

## Gender Differences in Risk Factors, Etiological Subtypes, Stroke Severity, and Functional Outcomes of Young Adult Ischemic Stroke in Northeast India: A Prospective Observational Study

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### Abstract

**Background:** Stroke remains a major contributor to mortality and disability worldwide. Although traditionally considered a disease of older individuals, the incidence of ischemic stroke among young adults has increased substantially over recent decades. Emerging evidence suggests important sex-specific differences in risk factor profiles and etiological mechanisms among young stroke patients.

**Objectives:** To evaluate gender-based differences in vascular risk factors, stroke subtypes, severity, and functional outcomes among young adults with arterial ischemic stroke.

**Methods:** This prospective observational study was conducted at the Department of Neurology, Gauhati Medical College and Hospital, Guwahati, India, from November 2024 to August 2025. Fifty-two consecutive patients aged 15–45 years with acute ischemic stroke were enrolled. Demographic characteristics, vascular risk factors, neuroimaging findings, etiological classification according to TOAST criteria, stroke severity using the National Institutes of Health Stroke Scale (NIHSS), and 3-month outcomes using the modified Rankin Scale (mRS) were assessed. Statistical analyses compared male and female patients.

**Results:** Among 52 patients, 34 (65.4%) were male and 18 (34.6%) were female. Smoking (64.7% vs. 16.7%,  $p < 0.001$ ) and diabetes mellitus (32.4% vs. 11.1%,  $p = 0.018$ ) were significantly more common among males. Females demonstrated higher frequencies of mitral stenosis (33.3% vs. 0%,  $p = 0.019$ ), vasculitis (11.1% vs. 0%,  $p = 0.042$ ), oral contraceptive use (11.1% vs. 0%,  $p = 0.031$ ), and pregnancy/puerperium-related stroke (5.6% vs. 0%,  $p = 0.042$ ). Large artery atherosclerosis predominated among males (44.1% vs. 22.2%,  $p = 0.048$ ), whereas other determined etiologies were more frequent among females (33.3% vs. 8.8%,  $p = 0.021$ ). No significant gender differences were observed in NIHSS severity categories or 3-month functional outcomes.

**Conclusions:** Young ischemic stroke demonstrates distinct sex-related differences in risk factors and etiological patterns. Males are predominantly affected by modifiable vascular risk factors, whereas females exhibit greater contributions from cardioembolic, inflammatory, and reproductive factors. Recognition of these differences may facilitate targeted prevention strategies and individualized clinical management.

**Keywords:** Young Stroke; Ischemic Stroke; Gender Differences; TOAST Classification; Risk Factors; Functional Outcome; NIHSS; Northeast India.

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### Introduction

Stroke is the second leading cause of death and one of the leading causes of long-term disability worldwide. Recent estimates from the Global Burden of Disease study indicate that more than 12 million new strokes occur annually, accounting for

substantial healthcare expenditure and societal burden. Although stroke incidence increases with age, the proportion occurring in younger adults has shown a concerning rise over the last two decades. [1,2] Young stroke, generally defined as stroke

occurring before 50 years of age, constitutes approximately 10–20% of all ischemic strokes globally. The consequences of stroke in younger populations are particularly devastating because affected individuals are often in their most productive years of life, resulting in prolonged disability, economic losses, and psychosocial consequences.[2,6]

India contributes nearly one-tenth of the global stroke burden. Epidemiological studies suggest that approximately 10–15% of all strokes in India occur in individuals younger than 45 years. Rapid urbanization, changing dietary habits, increasing prevalence of diabetes mellitus, hypertension, obesity, tobacco use, and environmental exposures have contributed significantly to this trend.[2,5]

Sex differences in stroke have gained increasing attention in recent years. Men generally demonstrate higher stroke incidence during young adulthood, largely attributable to behavioral and metabolic risk factors.

Women, however, possess unique biological and reproductive determinants, including pregnancy, puerperium, oral contraceptive use, autoimmune disorders, and valvular heart disease.[3]

Several international studies, including the Helsinki Young Stroke Registry reported by Putaala et al., have demonstrated distinct gender-specific etiological patterns. Similarly, European studies by Ekker and colleagues have highlighted the importance of sex-specific prevention strategies.

Despite growing global evidence, data from Northeast India remain scarce. The region has unique ethnic diversity, distinct cardiovascular risk profiles, high prevalence of rheumatic heart disease, and differing healthcare access patterns that may influence stroke epidemiology.

Understanding gender-based differences in young ischemic stroke may improve risk stratification, diagnostic evaluation, and preventive interventions.

**Primary Objective:** To evaluate gender-based differences in vascular risk factors, stroke subtypes, severity, and functional outcomes among young adults with ischemic stroke.

**Secondary Objectives:** To characterize etiological patterns according to TOAST classification and assess differences in stroke severity and outcomes between males and females.

**Study Hypothesis:** Young men and women exhibit significantly different risk factor profiles and etiological mechanisms despite similar stroke severity and functional outcomes.

## Materials and Methods

**Study Design:** Prospective observational hospital-based study.

**Study Setting:** Department of Neurology, Gauhati Medical College and Hospital, Guwahati, Assam, India.

**Study Duration:** November 2024 to August 2025.

**Study Population:** Consecutive young adults presenting with acute ischemic stroke.

**Inclusion Criteria:** Patients aged 15–45 years presenting within 28 days of onset of ischemic stroke.

**Exclusion Criteria:** Patients with transient ischemic attack, hemorrhagic stroke, or pre-existing disability (mRS  $\geq 3$ ).

**Clinical Assessment:** Detailed demographic and clinical evaluation was performed. Information regarding hypertension, diabetes mellitus, smoking, alcohol use, dyslipidemia, family history of stroke, and previous cerebrovascular events was obtained.

**Neuroimaging:** All patients underwent CT brain and/or MRI brain. Vascular imaging was performed where clinically indicated.

**Cardiac Evaluation:** Electrocardiography and echocardiography were performed to identify cardioembolic sources.

**Laboratory Evaluation:** Routine hematological and biochemical investigations were performed. Selected patients underwent thrombophilia and autoimmune screening based on clinical suspicion.

## TOAST Classification

Patients were categorized into:

1. Large artery atherosclerosis
2. Cardioembolism
3. Small vessel disease
4. Other determined etiology

## Stroke Severity Assessment

- NIHSS at admission.
- Outcome Assessment
- Modified Rankin Scale at three months.

**Statistical Analysis:** Continuous variables were expressed as mean  $\pm$  SD and categorical variables as frequencies and percentages. Normality assessment was performed using the Shapiro–Wilk test.

Comparisons were performed using:

- Student's t-test
- Mann–Whitney U test
- Chi-square test
- Fisher's exact test

A two-tailed p-value <0.05 was considered statistically significant.

## Results

**Baseline Characteristics:** A total of 52 patients were enrolled, comprising 34 males (65.4%) and 18

females (34.6%). Mean age was  $36.5 \pm 5.2$  years among males and  $34.8 \pm 6.1$  years among females. The majority belonged to the 36–45-year age group.

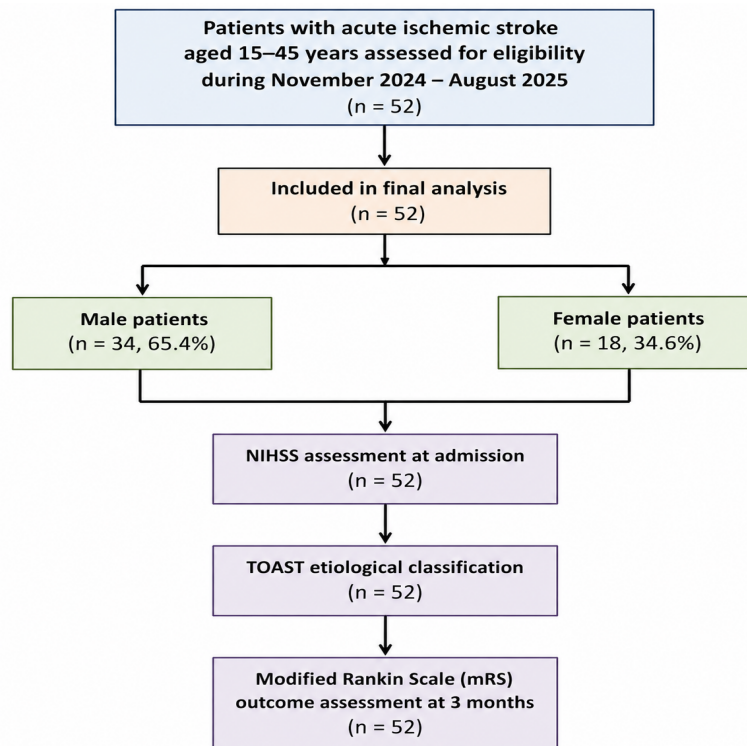


Figure 1: STROBE Flow Diagram of Patient Recruitment and Follow-up.

Table 1: Demographic Characteristics

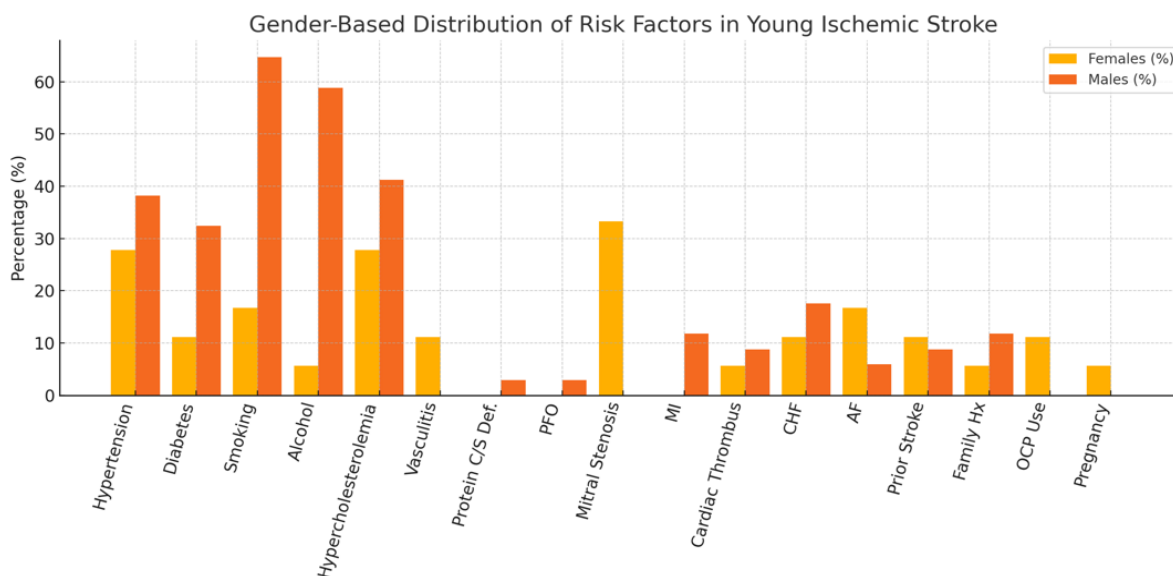
Parameter	Male (n=34)	Female (n=18)	Total (n=52)
Mean Age (years)	$36.5 \pm 5.2$	$34.8 \pm 6.1$	$35.9 \pm 5.6$
Age 15–25	5 (14.7%)	4 (22.2%)	9 (17.3%)
Age 26–35	10 (29.4%)	6 (33.3%)	16 (30.7%)
Age 36–45	19 (55.9%)	8 (44.5%)	27 (52.0%)

**Vascular Risk Factors:** Smoking was the most prominent risk factor among males. Diabetes mellitus showed significant male predominance. Females demonstrated significantly higher rates of mitral stenosis, vasculitis, oral contraceptive use, and pregnancy-related stroke.

Table 2: Gender-Based Vascular Risk Factors

Risk Factor	Females (n=18)	Males (n=34)	p-value
Hypertension	5 (27.8%)	13 (38.2%)	0.146
Diabetes Mellitus	2 (11.1%)	11 (32.4%)	<b>0.018*</b>
Tobacco Smoking/Chewing	3 (16.7%)	22 (64.7%)	<b>&lt;0.001*</b>
Alcohol Abuse	1 (5.6%)	20 (58.8%)	0.118
Hypercholesterolemia	5 (27.8%)	14 (41.2%)	0.205
Vasculitis	2 (11.1%)	0 (0%)	<b>0.042*</b>
Protein C/S Deficiency	0 (0%)	1 (2.9%)	0.312
Patent Foramen Ovale	0 (0%)	1 (2.9%)	0.619
Mitral Stenosis	6 (33.3%)	0 (0%)	<b>0.019*</b>
Myocardial Infarction	0 (0%)	4 (11.8%)	<b>0.001*</b>
Cardiac Thrombus	1 (5.6%)	3 (8.8%)	0.257
Congestive Heart Failure	2 (11.1%)	6 (17.6%)	0.187
Atrial Fibrillation	3 (16.7%)	2 (5.9%)	0.125
Prior Stroke	2 (11.1%)	3 (8.8%)	0.381

Family History of Stroke	1 (5.6%)	4 (11.8%)	0.187
Oral Contraceptive Pills	2 (11.1%)	0 (0%)	<b>0.031*</b>
Pregnancy/Puerperium	1 (5.6%)	0 (0%)	<b>0.042*</b>



**Figure 2: Gender based distribution of risk factors in young ischemic stroke**

**Stroke Etiology:** Large artery atherosclerosis represented the most frequent subtype among males, whereas other determined etiologies predominated among females.

**Table 3: TOAST Classification**

TOAST Subtype	Females (n=18)	% (Females)	Males (n=34)	% (Males)	p-value
Large Artery Atherosclerosis	4	22.2%	15	44.1%	0.048*
Cardioembolic (AF, CHF, MI, MS, PFO)	5	27.8%	9	26.5%	0.913
Small Vessel Disease	3	16.7%	7	20.6%	0.712
Other Determined Etiology (Vasculitis, Protein C/S Deficiency, etc.)	6	33.3%	3	8.8%	0.021*

**Stroke Severity:** Most patients presented with mild-to-moderate stroke severity. No statistically significant sex-related difference was identified.

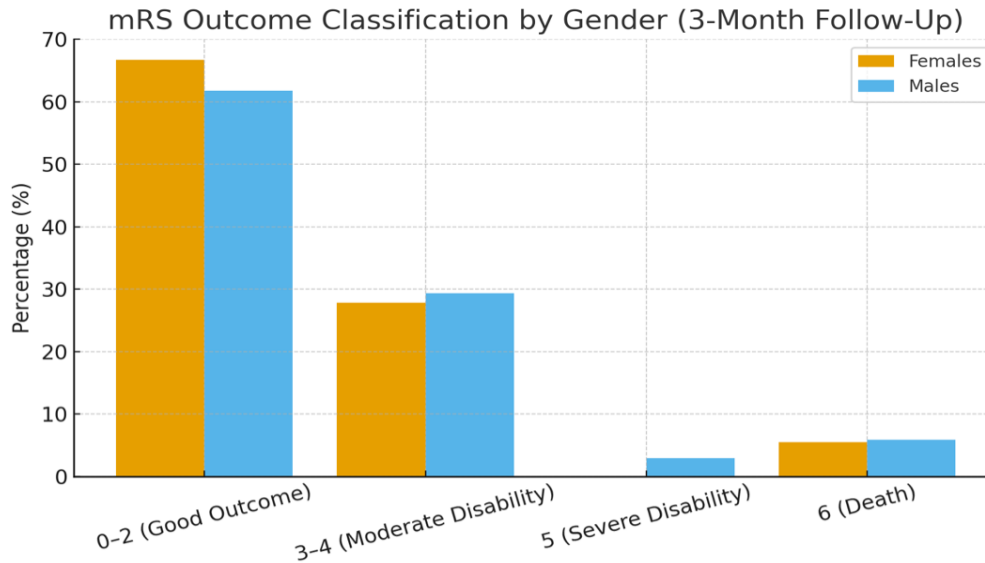
**Table 4: NIHSS Severity Distribution**

NIHSS Severity Category	Females (n=18)	% (Females)	Males (n=34)	% (Males)	p-value
Mild (NIHSS 0–4)	8	44.4%	14	41.2%	0.812
Moderate (NIHSS 5–15)	7	38.9%	14	41.2%	0.864
Severe (NIHSS >15)	3	16.7%	6	17.6%	0.932

**Functional Outcome:** At three months, favorable outcome (mRS 0–2) was achieved by 61.8% of males and 66.7% of females. No significant gender difference was observed.

**Table 5: Functional Outcome**

mRS Category	Females (n=18)	% (Females)	Males (n=34)	% (Males)	p-value
0–2 (Good Outcome)	12	66.7%	21	61.8%	0.704
3–4 (Moderate Disability)	5	27.8%	10	29.4%	0.888
5 (Severe Disability)	0	0%	1	2.9%	0.412
6 (Death)	1	5.5%	2	5.9%	0.972



**Figure 3: mRS outcome distribution**

## Discussion

**Principal Findings:** This prospective study demonstrates substantial gender-related heterogeneity in risk factors and etiological mechanisms among young ischemic stroke patients from Northeast India. Male patients exhibited significantly greater exposure to conventional vascular risk factors, whereas female patients demonstrated predominance of reproductive, inflammatory, and valvular cardiac factors.

**Comparison with Global Literature:** The male predominance observed in our study is consistent with findings from the Helsinki Young Stroke Registry reported by Putaala et al., where men constituted the majority of young stroke patients. Similar observations have been reported by Ekker et al. and Aigner et al. in European cohorts.[6,8]

**Gender Differences in Modifiable Risk Factors:** Smoking emerged as the strongest male-associated risk factor. Tobacco exposure promotes endothelial dysfunction, platelet activation, oxidative stress, and accelerated atherosclerosis.[7] Diabetes mellitus also demonstrated a significant association among men, supporting observations from contemporary global studies indicating increasing metabolic risk among young adults.[8]

**Female-Specific Etiological Factors:** Women demonstrated higher prevalence of mitral stenosis, vasculitis, oral contraceptive exposure, and pregnancy-related stroke.[9,10] The high prevalence of mitral stenosis likely reflects the continuing burden of rheumatic heart disease in Northeast India.

Autoimmune-mediated vasculitis predominantly affects women and contributes to endothelial

injury, thromboinflammation, and cerebral ischemia.

**Cardioembolic Stroke and Valvular Disease:** Cardioembolism accounted for approximately one-quarter of strokes in both sexes. However, underlying mechanisms differed. Female cardioembolic events were frequently linked to valvular pathology and atrial fibrillation.

**Large Artery Atherosclerosis:** Large artery atherosclerosis was significantly more common among males. This observation likely reflects cumulative exposure to smoking, diabetes, dyslipidemia, and hypertension.[8-10]

**Stroke Severity and Outcomes:** Despite differing etiologies, NIHSS severity and mRS outcomes were similar between sexes. This finding suggests that once stroke occurs, biological sex may exert less influence on early neurological impairment and short-term recovery than previously believed.[9]

**Clinical Implications:** Sex-specific risk assessment should become an integral component of young stroke evaluation. Female patients require thorough investigation for valvular heart disease, autoimmune disorders, and reproductive risk factors, whereas aggressive vascular risk modification is essential among men.

**Public Health Implications:** Targeted smoking cessation programs, diabetes control initiatives, reproductive counseling, and screening for rheumatic heart disease may substantially reduce young stroke burden in Northeast India.

**Strengths:** The study possesses several strengths. It employed a prospective design, comprehensive etiological workup, standardized TOAST classification, NIHSS severity assessment, and 3-month outcome evaluation using mRS.

Additionally, it contributes valuable epidemiological data from an underrepresented region of India.

**Limitations:** The study was conducted at a single tertiary care center and included a relatively small sample size. Referral bias may have influenced case selection. Long-term outcomes beyond three months were not assessed. Residual confounding cannot be excluded. Multivariable regression analysis was not performed due to limited sample size.

### Conclusion

The present study demonstrates significant gender-based differences in the risk factor profile and etiological spectrum of young ischemic stroke in Northeast India. Men are predominantly affected by conventional vascular risk factors, particularly smoking and diabetes mellitus, whereas women exhibit a greater contribution from valvular heart disease, vasculitis, hormonal exposure, and pregnancy-related mechanisms. Despite these differences, stroke severity at presentation and short-term functional outcomes remain comparable between sexes. These findings highlight the necessity for sex-specific preventive strategies, comprehensive etiological evaluation, and targeted public health interventions. Future multicenter studies with larger cohorts and long-term follow-up are warranted to further elucidate the biological and sociocultural determinants of young stroke in India.

### Declarations

**Ethics Approval:** The study was conducted after approval from the Institutional Ethics Committee of Gauhati Medical College and Hospital.

**Informed Consent:** Written informed consent was obtained from all participants or legally authorized representatives.

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