

ANALYSIS OF RISK FACTORS OF ACUTE ISCHEMIC STROKE FOR DIFFERENT ETHNIC GROUPS IN CHANGDE

Objectives: The aim of our study was to explore the risk factors of acute ischemic stroke (AIS) for different ethnic groups in Changde city (a multi-ethnic residence inhabited mainly by Han and Tujia), Hunan Province, China.

Design, Setting and Participants: A multi-center study was performed and the demography data, etiology data and clinical features of 5338 AIS patients from 17 hospitals in Changde city were collected from January 2011 through December 2011.

Main Measures: Student's t-test and χ^2 -test were used to compare the differences between the Han and Tujia ethnic group in the AIS.

Results: In Changde, the incidence of AIS in the Tujia ethnic group was higher than that in the Han ethnic group (233.14 per million vs. 84.38 million, respectively). We found statistically significant differences between the Tujia and Han ethnicities in demographic, etiology and clinical data (eg, sex, living environment, diet, smoking, payment methods, cerebral hemorrhage and transient ischemic attack [$P < .05$]). In addition, compared with the Han population, the Tujia patients had a higher rate of the incidence of the anterior circulation infarction, partial anterior circulation infarction, lacunar infarction and cerebral hemorrhage.

Conclusions: Our results indicate that lifestyle choices (eg, diet, smoking cigarettes), location, family heritage, and sex are associated with AIS and is useful for informing AIS rates and treatment for AIS. (*Ethn Dis.* 2014;24[3]:310-315)

Key Words: Acute Ischemic Stroke, Risk Factors, Ethnic Groups

From Department of Neurology, No.1 People's Hospital, Changde (PX, X-LX, G-XG, C-YG, S-JZ, Q-HS, JW, Y-DL); and Department of Neurology, Xiangya Hospital, Central South University (JK, BX).

Address correspondence to Bo Xiao; Department of Neurology, Xiangya Hospital, Central South University; Changsha 410008, China; +86-0731-84327236; +86-0731-84327236 (fax); boxxiao@hotmail.com

Ping Xu, BS; Jin Kang, MD; Xu-Lin Xiang, BS; Gui-Xiang Guo, BS; Chun-Yun Gao, BS; Shi-Jin Zhu, BS; Qing-Hua Su, BS; Jun Wen, BS; Yan-Deng Li, BS; Bo Xiao, MD

BACKGROUND

Ischemic stroke has become a leading cause of morbidity and mortality in the developing and developed world,¹ and a substantial portion of those deaths occur during hospitalization for acute ischemic stroke (AIS).² In the United States and Europe, AIS was the third leading cause of death³ and the incidence of stroke in China has increased year by year.⁴ Thus, predicting risk factors of stroke may be useful to determine prognosis and care for patients at risk. So far, many studies have reported about the etiology and pathogenesis of stroke.⁵ Previous studies have shown that stroke has some relationship with regional and genetic factors.⁶⁻⁸ Additionally, cholesterol levels are risk factors for cerebrovascular disease,⁹ and hypertension has been shown to be associated with stroke.¹⁰ Previous results have suggested that the low-density lipoprotein cholesterol (LDL-C) and the risk of atherosclerosis infarction were significantly associated.¹¹

Changde is a multi-ethnic city in China and is home to 5,703,000 residents; the majority of these residents (5,280,000) are Han Chinese. Minority populations accounted for 7.52% of the total population, including 350,000 Tujia people, 40,000 Hui people, more than 6,000 Uighurs people and other 33 ethnic minorities.^{12,13} Some research has focused on stroke in the Tujia ethnic group¹⁴; however, the comparative data between the Han and Tujia ethnic group have not been reported.¹⁵ Changde provides a favorable environment for the investigation of Tujia and Han among AIS because of the multi-ethnic mix.¹³ Our study attempted to investigate the difference between the Han and

Tujia ethnicities for incidence of, and risk factors for, AIS. Our findings will inform AIS prediction, diagnosis and treatment in Changde, Hunan province, China.

METHODS

Study Population

According to the multi-center study method,¹⁶ we enrolled 5338 patients with AIS from 17 hospitals of Changde in China between January 2011 and December 2011. The enrolling patients: 1) were aged 18-95 years; 2) had lived in Changde for more than two years; 3) had experienced a cerebrovascular event, (eg, cerebral infarction, transient ischemic attack, cerebral hemorrhage, spontaneous subarachnoid hemorrhage) within the previous 3 months as diagnosed by a neurologist according to clinical symptoms and imaging studies; and 4) signed informed consent. The patients who had a malignant tumor or venous system thrombosis were excluded.

Assessment and Laboratory Data

We prospectively investigated the demographic data of patients including age, sex, ethnicity and risk factors according to international diagnosed criteria (eg, history of smoking and hypertension, diabetes, ischemic heart disease and atrial fibrillation). Smoking was defined as smoking >1 year or >5 cigarettes per day. Patients were considered hypertensive if they had a well-defined hypertension history or their blood pressure was more than 140/90 mm Hg at least two times. Patients were diagnosed with diabetes if their fasting glucose level was >7.8 mmol/L or they were treated with antidiabetic medicine. Patients with blood cholesterol >6.5 mmol/L, low-density

Table 1. Sources of patients

Source	n	%
First People's Hospital of Changde	1127	21.11
Second People's Hospital of Changde	132	2.47
Third People's Hospital of Changde	78	1.46
Fourth People's Hospital of Changde	782	14.65
Fifth People's Hospital of Changde	74	1.39
Sixth People's Hospital of Changde	76	1.42
Seventh People's Hospital of Changde	77	1.44
Changde Hanshou People Hospital	235	4.4
Changde Shimen People's Hospital	347	6.5
First Chinese medicine hospital of Changde	351	6.58
Changde Lixian People's Hospital	294	5.51
Tsu People's Hospital	329	6.16
The Linli People Hospital	375	7.03
Taoyuan People's Hospital	762	14.28
An Township People's Hospital	190	3.56
The West Dongting People Hospital	81	1.52
West Lake People's Hospital	28	.52
Total	5338	100

lipoprotein (LDL) >3.2mmol/L, or hypercholesterolemia history were defined as patients with hyperlipidemia. Atrial fibrillation, ischemic heart disease, arrhythmia and intermittent postscript line were diagnosed in accordance with relevant international standards. The clinical severity status of the patients was assessed within 24 hours by the National Institute of Health Stroke Scale (NIHSS) and Scandinavian Stroke Scale (SSS).¹⁷⁻¹⁹

Statistical Analyses

Differences overall and between the ethnic groups in the characteristics and potential risk factors were analyzed by SPSS ver.13.0. Student's *t* test was used to compare continuous variables between groups. The chi-square test or Fisher's exact test were used to compare categorical variables. The significance level was defined as $P < .05$.

RESULTS

Participants

All 5338 AIS patients came from 17 hospitals in Changde, Hunan Province, China (Table 1). Among them, 1127, 782 and 762 patients came from the First People's Hospital of Changde, Fourth People's Hospital of Changde and Taoyuan People's Hospital, accounting for 21.11%, 14.65% and 14.28%, respectively.

We found a significant difference in AIS incidence among different ethnic groups ($P < .001$) (Table 2). The AIS incidence in Tujia was 233.14 per 100,000, which was significantly higher than that in the other ethnicities ($P < .05$) (Table 3). The AIS incidence in Han, Hui and Uighur was 84.38, 95 and 66.66 per 100,000, respectively. No statistical difference in the incidence

of AIS was found between the three ethnicities (Table 3).

Sample size calculations suggested that 461 participants per ethnic group would provide 80% power to detect important differences in AIS and risk factor prevalence between ethnic groups. In our study, 4450 Han and 816 Tujia patients were enrolled, and their baseline characteristics are summarized in Table 4. Most of the patients were aged 45 to 84 years (84.39% and 93.38% in Han and Tujia ethnic, respectively). No significant difference was found in the age and body mass index (BMI) between the Han and Tujia patients ($P > .05$). There were, however, differences between the Han and Tujia patients in sex, living environment, eating habits, smoking, education level, payment of medical expenses and cerebrovascular accident type ($P < .05$) (Table 4). More AIS patients in the Tujia group suffered from cerebral hemorrhage ($P = .004$), whereas more Han patients experienced transient ischemic attack ($P = .001$). And cerebral infarction occurred equally in the two ethnic groups.

To examine why the Tujia group had a higher AIS incidence than the Han group, we calculated the rates of conventional and novel risk factors between the two ethnic groups. Compared with the Han patients, the Tujia patients had greater risk factors for AIS (ie, sex, hypertension, myocardial infarction, other heart diseases). However, there were no significant differences in age, diabetes, hyperlipidemia, atrial fibrillation, history of stroke, SSS score and NIHSS score ($P > .05$) (Table 5). We found that the clinical types of

Table 2. The incidence of AIS in different ethnic groups recorded in the hospitals of Changde

	Han	Tujia	Hui	Uighur	Other	Overall P
Population in Changde	5,280,000	350,000	40,000	6,000	31,000	
Registration number of AIS	4450	816	38	4	30	
The incidence of registered AIS (per 100,000)	84.38	233.14	95	66.66	96.77	<.001 ^a

Statistical differences were analyzed using chi-square test.

^a $P < .001$.

RISK FACTORS OF AIS FOR DIFFERENT ETHNIC GROUPS - Xu et al

Table 3. Pairwise comparisons in the incidence of AIS between ethnic groups

	Han	Tujia	Hui	Uighur
Tujia	<.001 ^b			
Hui	.462	<.001 ^b		
Uighur	.638	.008 ^a	.498	
Other	.45	<.001 ^b	.94	.481

Statistical differences were analyzed using chi-square test.

^a $P < .01$.

^b $P < .001$.

stroke in the Han and Tujia populations were different; compared with the Han patients, the incidence rates of anterior circulation infarction, partial anterior circulation infarction, lacunar infarction and cerebral hemorrhage in Tujia patients were significantly increased ($P < 0.05$) (Table 6). According to the mortality rate, the anterior circulation infarction and cerebral hemorrhage mortality in the Tujia were higher than in the Han, and Tujia overall complication rate was higher as well (Table 6).

Table 4. Baseline characteristics of the patients

Characteristics	Han (N=4450), n	%	Tujia (N=816), n	%	P^a	
					Overall	Certain Category
Sex					.001 ^b	
Male	2512	56.45	512	62.75		
Female	1935	43.48	304	37.25		
Age					.708	
≤34	28	.63	6	.74		
35-44	131	2.94	24	2.94		
45-54	491	11.03	99	12.13		
55-64	1195	26.85	231	28.31		
65-74	1449	32.56	260	31.86		
75-84	1045	23.48	172	21.08		
≥85	111	2.49	24	2.94		
Environment					<.001 ^c	
Countryside	3342	75.1	667	81.74		
Town	1108	24.9	149	18.26		
BMI, mean ± SD	26.3 ± 14.7		25.7 ± 13.8		.279	
Eating pickled foods					<.001 ^c	
Yes	2672	60.04	713	87.38		
No	1778	39.96	103	12.62		
Smoking					<.001 ^c	
Yes	1378	30.97	453	55.51		
No	3072	69.03	363	44.49		
Education					<.001 ^c	
Primary school	3761	84.52	761	93.26		<.001 ^c
High school	541	12.16	37	4.53		<.001 ^c
University and above	148	3.33	18	2.21		.092
Payment methods					.005 ^b	
Health insurance	2047	46	332	40.69		
At their own expense	2403	54	484	59.31		
Cerebrovascular accident type					<.001 ^c	
Cerebral hemorrhage	1128	25.34	246	30.15		.004 ^b
Cerebral infarction	2726	61.25	490	60.04		.515
Transient ischemic attack	466	10.47	55	6.74		.001 ^b
Other	130	2.921	15	1.83		.082

^a Statistical differences were analyzed using T-test or chi-square test. P of the comparison in each characteristic is shown in the overall column. If there was significant different in the characteristic that contained more than 2 categories, differences in each category of the characteristic would be analyzed and the corresponding P are shown in the certain category column.

^b $P < .01$.

^c $P < .001$.

Table 5. Risk factors comparison between the Han and Tujia patients

Value	Han		Tujia		P
	n	%	n	%	
Age, mean ± SE	64.3 ± 12.9		61.9 ± 13.8		.115
Male	2512	56.45	512	62.75	.001 ^a
Hypertension	2136	48	440	53.92	.002 ^a
Diabetes	447	10.04	79	9.68	.75
Hyperlipidemia	193	4.34	31	3.8	.484
Atrial fibrillation	413	9.28	89	10.91	.146
Myocardial infarction	759	17.06	171	20.96	.007 ^a
Other types of heart disease	1034	23.24	237	29.04	<.001 ^b
History of stroke	442	9.93	75	9.19	.513
SSS score on admission, mean ± SD	39.8 ± 16.7		38.8 ± 17.2		.118
Admission NIHSS score, mean ± SD	9.8 ± 10.9		10.1 ± 11.2		.472

Statistical differences were analyzed using T-test or chi-square test.
 NIHSS, National Institute of Health Stroke Scale; SSS, Scandinavian Stroke Scale.

^a P<.01.

^b P<.001.

DISCUSSIONS

In our study, we investigated the incidence of AIS in different ethnic groups in Changde and compared the risk factors for AIS between the Han and Tujia ethnicities. We found that Tujia had a higher AIS incidence compared with other groups. We also found differences in the baseline characteristics and risk factors between the AIS patients in Tujia and Han groups.

In our study, 17 hospitals took part in the investigation of the Changde area population, covering different levels of hospitals in this region.²⁰ We found the incidence of reported AIS in Tujia ethnic was much higher than that of other ethnic groups. We also found that being male, living in a rural environment, eating pickled foods and smoking were more likely risk factors for the Tujia people as compared with the Han.

Currently, the relationship between sex and stroke is still debatable. Some previous results suggested that being female is a risk factor for stroke because of the declining estrogen levels.²¹ However, in our study, we found that the incidence of stroke in males was higher in both Han and Tujia groups, with Tujia males having higher incidence than Han males (P<.05). Considering that men are the ones who undertake

Table 6. Clinical type and characteristic comparison between the Han and Tujia patients

Type of stroke	Cases					Stay in the Hospital, Days, Mean ± SD		
	Han, n	Probability %	Tujia n	Probability %	P	Han	Tujia	P
Completely anterior circulation infarction	389	10.09	103	13.99	.002 ^b	15 ± 14	14 ± 15	>.05
Partial anterior circulation infarction	851	22.08	71	9.65	<.001 ^c	12 ± 9	11 ± 9	>.05
Posterior circulation infarction	373	9.68	65	8.83	.474	16 ± 10	14 ± 12	>.05
Lacunar infarction	1113	28.88	251	34.1	.004 ^b	8 ± 7	7 ± 8	>.05
Cerebral hemorrhage	1128	29.27	246	35.86	.024 ^a	11 ± 11	14 ± 13	<.05 ^a
Total	3854		736			12 ± 10	11 ± 12	>.05

Type of stroke	Death Cases					Complication Cases				
	Han, n	Probability %	Tujia	Probability %	P	Han, n	Probability %	Tujia, n	Probability %	P
Completely anterior circulation infarction	90	23.13	25	24.27	.239	220	56.56	61	59.22	.095
Partial anterior circulation infarction	124	14.57	12	16.9	<.001 ^c	208	24.44	21	29.57	<.001 ^c
Posterior circulation infarction	35	9.38	7	10.77	.832	86	23.06	17	26.15	.623
Lacunar infarction	91	8.18	19	7.56	.856	124	11.14	29	11.55	.824
Cerebral hemorrhage	257	22.78	67	27.23	.078	420	37.73	109	43.9	.075
Total	597	15.49	130	17.66	.139	1058	27.45	237	29.3	.009 ^b

Statistical differences were analyzed using T-test or chi-square test.

^a P<.05.

^b P<.01.

^c P<.001.

Our study attempted to investigate the difference between the Han and Tujia ethnicities for incidence of, and risk factors for, acute ischemic stroke.

financial responsibility in most Tujia families, the Tujia men may have greater economic pressure compared with Han, which could lead to the higher incidence of hypertension and heart disease in the AIS patients. In addition, compared with the Tujia, the Han people possess better living conditions and have a stronger commitment to medical treatment. After adjusting for poor living conditions and poor awareness of medical treatment, incidence of reported AIS in the Tujia group was still much higher than that in Han ethnic, suggesting that the Tujia population have a much higher risk of AIS. Previous results²² have reported that the hypertension is an independent risk factor in cerebral hemorrhage and that heart disease is an independent risk factor in the anterior circulation infarction.²³ In the Tujia AIS patients, the hypertension incidence was higher than that in the Han AIS patients ($P < .05$), which could suggest that long-term hypertension would lead to atherosclerosis and abnormal dilation of small blood vessels, loss of autoregulation leukoencephalopathy, cerebral metabolism and damaged brain structures. In eating habits, we found that the Tujia favor pickled foods, which are not rich in the nutrients

We found that Tujia had a higher AIS incidence compared with other groups.

known to contribute to healthy brain function and found in fresh vegetables and fruits: vitamin C, vitamin E, B-carotene and other antioxidants.

The Tujia ethnic group have long been an important minority in China.²⁴ To our knowledge, this is the first validated data for comparison between the Han and Tujia ethnic in AIS incidence and risk factors.

CONCLUSIONS

According to our study, the interaction between the Tujia ethnic group and the risk factors of AIS patients might be confounded by other factors such as diabetes, hyperlipidemia, AF, smoking status, BMI and the treatments. We also found, however, that the Tujia have more AIS risk factors compared with the Han.

ACKNOWLEDGMENTS

This survey was supported by “Eleventh Five-Year” National Science and Technology Support Program sub-topics (No. 2006BA104A02) and grants from the explore program of Science and Technology Bureau of Changde (No. 2012sk45).

REFERENCES

1. Lucke-Wold BP, Turner RC, Lucke-Wold AN, Rosen CL, Huber JD. Age and the metabolic syndrome as risk factors for ischemic stroke: improving preclinical models of ischemic stroke. *Yale J Biol Med.* 2012;85(4):523–539.
2. Allen NB, Holford TR, Bracken MB, et al. Geographic variation in one-year recurrent ischemic stroke rates for elderly Medicare beneficiaries in the USA. *Neuroepidemiology.* 2010;34(2):123–129.
3. Braestrup C, Nielsen M. Ontogenetic development of benzodiazepine receptors in the rat brain. *Brain Res.* 1978;147(1):170–173.
4. Wang YL, Xu J, Xie XP, Wang YJ. Study of day-time rhythm of stroke onset in chinese population. *Value Health.* 2013;16(3):A278.
5. Dong X, Tao DB, Wang YX, et al. Plasma copeptin levels in Chinese patients with acute ischemic stroke: a preliminary study. *Neural Sci.* 2013;34(9):1591–1595.
6. Bennett D, Yan B. Suboptimal response to clopidogrel: A genetic risk factor for recurrent ischaemic stroke. *J Clin Neurosci.* 2013;20(6):767–770.
7. Van Schie MC, Wieberdink RG, Koudstaal PJ, et al. Genetic determinants of von Willebrand factor plasma levels and the risk of stroke: the Rotterdam Study. *J Thromb Haemost.* 2012;10(4):550–556.
8. Kawai T, Ohishi M, Takeya Y, et al. Adiponectin single nucleotide polymorphism is a genetic risk factor for stroke through high pulse wave pressure: a cohort study. *J Atheroscler Thromb.* 2013;20(2):152–160.
9. Papademetriou V, Narayan P, Rubins H, Collins D, Robins S. Influence of risk factors on peripheral and cerebrovascular disease in men with coronary artery disease, low high-density lipoprotein cholesterol levels, and desirable low-density lipoprotein cholesterol levels. HIT Investigators. Department of Veterans Affairs HDL Intervention Trial. *Am Heart J.* 1998;136(4 Pt 1):734–740.
10. Gorelick PB, Aiyagari V. The management of hypertension for an acute stroke: what is the blood pressure goal? *Curr Cardiol Rep.* 2013;15(6):366.
11. Howard WJ, Russell M, Fleg JL, et al. Prevention of atherosclerosis with LdL-C lowering - lipoprotein changes and interactions: The Sands Study. *J Clin Lipidol.* 2009;3(6):322–331.
12. Zou J, Zhu Y, Sheng G. [Genetic polymorphisms of fifteen short tandem repeats in Tujia ethnic group of Hubei province]. *Zhonghua Yi Xue Yi Chuan Xue Za Zhi.* 2009;26(6):701–704.
13. Wang XW, Hu LM. [Trend of death cause of residents in Changde from 1973 to 2002]. *Zhong Nan Da Xue Xue Bao Yi Xue Ban.* 2006;31(6):952–959.
14. Xi S, Zhao J, Zhao H, et al. [Theoretical study on thirteen or fourteen incompatible medications and opposite drug properties of Tujia ethnic medical science]. *Zhongguo Zhong Yao Za Zhi.* 2012;37(10):1500–1505.
15. Yuan GL, Shen CM, Wang HD, et al. Genetic data provided by 21 autosomal STR loci from Chinese Tujia ethnic group. *Mol Biol Rep.* 2012;39(12):10265–10271.
16. Robledo JA, Mejia GI, Morcillo N, et al. Evaluation of a rapid culture method for tuberculosis diagnosis: a Latin American multi-center study. *Int J Tuberc Lung Dis.* 2006;10(6):613–619.
17. Berthier E, Decavel P, Vuillier F, et al. Reliability of NIHSS by telemedicine in non-neurologists. *Int J Stroke.* 2013;8(4):E11.
18. Luvizutto GJ, Monteiro TA, Braga G, et al. Validation of the scandinavian stroke scale in a multicultural population in Brazil. *Cerebrovasc Dis Extra.* 2012;2(1):121–126.
19. Gray LJ, Ali M, Lyden PD, Bath PM. Interconversion of the National Institutes of

- Health Stroke Scale and Scandinavian Stroke Scale in acute stroke. *J Stroke Cerebrovasc Dis.* 2009;18(6):466–468.
20. Li B, Zhong F, Yi H, et al. Genetic polymorphism of mitochondrial DNA in Dong, Gelao, Tujia, and Yi ethnic populations from Guizhou, China. *J Genet Genomics.* 2007;34(9):800–810.
21. Roivainen R, Haapaniemi E, Putaala J, Kaste M, Tatlisumak T. Young adult ischaemic stroke related acute symptomatic and late seizures: risk factors. *Eur J Neurol.* 2013;20(9):1247–1255.
22. Gladwin MT. Prevalence, risk factors and mortality of pulmonary hypertension defined by right heart catheterization in patients with sickle cell disease. *Expert Rev Hematol.* 2011;4(6):593–596.
23. Wang W, Lee ET, Fabsitz RR, et al. A longitudinal study of hypertension risk factors and their relation to cardiovascular disease: the Strong Heart Study. *Hypertension.* 2006;47(3):403–409.
24. Xie XH, Li H, Mao XY, et al. Genetic structure of Tujia as revealed by Y chromosomes. *Yi Chuan Xue Bao.* 2004;31(10):1023–1029.

AUTHOR CONTRIBUTIONS

Study design and concept: Xu, Kang, Xiang, Guo, Gao, Zhu, Su, Wen, Li

Acquisition of data: Xu, Kang, Xiang, Guo, Gao, Zhu, Su, Wen, Li, Xiao

Data analysis and interpretation: Xu, Kang, Xiang, Guo, Gao, Zhu, Su, Wen, Li

Manuscript draft: Xu, Kang, Xiang, Guo, Gao, Zhu, Su, Wen, Li, Xiao

Statistical expertise: Xu, Kang, Xiang, Guo, Gao, Zhu, Su, Wen, Li

Acquisition of funding: Xu, Kang, Xiang, Guo, Gao, Zhu, Su, Wen, Li, Xiao

Administrative: Xu, Kang, Xiang, Guo, Gao, Zhu, Su, Wen, Li

Supervision: Xu, Kang, Xiang, Guo, Gao, Zhu, Su, Wen, Li