

Original Article

Prevalence, Demographics and Risk Factors of Intracranial Stenosis in Ischemic Stroke Patients Admitted at a Teaching Government Hospital in Central Gujarat

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Introduction : Ischemic Strokes (IS) occur when an artery of brain is occluded by thrombosis or embolus. It can be caused either by large artery atherosclerosis, cardioembolic source, small vessel disease and in some rare cases such as hypercoagulable state or in few cases can't be determined (cryptogenic stroke). We chose to compare Intracranial Arterial Stenosis (ICAS) IS with non-ICAS IS patients to determine whether particular risk factors, demographics or clinical characteristics were particularly associated with ICAS.

Material and Method : We collected data of 153 stroke patients admitted at GMERS General Hospital, Gotri, Vadodara for three months from March 2018-May 2018. Out of which 50 IS patients passed our inclusion criteria. Their history, laboratory values and imaging. MRA and CTA imaging results were assessed and recorded. Statistics was carried out using Excel, MedCalc and Graph Pad Prism.

Results : In our study, out of 73 Stroke patients, 21 (29%) were diagnosed as stenotic and classified as ICAS. The remaining IS were classified as Non-ICAS. Among the IS patients (N=50), ICAS accounted for 21 (42%); females had a dramatically lower Time since onset (TSO) than males, with few arriving within one hour. Majority (71.4%) of the males arrived after 24 hours while half (53%) of the females arrived after 24 hours to the hospital. The TSO was longest in rural lower-middle class patients (mean 20 days). On comparison of age, median age was higher in ICAS than non-ICAS patients. High neutrophil count was found both in ICAS as well as Non-ICAS groups and neutrophil to lymphocyte ratio (NLR) was different between both the groups. Tobacco and Alcohol abuse, Diabetes Mellitus were major risk factors. Cardiac disorder were seen in very few patients whereas Past Stroke event had occurred in several of the IS patients, with no significant differences observed in the two groups (ICAS and non-ICAS) studied.

Conclusion : Demographics, risk factors and laboratory values were obtained from all the patients. Higher proportion of males was observed in all IS patients, Lower-middle class patients had the longest TSO. There was no significant difference in risk factors. Significant difference in neutrophilia was striking and showed strong inverse relationship to lymphocytes in ICAS IS patients and moderate inverse relationship in non-ICAS IS patients.

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Key words : Ischemic Stroke, Intracranial Arterial Stenosis (ICAS), Non-ICAS, MRI and MR Angiography, Treatment.

Ischemic Stroke is an episode of neurological dysfunction caused by focal brain, spinal cord or retinal infarction¹. Ischemic Strokes (IS) occur when an artery to the brain is blocked (occluded), typically by occlusion of the vessel by thrombosis or migration of a blood clot (embolus). This deprives the brain cells

Editor's Comment :

- Time Since Onset plays a major role in delayed treatment in Rural and Lower-middle class population.
- Diabetes Mellitus, Tobacco, Alcohol and cardiac illness forms a major risk group.
- Early recognition of the risk factor, awareness of stroke and early treatment shall be helpful.

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supplied by that artery of essential oxygen and nutrients².

Stroke has a high fatality rate in India^{3,4} and Intracranial Arterial Stenosis (ICAS) is known to be a common cause of IS in the Asian population⁵. ICAS has a prevalence of 20-53% depending on the population being studied³⁻⁶. There is limited awareness

in India⁷ and particularly in Gujarat⁶ about the symptoms and risk factors of stroke. Indian population is diverse ethnically as well as socio economically and so, could be exposed to different modifiable and non-modifiable risk factors. In a developing country such as India, communicable and chronic diseases pose a combined burden and pose additional challenges from socio-economic and availability of resources perspective⁷.

Knowing the risk factors, demographics and prevalence of ICAS helps in better diagnosis and subsequently prognosis, outcome and management of the patients. Furthermore, ICAS IS is known to be associated with higher rates of recurrent stroke^{8,9}. So, it is important to identify, diagnose and treat the patients early as well as develop a better understanding of the etiology. It would be of great benefit to understand the factors that might influence the etiology of stroke in a larger future study and thus help in the proper management (aggressive medical therapy, management of risk factors and/or intervention such as percutaneous transluminal angioplasty and stenting), as well as prevent recurrence¹⁰⁻¹². Only few study found in Gujarat area.

So, the overall objective of the study was to determine the prevalence of IS and also to identify specific risk factors associated with ICAS among all patients admitted with IS at a Government Hospital.

MATERIALS AND METHODS

Study Design : The study design was prospective and analytical for all IS patients. A Case Record Form was prepared by the investigator.

Study Setting : Tertiary care teaching hospital (GMERS General Hospital)

Ethics : All ethical guidelines will be followed as per ICMR. The study protocol was approved by the institutional ethics committee and guidelines were adhered to throughout the study. All data was collected and analyzed by the investigator.

Inclusion and Exclusion criteria : All patients were admitted in the medicine department with stroke were included. Patients included were all those with strokes and in which Magnetic Resonance Angiography (MRA) and/or Computed Tomography Angiography (CTA) imaging of intracranial vessels was performed. Patients were excluded if MRA/CTA had not been performed.

Participants or guardian of all participants were explained about the nature of study in detailed. And written informed consent was taken.

Sample Size: In present study, total 153 patients with stroke were assess. Out of that total 50 patients

could be included according to inclusion and exclusion criteria.

Study Procedure : A Patient Study ID number was assigned to every patient and we collected data on Age, Gender, Height, Weight, Waist, BMI, BP, Residence (Rural/Urban), Socio-economic Status, Education, Diet (Vegetarian or Non-Vegetarian), Stroke date/time, Time since onset. Socioeconomic Status was classified according to the modified Kuppuswamy scale¹³.

Additionally, the following risk factors were assessed based on prior history and laboratory results/ blood pressure and were noted in the questionnaire: Diabetes Mellitus, Hypertension, Exercise, Smoking/ Tobacco abuse, Alcohol, Family History of Stroke, Cardiac disorder, Past Stroke event. Laboratory analyses (Hb, CBC, Blood glucose) were included in the study to determine any risk factors which may not have been evident in the history. MRA and CTA were performed by the hospital-affiliated imaging facility for the patients enrolled in the study. Interpretation of the imaging results was done under guidance of qualified Radiologists and Neurophysicians.

Strokes were classified into subtypes based on Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification². MRA and CTA imaging results were assessed and recorded. The cross-sectional nature of this study limited our data to one time point, which included imaging, history and laboratory values.

Data Analysis: Data was collected and tabulated using Microsoft Excel. All data analysis and tabulation was performed using Excel, MedCalc and Graph Pad Prism. Means and Median values along with Standard deviations were calculated. Categorical data was analyzed using univariate and multivariate Chi Square analysis or Fisher's exact test. Continuous variables were analyzed using unpaired t-tests and linear regression. Results were considered significant if the p value was less than 0.05.

RESULTS

In Fig 1, the percentage of patients that present with ICAS among the IS patients.

Tables 1 and 2 show the comparative demographics, clinical characteristics and risk factors of ICAS patients and non-ICAS patients. No significant difference was seen between the two groups for all parameters except Neutrophils, which were significantly higher in the non-ICAS group. Lymphocytes trended towards higher mean in ICAS, although it was not significant at $p < 0.05$. Males were clearly predominant in the ICAS group (67%).

In Fig 2, comparison of age (medians shown by

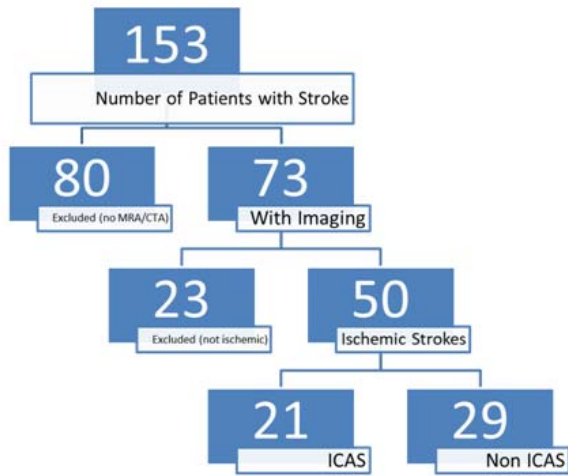


Fig 1 — the percentage of patients that present with ICAS among the IS patients

Demographics	ICAS (N=21)	Non-ICAS (N=29)
Males/Females	14/7	21/8
age (median)	65	55
age (mean)	62	55
education		
None	4	7
Upto 5th Standard	6	9
5th-10th Standard	6	5
10th pass to 12th pass	3	4
Graduate	2	4
residence		
Rural	9	12
Urban	12	17
Socio-economic status		
Lower	11	16
Lower-Middle	5	6
Middle	5	5
Upper-Middle	0	2
Vegetarian	13	23
Time since onset (mean)	4.7days	3.1days
Diabetes Mellitus	6	15
Hypertension	11	20
Past H/O Stroke	10	14
Tobacco	7	8
Alcohol	3	5
Cardiac History	10	18
Respiratory history	5	2

horizontal line) is shown for both groups. Although median age was higher in ICAS than non-ICAS patients, no statistically significant difference was seen. In Fig 3, the mean time since onset (TSO) in days is plotted on the y axis, with error bars showing standard deviation, against the stroke subtype and gender on the x axis. Males had longer mean TSO than females. This held true

irrespective of whether the stroke was ICAS or non-ICAS IS. In addition to the gender differences seen in TSO, we observed a difference based on socio-economic status as well. Individuals belonging to the lower-middle socio-economic strata showed the longest TSO, as shown in Fig 4. This held true for both rural and urban residing patients. However, the rural lower middle class patients showed the highest TSO at 20 days. Diabetes Mellitus, Hypertension, Past

history of Stroke in ICAS patients were not mutually exclusive risk factors, as shown in the Venn diagram in Fig 5. Tobacco and Alcohol abuse although prevalent (Table 1) in both ICAS and non-stenotic patients, did not show any remarkable difference. However, of the ICAS patients with history of Diabetes Mellitus, over 80% also had history of Tobacco and/or Alcohol abuse. Cardiac and Respiratory disorder were seen in very few patients whereas Past Stroke event had occurred in several of the IS patients, with no significant differences observed in the two groups (ICAS and non-ICAS) studied.

Fig 6 shows the inverse correlation

seen between neutrophils and lymphocytes in stenotic and non-stenotic IS patients. The regression analysis showed strong inverse linear correlation (R²=0.89) between neutrophils and lymphocytes in stenotic and a moderate inverse correlation in non-stenotic patients; the slope was also more negative in ICAS.

DISCUSSION

In present study demographics appeared similar to those reported in other studies from South India and event same region^{3,6}. In a multinational study published in 2013, data was compared from Prospective Hospital Stroke Registries in China (n = 752 acute stroke patients), Germany (n = 96054), India

Demographics	ICAS (N=21)	Non-ICAS (N=29)	p-value
Hb	12.81	12.80	0.981
PCV	38.94	39.60	0.497
MCV	84.81	87.28	0.490
MCH	27.51	28.54	0.466
MCHC	32.33	32.74	0.268
Total RBC	4.79	4.50	0.224
Total WBC count	10719	10181	0.647
Neutrophils	68.9	74.8	0.028
Lymphocytes	20.5	16.8	0.102
Eosinophils	3.8	2.7	0.179
Monocytes	6.2	5.6	0.272
ESR	45.6	55.5	0.531
PLT	2.7	3.1	0.396

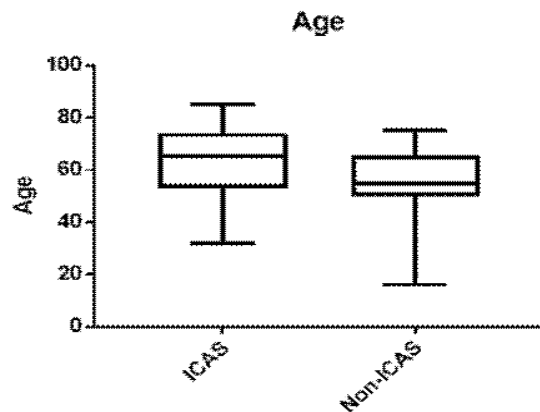


Fig 2 — comparison of age among ICAS and non-ICAS patients

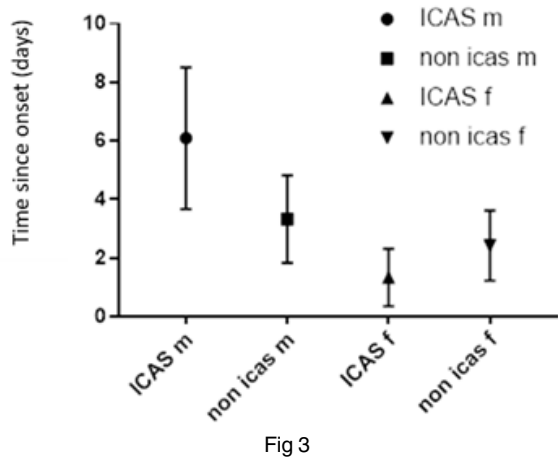


Fig 3

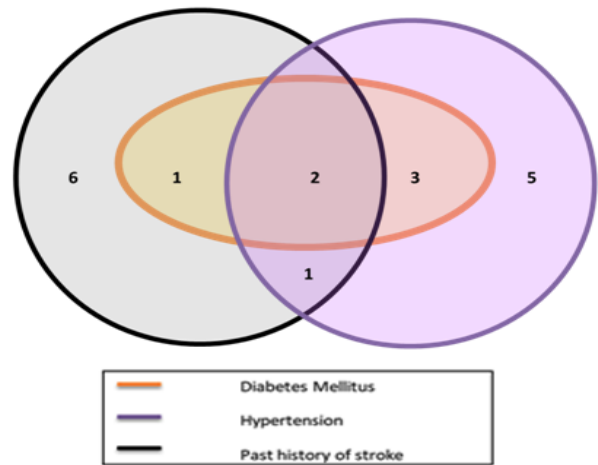


Fig 5 — Diabetes Mellitus, Hypertension, Past history of Stroke in ICAS patients

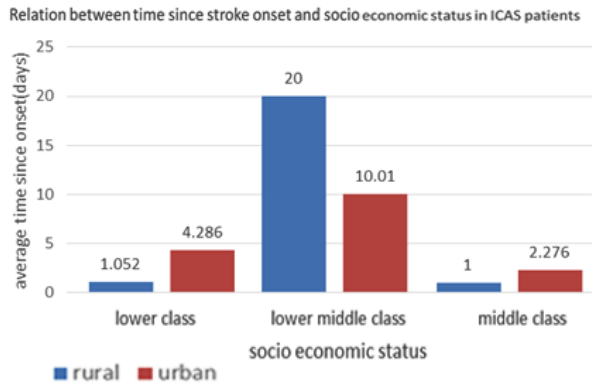


Fig 4 — Relation between time since stroke onset and socioeconomic status in ICAS patients

(n = 1500), and Iran (n = 1392) to determine gender distribution of stroke patients and associated factors¹⁴. Gender distribution was highly different between countries. For example, whereas India and China showed a male preponderance, Iran had more females in their stroke patient population. In the current study, a gender difference was apparent in our sample of patients – there were more men who were admitted with IS than women, both in ICAS and non-ICAS patient categories.

The present study shows among all IS patients, females had a dramatically lower Time since onset (TSO) than males, with few of them arriving within one hour. Majority (71.4%) of the males in our study arrived after 24 hours while half (53%) of the females arrived after 24

hours to the hospital. This may indicate a possible heightened awareness of the critical nature of stroke among the small proportion of women that reached the hospital. Further, the TSO was longest in rural lower-middle class patients (mean 20 days). This length of time is much longer than that reported by other studies in our region and elsewhere^{3,5,6,15}. This sheds light on a major area for improvement for timely care of patients in a Government Hospital setting. Future directions of our study would be to increase stroke awareness in the community.

An observation that stood out in this study was the large number of patients with a high neutrophil count both in ICAS as well as Non-ICAS groups. In addition to the unusually high count of neutrophils in several patients, we also noted a statistical difference in the mean neutrophils between the ICAS and non-ICAS groups. We also assessed the neutrophil to lymphocyte ratio (NLR) but there was no statistical significance between the NLR of the 2 groups. Previously, high neutrophils have been shown to be

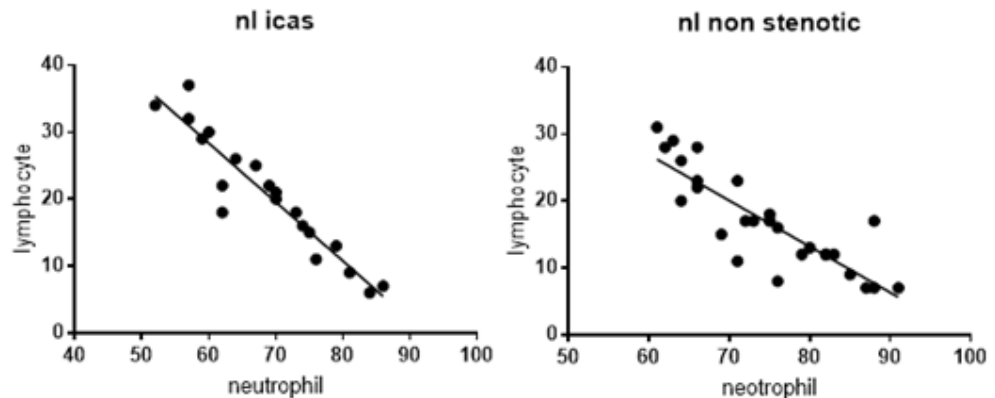


Fig 6 — correlation between neutrophils and lymphocytes in stenotic and non-stenotic IS patients.

associated with recurrent strokes¹⁵. This relationship warrants further investigation in future studies comparing ICAS and Non-ICAS and neutrophil involvement. ICAS IS association with higher rates of recurrent stroke^{8,9} is dependent on the time window following first event and unfavorable outcome is more likely in older patients^{6,16}. It is important to identify, diagnose and treat the ICAS IS patients early as well as develop a better understanding of the etiology to improve outcome.

This study provides insight for future investigators who can focus on taking a proactive approach to implement preventive measures. In-hospital psychological, medical and follow-up care may not be a feasible option for many patients and their families, and community involvement in Stroke prevention and care might be a better way to tackle this issue. The constraints to arriving at the hospital in time as well as the costs associated with in performing required tests and retaining patients until treatment is complete is a major hurdle that needs to be addressed. Stroke awareness campaigns would be of great benefit for long term involvement of the community in prevention and care.

The major limitation of the study is less sample size which is mainly because the total duration of the study. As most of the patients admitted belonged to lower socio-economic strata, imaging was not available/done for all patients owing to their economical limitations. That also decrease recruitment rate in the study.

In conclusion higher proportion of males was observed in all IS patients, however the small number of females admitted all came in a much smaller time window following onset than males. Lower-middle class patients had the longest TSO, both from rural and urban residential areas. No significant differences were obtained for most risk factors and laboratory values that were assessed owing to small sample size. Significant difference in neutrophilia was striking, and showed strong inverse relationship to lymphocytes in ICAS IS patients and moderate inverse relationship in non-ICAS IS patients.

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