from 26 villages in the subdistrict (mandal). Among them, approximately 29,000 (52%) are male and approximately 27,000 (48%) are female. Seventy-five percent of the whole population are from general caste, 25% are from schedule caste, and none from schedule tribes.

Recruitment and Enrolment

The patients were recruited by line listing from the village of Moinabad through a door to door survey. Cases were live stroke patients. Controls were live subjects without history of stroke who are from the same neighborhood and from similar socioeconomic status as cases. Controls were not taken from the same family as the cases. For every case, one control was enrolled.

Data Collection

All the houses of Moinabad were approached by a door to door survey. Families with a history of stroke and a live stroke patient were considered for enrolment. The subject was examined by a Medical Officer in the field, who has confirmed the diagnosis clinically. Data collected included the variables—demographic details including age, gender, and educational qualification, history of stroke (previous/family), hospital visits, current medical treatment, medical reports, computed tomography scan, or magnetic resonance imaging reports where available. Physical examination included blood pressure (BP) check, blood sample collection for lipid profile evaluation, and a random blood sugar.

Exclusion Criteria

Patients who are not willing to consent, patients who are not available at the time of study, patients who have expired following stroke, patients with history suggestive of transient ischemic attack were excluded for the study.

Kelsey's sample size method for unmatched case–control study was used.¹⁰ A two-sided confidence level (1 α) of 95, power (% chance of detecting) of 80, ratio of controls to cases of 1, least extreme odds ratio (OR) to be detected, 1.99, based on OR for hypertension in stroke and proportion of controls with exposure of 40 in previous studies were used as input parameters.^{6,11} The minimum sample size was calculated to be 136 cases and 136 controls with a total sample size of 272. Proportion of cases with exposure was derived to be 57.02. Finally, 144 cases and 144 controls participated.

Data Analysis

Data are analyzed at two levels. At primary level, prevalence and association of various risk factors were assed using Chi-square test. To derive age and gender adjusted odds ratios (AORs) of various risk factors, binary logistic regression analysis was performed with age and gender being controlled.

Operational Definitions

We defined stoke to be "a clinical syndrome characterized by rapidly developing clinical symptoms and/or signs, and at times global, loss of cerebral function, with symptoms lasting more than 24 hours or leading to death, with no apparent cause other than a vascular one."¹²⁻¹⁴ Those who gave a history of hypertension or who had an elevated blood pressure of either systolic above or equal to 140 mm of Hg and or a diastolic above or equal to 90 mm of Hg as a mean of three reading were termed as hypertensives.¹⁵ Diabetics were those who had a history of diabetes mellitus or a GRBS (glucometer random blood sugar) \geq 200 mg/dL.^{16,17} Generalized obesity was termed as a body mass index (BMI) above or equal to 25.¹⁸

WHO STEP-wise Approach to Stroke Surveillance Manual¹⁹ was used as reference, in design and conduct of the study including anthropometry and laboratory procedures.

Results

Demographic Characteristics of the Study Population

Out of the 144 controls, 59 were women and 85 were men with a mean age of 45.69 and 47.40, respectively. Out of 144 cases, 44 were women and 100 were men with a mean age of 60.77 and 62.49.

Estimated crude prevalence of stroke in Moinabad mandal is found to be 257(220–300) per 1, 00,000 population. Prevalence of stroke among men is 344(280–410) per lakh men and among women it is 163(110–210) per lakh women.

A higher prevalence of stroke was seen in higher age groups, men, smokers, alcohol consumers, hypertensives, and diabetics (**-Table 1**). This association was tested for statistical significance by Chi-square which has revealed that age and hypertension were significantly associated with stroke patients.

Binary Logistic Regression Model for Deriving AOR of Various Risk Factors

Modifiable Risk Factors

After adjusting the effects of age and gender in the model, the final binary logistic regression model has shown that cases are more likely to have a total cholesterol >200 mg/dL (AOR 2.278, 95% confidence interval [CI]: 1.101–4.713, p = 0.026), a systolic blood pressure \geq 140, (AOR 2.234, 95% CI: 1.299–3.842, p = 0.004), followed by being consumers of alcohol, (AOR 1.997 95% CI: 1.134-3.516, *p* = 0.017), or a smoker (AOR 1.812, 95% CI: 0.974–3.372, p = 0.060), or with a diastolic blood pressure ≥ 90 , (AOR 1.795, 95% CI: 1.057–3.049, *p* = 0.030) or those with HDL <40 mg/dL. The odds of having stroke is higher among men with waist circumference> 90 cm (AOR 1.333, 95% CI: 0.686-2.588 p = 0.396). The odds of having stroke is faintly higher among women with waist circumference >80 cm (AOR 1.055, 95% CI: 0.331-3.369, p = 0.927). Obesity as measured by BMI was not identified as a risk factor in our study (**Table 2**).

Among nonmodifiable risk factors, stroke patients, were those from higher age groups (AOR 1.971, 95% CI: 1.624–2.393, p = 0.000) or having a higher risk of being male (AOR 1.331, 95% CI: 0.774–2.291, p = 0.301).

Comparison of Means of Risk Factors of Cases and Controls

The mean systolic (138.73 \pm 19.59 mm Hg vs. 127.43 \pm 13.05 mm of Hg, p = 0.000) and diastolic (88.26 \pm 13.81 mm of Hg vs.

83.75 mm of Hg, p = 0.002) blood pressures were significantly higher in stoke cases compared with controls. Similarly, the means of, "mean arterial pressures," abdominal girth (inches) were significantly higher in stroke cases than controls. The means of GRBS and total cholesterol were also higher in cases than controls; however, they are not statistically significant. The mean BMI among stroke patients was a unit less compared with controls (**– Table 3**).

Discussion

Estimated crude prevalence of stroke in Moinabad mandal is 257 per 100, 000 people, which is significantly less than in the rural district of Gadchiroli in Maharashtra.²⁰ Adjusted incidence rate of stroke in rural Kerala is 138 per 100, 000 people according to the Trivandrum Stroke Registry⁶ which suggests lower prevalence in that region compared with Moinabad. Prevalence data reveal considerably lower prevalence of stroke in states such as rural West Bengal, rural Karnataka, and Kuthar Valley Kashmir.^{5,6,21} Regional variation in stroke prevalence has also been observed in the United States where there is a defined stroke belt.²² Differences in local socioeconomic conditions, risk factors, and study methodology probably contribute to the variation in prevalence.

Risk Factors for Stroke

Age and gender trends were similar to earlier stroke studies²³ with greater prevalence of stroke, hypertension, and tobacco use in older subjects^{5,6}; and greater number of males with exposure to tobacco and alcohol consumption.

Hypertension was the most frequent risk factor in our study with an OR of 2.234, consistent with data from other rural and urban studies in India,^{11,24} the United States,²⁵ as well as the international multicenter INTERSTROKE study.²⁶ Reports from AIIMS, New Delhi and SCTIMST, Trivandrum also reveal hypertension as the leading risk factor in "young stroke" (stroke < 45 years).^{27,28}

An estimated 54% of all stroke-related deaths in low income countries² have been linked to hypertension²⁰ as have 40% of all stroke-related deaths in Gadchiroli district. The Earth Institute report in 2004 stated that cardiovascular disease-related death rates across all age groups and both genders are much higher in India than in Portugal and the United States.²⁹ These observations are indicative of both urban and rural India going through phase 2 of the epidemiological transition.

The prevalence of diabetes in our study is similar to what has been observed in rural Kerala.⁶ With an OR of 1.6, diabetes has a weaker stroke risk association than hypertension, smoking, and alcohol consumption.

Alcohol consumption was the major stroke risk factor in our population (OR 1.997) and was also linked to 24.6% of male stroke deaths in Gadchiroli.⁷ Many Indian studies however did not document such a relationship.^{6,30} In rural Karnataka, although alcohol consumption was prevalent in 30% of the population, it did not significantly correlate with direct cardiovascular risk factors for MI or stroke outcome.⁸Binge drinking increased stroke risk by an OR of

Risk factor	Exposure	Control		Case (Stroke)		Total	p-Value	
		n	%	n	%	n		
Age	<55 y	93	76.2%	29	23.8%	122	0.000	
	≥55 y	51	30.7%	115	69.3%	166		
Gender	Female	59	57.3	44	42.7	103	0.065	
	Male	85	45.9	100	54.1	185		
Smoking	No	98	51.9	91	48.1	189	0.385	
	Yes	46	46.5	53	53.5	99		
Alcohol	No	70	53.4	61	46.6	131	0.287	
	Yes	74	47.1	83	52.9	157		
Hypertension SBP ≥140 mm Hg	Normotensive	106	61.6	66	38.4	172	0.000	
	Hypertensive	38	32.8	78	67.2	116		
Hypertension DBP ≥90 mm Hg	Normotensive	83	61.5	52	38.5	135	0.000	
	Hypertensive	61	39.9	92	60.1	153		
Obese by BMI	Normal BMI	92	49.5	94	50.5	186	0.805	
	Overweight and obese	52	51.0	50	49.0	102		
Diabetes	Nondiabetic	126	51.2	120	48.8	246	0.316	
	Diabetic	18	42.9	24	57.1	42		
Total		144	50.0	144	50.0	288		

 Table 1
 Frequency of demographic and modifiable risk factor variables

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure.

Note: Test of Significance of Association by X (Odds Ratio)²; (p-value in italics = statistically significant).

Table 2 Binary logistic regression

Risk factor	Adjusted odds	95% CI	p-Value	
	ratio	Lower	Upper	-
Non-modifiable risk factor				
Gender (male vs. female)	1.331	0.774	2.291	0.301
Age (≥ 55 vs. < 55 y)	1.971	1.624	2.393	0.000
Modifiable risk factor				
Smoking	1.812	0.974	3.372	0.060
Alcohol	1.997	1.134	3.516	0.017
Systolic blood pressure ≥140	2.234	1.299	3.842	0.004
Diastolic blood pressure ≥90	1.795	1.057	3.049	0.030
Obesity or overweight (BMI ≥25)	0.906	0.527	1.557	0.721
Waist circumference >90 cm in men	1.333	0.686	2.588	0.396
Waist circumference >80 cm in women	1.055	0.331	3.369	0.927
Diabetes (GRBS ≥200 mg/dL)	1.648	0.747	3.637	0.216
Total cholesterol >200 mg/dL	2.278	1.101	4.713	0.026
HDL <40 mg/dL	1.658	0.976	2.817	0.062

Abbreviations: AOR, adjusted odds ratios; BMI, body mass index; CI, confidence interval; GRBS, glucometer random blood sugar; HDL, high-density lipoprotein.

Note: Predictive probability for stroke; (p-values in bold = statistically significant).

1.5 in the INTERSTROKE study conducted across 22 countries including India. 26

Current or past history of smoking increased stroke risk by the odds of 1.81; high-risk association of smoking and stroke is well established by many Indian urban and rural studies with very high ORs ranging from 3.92 in WB³¹ to 7.8 in Kerala.⁶ Tobacco inhalation was a direct cardiovascular risk factor in the rural Karnataka population.⁸ Nearly 37% of our subjects either smoked or chewed tobacco, a number similar to the Trivandrum Rural Stroke Registry; whereas there were significantly more documented smokers (59%) in a hospital-based case-referent study.²⁸

Variable	Case (Stroke)	Cor	ntrol	p-Value	95% CI of the difference	
	Mean	SD	Mean	SD		Lower	Upper
BMI	22.78	4.35	23.79	3.73	0.036	1.95	0.07
SBP	138.73	19.59	127.43	13.05	0.000	7.44	15.16
DBP	88.26	13.81	83.75	11.15	0.002	1.60	7.43
MAP	105.06	13.63	98.21	10.72	0.000	4.00	9.69
ABDG	46.83	21.99	41.83	15.19	0.025	0.62	9.39
GRBS	148.66	94.54	131.36	78.68	0.093	2.88	37.47
ТС	171.03	44.19	165.82	40.01	0.295	4.57	14.99
HDL	41.76	11.72	43.81	11.59	0.137	0.66	4.75

 Table 3
 Comparison of means of risk factors of cases and controls

Abbreviations: ABDG, abdominal girth in inches; BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; GRBS, glucometer random blood sugar; HDL, high density lipoprotein; MAP, mean arterial pressure; SBP, systolic blood pressure; SD, standard deviation; TC, total cholesterol.

Interestingly, young strokes in the AIIMS study had low exposure to smoking.²⁷ Whether such differences in behavioral risk factors influence stroke incidence and subtypes is not known.

Obesity as measured by waist circumference rather than BMI was more prevalent in our stroke subjects compared with controls with an OR of 1.033 (female) and 1.33 (male) stroke risks. Abdominal obesity rather than BMI seemed to be a better indicator of stroke risk in other Indian and international stroke studies.³²⁻³⁴ Two large population-based cardiovascular risk factor studies in rural AP⁹ and Karnataka⁸ utilized high BMI as an indicator of obesity and a direct cardiovascular risk factor for stroke or MI.

Elevated serum, total cholesterol, and a low HDL were significant stroke risk factors in this study with ORs of 2.278 and 1.658, respectively. One-third of our stroke subjects had dyslipidemia as did 26% of those in the Trivandrum Registry.⁶ Urban and rural differences in risk factor profiles are disappearing in epidemiological transition. It is note-worthy that unlike well-established links between dyslipidemia (lipid factors) and cardiac ischemic events,³⁵ the impact of dyslipidemia on stroke in the Indian context requires further study.

Conclusion

To our knowledge, this is the first study to estimate the burden of stroke in rural Telangana. The high burden of stroke in rural Telangana makes it a significant public health challenge for the State. In the current study, we found that the leading modifiable risk factors for stroke were in order, total cholesterol of above 200 mg/dL, systolic blood pressure above 140, alcohol consumption, smoking, diastolic blood pressure above 90, an HDL below 40 mg/dL, GRBS above 200 mg/dL, waist circumference above 90 cm in men, and 80 cm in women. Generalized obesity as measured by BMI was not associated with stroke, unlike central obesity as measured by waist circumference. Among nonmodifiable risk factors, age is a leading risk factor followed by male gender. The age association could be due to the fact that advances in age are accompanied by an accretion of associated risk factors. While nonmodifiable risk factors have limited potential for amendment, all modifiable factors can

be targeted in the same order of priority as the ORs demonstrated in our study. The National Program is there in place to strategically target the prevention of modifiable risk factors through primary health care in India.³⁶ We recommend including prevention protocols for stroke victims including rehabilitation services for rural populations with limited resources.

Ethical Approval

The project got clearance from IEC of Apollo Medical College, Hyderabad. Information was given to participants and voluntary consent obtained in writing. All participants were given health education on importance of periodic screening for risk factors of noncommunicable disease, timely management, and adherence to therapy.

Funding

None.

Conflict of Interest

None declared.

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