Risk factors predisposing to acute stroke in India: a prospective study

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Background: Stroke is an important neurological disorder with significant morbidity and mortality. In India, the risk factors for stroke (obesity, diabetes mellitus, alcoholism, hypertension, and sedentary lifestyle) are mounting with economic growth and increasing the disease burden.

Objective: To assess the severity and risk factors of stroke in India and identify any new predisposing factors.

Methods: A multicentric (six tertiary care hospitals across India) prospective observational study (from September 2016 to July 2017) was conducted on 526 stroke patients, presenting within the first 24 h to examine the risk factors for ischemic and hemorrhagic strokes. Severity was determined using the National Institutes of Health Stroke Scale (NIHSS).

Results: Predominantly male (72.3%), 75% of the sample was >50 years old, with a mean body mass index (BMI) of 25.8 ± 4.3 kg/m² and 14.6% obese patients. Hypertension and diabetes mellitus were the commonest comorbidities, followed by a history of ischemic heart disease and familial history of stroke. 20.5% of patients had mild strokes, 57.4% had moderate, 8.4% experienced moderate-severe strokes, whereas 7.2% had severe strokes. Regarding the admission diagnoses, 56.8% were ischemic, 18.6% were hemorrhagic, 1.1% had a transient ischemic attack, 6.6% suffered recurrent strokes, and 17% were other forms.

Conclusion: The foremost risk factors for stroke in India, hypertension and diabetes, need to be controlled and treated like other global high-risk populations for stroke prevention. The NIHSS scores highlight the relationship between risk factors and stroke severity.

Keywords: diabetes, hemorrhagic stroke, hypertension, ischemic stroke, National Institutes of Health Stroke Scale, risk factors, stroke

INTRODUCTION

The Global Burden of Disease report of 2017 has described stroke as the second most common cause of death globally, and the third commonest reason for disability [1,2]. Affecting approximately 104.2 million people worldwide, the prevalence of stroke increased by 10.1% from 1990 to 2017. Toward the end of the decade from 2007 to 2017, the worldwide incidence of ischemic stroke was at 16.1%. Considering region-wise prevalence, the South Asian countries have the highest stroke-related mortality rates, and both ischemic and hemorrhagic stroke is highly prevalent in Central and East Asia as well [3].

Feigin et al. [4] revealed that while the incidence of stroke saw a 42% decline in the high-income countries, it increased steeply by >100% in the low and middle-income countries. Approximately 11.6 million cases of ischemic and 5.3 million hemorrhagic strokes were reported globally in the year 2010, of which 63% of ischemic stroke and 80% of hemorrhagic strokes occurred in the low and middle-income countries. As per the Framingham study, one in five women and one in six men above the age of 55 years had a lifetime risk of stroke [5]. However, as compared to a 17–33% case fatality rate (CFR) for stroke in the western countries, in India, CFR rates vary from a significant 41.08% (30-day CFR) in Kolkata to 24.5% in the urban Trivandrum (28-day CFR) [6]. The mortality rate in the first 7–10 days was about 20% in the state of Kerala, versus 33% in Kolkata, West Bengal. Overall, by the year 2010, approximately 39.4 million disability-adjusted life years (DALYs) were lost globally to ischemic stroke (64% in low and middle-income countries) and 62.8 million DALYs lost to hemorrhagic stroke (86% in low and middle-income countries) [3]. These data reveal the contrast between stroke-related death in the high-income versus low and middle-income countries [3].

The overwhelming incidence of stroke in India makes it essential to examine the predisposing and modifiable factors in the Indian population. Several risk factors like diabetes mellitus, heart disease, dyslipidemia, alcohol...
consumption, drug abuse, hypertension, and smoking are established contributors. Additionally, many undetermined social and cultural factors also influence the disease process significantly, evident as lifestyle-change and economic growth that are easily identifiable in India [7]. Hypertension, smoking, diabetes, and dyslipidemia are major modifiable risk factors for stroke in India, with hypertension accounting for about 57% of all stroke-related deaths [8]. Diabetes mellitus, anemia, hypertension, and tobacco use, rather than dyslipidemia alone, are documented to be associated with ischemic stroke. With varying disease risks and unknown associations in different regions of the world, there is a dire need for population-specific risk assessment [9]. In this light, the present study aims to evaluate a spectrum of risk factors contributing to ischemic and hemorrhagic stroke in the Indian population and examine stroke severity using the National Institutes of Health Stroke Scale (NIHSS). Additionally, the study assesses sex-based deviations in risk factors for acute stroke. It is of utmost importance to declare that authors only evaluated the risk factors in patients with acute stroke admitted to the involved hospitals. By design, the study did not intend to monitor or modify the treatment given. This decision was entirely made by the neurologists as per the hospital protocol, without any input from the authors.

PARTICIPANTS AND METHODS

An observational design was used to conduct this multicentric prospective study from 1 September 2016 to 31 July 2017, in which patients suffering from acute stroke symptoms in six select hospitals across India (Apollo Ahmedabad, Bhubaneswar, Chennai, Madurai, Hyderabad and Delhi) were included. The study was approved by the Apollo Hospitals’ ethics committee.

Sample selection

Six hundred and nine patients admitted to the hospital with an acute stroke (both ischemic and hemorrhagic) were screened by the research team as potential study participants. Those aging 18 years and above presenting within the first 24 h of symptom onset and with a confirmed diagnosis of stroke from the magnetic resonance imaging (MRI) or computed tomography (CT) scan were included in the study. Pregnant women and patients who were unable to provide, or others whose legally authorized representatives (LAR) refused to provide consent were excluded from the study. Written informed consent was obtained for all those who agreed to participate (by either the patient himself or the LAR). All patients were managed at the physician’s discretion according to the hospital’s stroke management protocol.

Data collection

Demographic details (age, gender, socioeconomic details, and body mass index [BMI] and baseline data for vital signs, medical history of hypertension, ischemic heart disease, vasculitis or other cardiovascular diseases, atrial fibrillation, dyslipidemia, and other cardiometabolic risk factors like history of smoking and alcohol consumption, family history of stroke, history of thrombolytic therapy and/or surgical procedures, and dietary details. Also, reports of 2D-echocardiogram and MRI/CT of the brain confirming the diagnosis were collected. All data were systematically retrieved from the hospital records and the process was closely monitored by a quality assurance monitor.

NIHSS scores were calculated for all patients. The scale consists of 11 items with a total score of 0–42 and based on this score, patients are categorized as having no stroke (score: 0), mild stroke (1–4), moderate stroke (5–15), moderate-to-severe stroke (16–20), and severe stroke (21–42).

Data analysis

Categorical variables were processed as percentages, while continuous variables have been described using mean ± standard deviation or median (range), as appropriate.

RESULTS

Of the 609 patients screened for the study, 526 patients were recruited as per the selection criteria. The predominantly male study sample (72.3%) had a mean age (±standard deviation [SD]) of 56.3 ± 11.7 years, and 75% of patients were above 50 years of age. The mean BMI for the sample was 25.8 ± 4.3 kg/m², of which 42% had a normal BMI (<25 kg/m²), 40% were overweight (25–30 kg/m²), 14.6% were obese (>30 kg/m²), and about 3% of the population was underweight (<18 kg/m²). The mean blood pressure at admission for all patients was 147/85 ± 28/16 mmHg. Table 1 presents the demographic details for all patients.

Risk factors for stroke

Preexisting risk factors, namely hypertension, diabetes mellitus, coronary artery disease, smoking, chronic renal

Table 1. Demographic details of the study population

<table>
<thead>
<tr>
<th>Mean</th>
<th>Age (years)</th>
<th>Weight (kg)</th>
<th>Height (m)</th>
<th>BMI (kg/m²)</th>
<th>BP SYS (mmHg)</th>
<th>BP DIA (mmHg)</th>
<th>SpO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>58</td>
<td>68</td>
<td>162</td>
<td>25.7</td>
<td>140</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>Mode</td>
<td>60</td>
<td>65</td>
<td>160</td>
<td>27.3</td>
<td>140</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>11.7</td>
<td>12.9</td>
<td>90</td>
<td>4.3</td>
<td>28.4</td>
<td>16.3</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>55</td>
<td>98</td>
<td>81</td>
<td>34.0</td>
<td>168</td>
<td>160</td>
</tr>
<tr>
<td></td>
<td>Minimum</td>
<td>20</td>
<td>32</td>
<td>130</td>
<td>12.8</td>
<td>70</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>Maximum</td>
<td>75</td>
<td>130</td>
<td>211</td>
<td>46.8</td>
<td>238</td>
<td>170</td>
</tr>
<tr>
<td></td>
<td>Count</td>
<td>523</td>
<td>475</td>
<td>464</td>
<td>445</td>
<td>516</td>
<td>515</td>
</tr>
</tbody>
</table>

SD, standard deviation.
disease, alcohol consumption, hypothyroidism, and dyslipidemia, for stroke were identified in 446 patients (Fig. 1). Hypertension \( (n = 365) \) and diabetes \( (n = 247) \) were the commonest comorbidities present in these stroke patients, while 214 patients had both diabetes and hypertension, followed by smoking \( (n = 85) \), obesity \( (n = 65) \), and regular alcohol consumption \( (n = 63) \). When considering cardiovascular factors, 43 patients had dyslipidemia, 43 had carotid or other arterial diseases, 28 had atrial fibrillation, and 12 had vasculitis. Furthermore, 10.2% of the sample had undergone surgeries or interventional procedures – percutaneous transluminal coronary angioplasty \( (n = 23) \), coronary artery bypass grafting \( (n = 20) \), and cataract surgery \( (n = 11) \) (Fig. 2).

**Symptoms of stroke**

The commonest symptoms were slurring of speech followed by limb weakness. 49% of patients had no upper limb weakness, whereas 40% had a mild weakness, 4% had a severe weakness, and 6.5% had total paralysis. Likewise, 52.2% of patients had no lower limb weakness, 40% with mild weakness, 1% had a severe weakness, and 5% developed total paralysis. Additional symptoms observed included headache, sweating, dizziness, palpitations, nausea, vomiting, unsteady gait, numbness, ataxia, convulsion, blurring of vision, and visual loss.

Of the 526 patients, 429 (81.5%) were conscious, 77 in a drowsy state, 10 were unconscious, and 10 were comatose (Fig. 3).

**Management of stroke**

In all the centers, acute management included thrombolytic therapy, followed by medications to reduce risk factors for recurrent stroke. Based on the patient's symptomatic profile and the hospital's stroke-care protocol, a combination of drugs, namely antihypertensives, hypoglycemics, antiplatelet agents, and neuro-and gastro-protective medicines with vitamin supplements were prescribed, along with drugs for other co-morbid conditions (statins, antiepileptic drugs, anti-inflammatories, antianxiety drugs, and antibiotics) as required.

Change and/or resistance to antihypertensives/antidiabetics were not recorded. Overall, 403 were treated for hypertension, 348 patients for diabetes mellitus, and 214 for both hypertension and diabetes. Hypertension was managed as per existing guidelines using calcium channel blockers \( (20\%) \), and angiotensin receptor blocker \( (17\%) \) (Fig. 4).

**MRI/CT scan reports**

The MRI/CT scans were examined for the standard findings for a brain lesion. The CT scan impressions revealed infarction and/or hypodense areas as the primary causes for stroke, followed by bleeding, midline shift, lacunar infarct, gliotic lesion, and other less frequent findings (Fig. 5). MRI impression reports also depicted infarction as the major reason for stroke, followed by basal ganglia bleed, lacunar infarct, ischemic changes, and gliotic lesion. Other MRI features \((<2\% \text{ incidence})\) were also seen (Fig. 6).

**Diagnosis at admission**

Although the symptoms reported were variable, the diagnoses recorded at admission showed 299 \((56.8\%)\) patients with ischemic stroke, 98 \((18.6\%)\) of hemorrhagic stroke, six \((1.1\%)\) with a transient ischemic attack, 35 \((6.6\%)\) of recurrent stroke, 39 \((7.4\%)\) with an acute stroke, 25 \((4.7\%)\) with infarction, and 24 \((4.5\%)\) with other diagnoses.

**Stroke severity as per National Institutes of Health Stroke Scale**

Of the 526 patients, 34 \((6.4\%)\) had a zero score as per NIHSS, 108 \((20.5\%)\) had a mild stroke score, 302 \((57.4\%)\) had a moderate stroke, 44 \((8.4\%)\) with moderate to severe stroke, and 38 \((7.2\%)\) suffered a severe stroke (Table 2).

**DISCUSSION**

The present novel study effectively identifies the risk factors for acute stroke in the Indian setting prospectively. It was...
observed that while a majority of patients presenting with stroke symptoms were diagnosed as ischemic stroke, the NIHSS criteria categorized them as 57.4% moderate and 7.2% severe strokes [11]. Hypertension and diabetes were the most commonly reported predisposing risk factors.

Even with the decreased incidence of stroke in the high-income countries, the incidence of stroke has seen a more-than-double rise in the lower and middle-income countries [2], where it contributes to increased morbidity and mortality in the younger population [12,13]. Ischemic stroke is the commonest variety in India, with the highest prevalence of 83.6% in Thiruvananthapuram (Indian Stroke Registry), followed by 80.2, 73.8, and 68% in Mumbai, Bengaluru, and Kolkata, respectively [14,15].

The risk factors for stroke can be categorized into modifiable (obesity, hypertension, chronic kidney disease, diabetes, coronary artery disease, smoking, alcohol intake, COPD, dyslipidemia, and sedentary lifestyle) and nonmodifiable factors. Our results concur with the existing literature to demonstrate the role of nonmodifiable risk factors (aging >55 years and male gender) in stroke. Age, a nonmodifiable factor, is reported to increase the risk of stroke by two-fold every 10 years after 55 years of age. Studies on Indians, Indian-Americans have shown that the Indian population tends to suffer a stroke at an early age, i.e., above 55 years [14,16]. Also, a meta-analysis of studies from 19 countries reported that the incidence (33%) and prevalence (41%) of stroke were higher in males compared to females.
females. Strikingly, females have a CFR of 24.7% with stroke, versus 19.7% for males [17]. The Neurological Society of India has reported the age-specific prevalence of stroke as higher rates in the sixth and seventh decades [18], similar to our findings (maximum in the fifth and sixth decades of life, followed by the fourth and seventh decades). The mean average age of 3126 patients identified in a stroke registry conducted by the Department of Health Research was observed to be 59 ± 15 years [19], which further corroborates the notion that the average age of stroke patients is 15 years lower in developing countries compared to developed countries [20]. Also, in India, nearly 20% of stroke patients on their first hospital admission were at ≤ 40 years.

The common modifiable risk factors were also found in our study. In addition, some incidental factors [21], such as vitamin deficiency, vasculitis, Parkinson’s disease, blood disorders, encephalopathy, and psoriasis, were also seen in some patients. A correlation between the established comorbidities and these newer factors may help understand the extent of their role. Previous hospital and community-based studies have highlighted the influence of tobacco consumption, anemia, hypertension, and diabetes mellitus in predisposing to stroke, especially ischemic stroke, rather than just higher cholesterol levels. Nearly 50% were of our study patients were diabetic. India reported the highest incidence of diabetes, 9%, in the year 2020, which is expected to rise by 2030 [10]. Hypertension, as evident in the literature, is an important contributor, and 69% of our patients had a history of hypertension and in 32%, it was the reason for stroke [22]. A case–control study conducted on the urban population of Kashmir state also documented 58% of its study as diagnosed hypertensives, although the cause for stroke differed [18]. Likewise, a Kerala-state community-based stroke study reported an 85% incidence of hypertension, 50% for diabetes, and 26% for dyslipidemia. Additionally, smoking was more prevalent among the rural population and 26.8% of their male patients were smokers [23].

Another North Indian case–control reported on the predisposing role of a sedentary lifestyle and psychological stress [24], along with the effect of heavy alcohol consumption and heart disease as risk factors for stroke in younger patients [25]. Also, the presence of >3 components of metabolic syndrome in the South India population is notable [4]. Overall, hypertension, along with other modifiable risk factors, largely predisposes the patient to the stroke. With a higher prevalence in the urban areas, the incidence of hypertension in India is projected to increase in the future [26].

The increasing burden of tobacco use, both as smoking (20%) and chewing (40%), is a major health concern in India [27]. Furthermore, the influence of lifestyle changes with urbanization and industrialization has led to a rise in non-communicable diseases. Supplemented by a lack of awareness about symptoms and risk factors, managing stroke has become a great challenge. Only 55% of the urban population recognized one presenting symptom, whereas only 6.2% could identify three stroke symptoms. Likewise, another study reported that 50% of patients were unfamiliar with the common risk factors and stroke prevention [28]. The median time of presenting to a hospital was 10h from symptom onset. Hence, the need for greater awareness about stroke-related symptoms, risk factors, and the importance of seeking prompt medical help [29].

In concordance with the existing data, 56.8% of our patients were diagnosed with ischemic stroke, while 18.6% suffered a hemorrhagic stroke. MRI findings of infarcts were seen in nearly 50%, followed by bleeding and midline-shift in 11–14%, 13% had lacunar infarcts, and 5% had lacunar infarcts and gliotic lesions. Contrastingly, studies have revealed that ischemic stroke is reported in 68–80% of patients and hemorrhagic stroke in 20–32%, with extracranial (25–26%) and intracranial (30%) carotid diseases as the etiological factors in ischemic stroke [6].

Limb weakness is a common presenting symptom for patients [19], and weakness in both upper and lower limbs was observed in our patients, whereas 51% of patients had normal limb function. Also, the NIHSS scores for the stroke types corresponded well to the patients’ complaints, clinical profile, and risk factors. The majority of patients (57–62%) had a moderate NIHSS score of 5–15 out of which 54% were ischemic stroke patients, 20% were hemorrhagic patients, 7% had a recurrent stroke, while 19% of patients presented with other reasons (acute, infarct, etc.). A mild stroke with a score of 1–4 constituted 11–23% of patients, moderate-severe forms constituted 6–14%, whereas severe forms (21–42) comprised only 5–12% of the sample.

A previous study from India (the above reference) has shown hypertension to be the main reason for the development of stroke in a major (single) city in India. Although this study is of clinical importance, the data were collected from a registry and not prospectively. In contrast, the present study was a prospective de Novo research investigation undertaken across various regions of India to evaluate the predisposing factors for acute stroke. Hence, the

<table>
<thead>
<tr>
<th>Stroke status</th>
<th>NIH score</th>
<th>No. of patients</th>
<th>Ischemic</th>
<th>Hemorrhagic</th>
<th>TIA</th>
<th>Recurrent</th>
<th>Others*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Stroke</td>
<td>0</td>
<td>34</td>
<td>24</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Mild</td>
<td>1–4</td>
<td>108</td>
<td>71</td>
<td>11</td>
<td>2</td>
<td>8</td>
<td>16</td>
</tr>
<tr>
<td>Moderate</td>
<td>5–15</td>
<td>302</td>
<td>162</td>
<td>61</td>
<td>1</td>
<td>20</td>
<td>58</td>
</tr>
<tr>
<td>Moderate to severe</td>
<td>16–20</td>
<td>44</td>
<td>26</td>
<td>11</td>
<td>1</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Severe</td>
<td>21–42</td>
<td>38</td>
<td>16</td>
<td>13</td>
<td>1</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>526</td>
<td>299</td>
<td>98</td>
<td>6</td>
<td>35</td>
<td>88</td>
</tr>
</tbody>
</table>

*Others – acute, infarct, and others. TIA, transient ischemia attack.
observations may be of broader cross-sectional significance across the country.

A previous study from India [30] has shown hypertension to be the main reason for the development of stroke in a major (single) city in India. Although this study is of clinical importance, the data were collected from a registry and not prospectively. In contrast, the present study was a prospective de novo research investigation undertaken across various regions of India to evaluate the predisposing factors for acute stroke. Hence, the observations may be of broader cross-sectional significance across the country.

Limitations of the study
Because of the observational study design, the quality of data collected from the hospital's medical records relied on the hospital's uniformity in maintaining records. The NIHSS scoring and the investigations conducted differed at each center; hence, the collected diagnostics for the study sample could not be compared completely. Still, meticulous efforts were undertaken to mitigate these differences in the descriptive data collected from various locations. However, the symptoms and risk factors observed in the study matched well with the published data. The NIHSS score, as per the hospital-admission data, corresponded to the different types of strokes diagnosed subsequently. Overall, the purpose of the study was to investigate the risk factors for stroke and was not designed to monitor the clinical management, which was left to the hospital protocols. Hence, the cholesterol levels were not investigated due to the study protocol.

Nevertheless, the results of this study provide useful insight for intervention programs, especially blood-pressure management, which has been addressed by the World Hypertension League. They noted that the trend toward BP reduction was associated with lower stroke mortality rates [31]. In conclusion, the present study successfully identified the well-established symptoms, risk factors, and stroke varieties in the Indian population. The NIHSS scores also corresponded with symptoms of different types of strokes. Conventional risk factors such as hypertension, diabetes, obesity, atrial fibrillation, carotid/peripheral artery disease, poor diet, and sedentary lifestyle were observed. However, the common symptoms like dropping of the face, arm/limb weakness, and slurring of speech were not as frequently reported, probably due to lack of awareness. Our results highlight the significant role of hypertension and diabetes as predisposing factors for acute stroke and recommend that future efforts should focus on early detection and aggressive control of hypertension to decrease the risk of stroke and its sequelae. Our study is the first prospective study of risk factors for acute stroke in the Indian subcontinent. Therefore, our findings are of great public health importance and call for aggressive detection and control of hypertension in the community.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES


