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

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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. Nonmodifiable risk factors identified were male gender and higher age group.

Conclusion The high prevalence of stroke in rural Telangana makes it an important public health challenge for the state. The identified risk factors need to be addressed 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...
across the world.\textsuperscript{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.\textsuperscript{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,\textsuperscript{5} the second is the Trivandrum stroke study\textsuperscript{6} which compared rural and urban population in Kerala, and the third examined stroke mortality in Gadchiroli district, Maharashtra.\textsuperscript{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.\textsuperscript{8,9} Data from Trivandum 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.\textsuperscript{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.\textsuperscript{3} 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.\textsuperscript{10} A two-sided confidence level (1\textalpha) 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.\textsuperscript{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 assessed 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 stroke 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.\textsuperscript{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.\textsuperscript{15} Diabetics were those who had a history of diabetes mellitus or a GRBS (glucometer random blood sugar) ≥200 mg/dL.\textsuperscript{16,17} Generalized obesity was termed as a body mass index (BMI) above or equal to 25.\textsuperscript{18} WHO STEP-wise Approach to Stroke Surveillance Manual\textsuperscript{19} 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 (\textsuperscript{\textendash}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 ≥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 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 1.053, 95% CI: 0.331–3.369, p = 0.927). Obesity as measured by BMI was not identified as a risk factor in our study (\textsuperscript{\textendash}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 ± 19.59 mm Hg vs. 127.43 ± 13.05 mm of Hg, p = 0.000) and diastolic (88.26 ± 13.81 mm of Hg vs. 83.75 mm of Hg, p = 0.002) blood pressures were significantly higher in stroke 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 (\textsuperscript{\textendash}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.\textsuperscript{20} Adjusted incidence rate of stroke in rural Kerala is 138 per 100,000 people according to the Trivandrum Stroke Registry\textsuperscript{4} 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.\textsuperscript{5,6,22} Regional variation in stroke prevalence has also been observed in the United States where there is a defined stroke belt.\textsuperscript{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 studies\textsuperscript{23} with greater prevalence of stroke, hypertension, and tobacco use in older subjects\textsuperscript{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,\textsuperscript{11,24} the United States,\textsuperscript{25} as well as the international multicenter INTERSTROKE study.\textsuperscript{26} Reports from AIIMS, New Delhi and SCTIMST, Trivandrum also reveal hypertension as the leading risk factor in “young stroke” (stroke < 45 years).\textsuperscript{27,28}

An estimated 54% of all stroke-related deaths in low income countries\textsuperscript{2} have been linked to hypertension\textsuperscript{29} 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.\textsuperscript{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.\textsuperscript{4} 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.\textsuperscript{7} Many Indian studies however did not document such a relationship.\textsuperscript{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.\textsuperscript{6} Binge drinking increased stroke risk by an OR of
1.5 in the INTERSTROKE study conducted across 22 countries including India. 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 WB to 7.8 in Kerala. Tobacco inhalation was a direct cardiovascular risk factor in the rural Karnataka population. 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.

### Table 1  Frequency of demographic and modifiable risk factor variables

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

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; SBP, systolic blood pressure.
Note: Test of Significance of Association by X² (Odds Ratio); (p-value in italics = statistically significant).

### Table 2  Binary logistic regression

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Adjusted odds ratio</th>
<th>95% CI for AOR</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-modifiable risk factor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender (male vs. female)</td>
<td>1.331</td>
<td>0.774</td>
<td>2.291</td>
</tr>
<tr>
<td>Age (≥ 55 vs. &lt; 55 y)</td>
<td>1.971</td>
<td>1.624</td>
<td>2.393</td>
</tr>
<tr>
<td>Modifiable risk factor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>1.812</td>
<td>0.974</td>
<td>3.372</td>
</tr>
<tr>
<td>Alcohol</td>
<td>1.997</td>
<td>1.134</td>
<td>3.516</td>
</tr>
<tr>
<td>Systolic blood pressure ≥140</td>
<td>2.234</td>
<td>1.299</td>
<td>3.842</td>
</tr>
<tr>
<td>Diastolic blood pressure ≥90</td>
<td>1.795</td>
<td>1.057</td>
<td>3.049</td>
</tr>
<tr>
<td>Obesity or overweight (BMI ≥25)</td>
<td>0.906</td>
<td>0.527</td>
<td>1.557</td>
</tr>
<tr>
<td>Waist circumference &gt;90 cm in men</td>
<td>1.333</td>
<td>0.686</td>
<td>2.588</td>
</tr>
<tr>
<td>Waist circumference &gt;80 cm in women</td>
<td>1.055</td>
<td>0.331</td>
<td>3.369</td>
</tr>
<tr>
<td>Diabetes (GRBS ≥200 mg/dL)</td>
<td>1.648</td>
<td>0.747</td>
<td>3.637</td>
</tr>
<tr>
<td>Total cholesterol &gt;200 mg/dL</td>
<td>2.278</td>
<td>1.101</td>
<td>4.713</td>
</tr>
<tr>
<td>HDL &lt;40 mg/dL</td>
<td>1.658</td>
<td>0.976</td>
<td>2.817</td>
</tr>
</tbody>
</table>

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).
Interestingly, young strokes in the AIIMS study had low exposure to smoking. 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. Two large population-based cardiovascular risk factor studies in rural AP and Karnataka 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. 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, 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. 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.

**References**

1 Feigin VL. Stroke in developing countries: can the epidemic be stopped and outcomes improved? Lancet Neurol 2007;6(2):94–97
14 Jane N, Improving Stroke Prevention and Outcomes in Uganda: Population Survey and Hospital Based Study. Uganda: Makerere University Kampala; 2011 Available at:
25 American Heart Association, Heart Disease and Stroke Statistics. Dallas: AHA; 2008
29 Leeder SR, Raymond S, A Race Against Time: The Challenge of Cardiovascular Disease in Developing Countries. New York, NY: Trustees of Columbia University; 2004
36 Training Module for Medical Officers for Prevention, Control and Population Level Screening of Hypertension, Diabetes and Common Cancer (Oral, Breast & Cervical), National Centre for Disease Control Directorate General of Health Services Ministry of Health and Family Welfare, GOI 22—Sham Nath Marg, New Delhi-110054, India, 2017