ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 16, Issue 11, 2023

Online - 2455-3891
Print - 0974-2441

Research Article

EVALUATION OF RISK FACTORS AND THEIR PROGNOSTIC VALUE IN PATIENTS WITH ISCHEMIC STROKE

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Received: 04 April 2023, Revised and Accepted: 13 June 2023

ABSTRACT

Objectives: The objectives of this study were to evaluate the risk factors in patients with ischemic stroke, to find out the prognosis of ischemic stroke regarding risk factors, and to identify the patients having modifiable risk factors so that care can be taken to prevent recurrences.

Methods: This was a prospective and observational study with 100 patients with ischemic stroke. Patients were recruited from November 2017 to October 2018. NIHSS score was used to classify the severity of the stroke. The Barthel index was used to assess prognosis at the time of discharge.

Results: The mean age of the study population was 61.4±13.7 years. There was no statistically significant (p=0.28) difference in the outcome of the patients with respect to gender. There was a statistically significant (p=0.04) difference in the severity of the patients respective to gender. Among 100 patients, 55 had hypertension and the relative risk of hypertension was found to be 1.22, indicating hypertension is the most predominant risk factor.

Conclusion: Hypertension is the most prevalent risk factor in the present study. As per our study findings, hypertension, diabetes mellitus, a history of smoking, and a history of alcohol intake were the preventable risk factors, leading to severe stroke and poor functional outcome. Patients with multiple risk factors had severe stroke and poor functional outcome when compared to patients with single or no risk factors. Patients with severe stroke based on NIHSS score had the poor functional outcome.

Keywords: Ischemic stroke, Hypertension, Risk factors, NIHSS score, Barthel Index.

 DOI: http://dx.doi.org/10.22159/ajpcr.2023v16i11.48012. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Ischemic stroke was defined as an episode of neurological dysfunction caused by focal cerebral, spinal, or retinal infarction [1]. Due to demographic changes and the rising frequency of the main modifiable risk factors, stroke is increasingly a leading cause of disability and premature mortality in low- and middle-income countries like India [2].

Because of their inability to pay for the high cost of stroke care as well as their shifting demographic exposure to risk factors, the poor are becoming more and more afflicted by stroke. The majority of stroke survivors continue to live with a disability, and because ongoing rehabilitation and long-term care are usually covered by family members, their families are left in a financially precarious situation [3].

Globally, there are 7.6 million new ischemic strokes each year, over 62% of all incident strokes are ischemic strokes and 3.3 million people die from ischemic strokes annually [4].

India has experienced a significant economic and demographic change, which has caused a shift away from infectious diseases and nutritional deficiencies caused by poverty toward lifestyle-related cardiovascular and cerebrovascular diseases [5]. India has a varied prevalence of stroke, with estimated prevalence rates starting at 0.3/1000 in people under the age of 40. The multiple risk factors contribute the risk of ischemic stroke [6,7].

Active risk-factor treatment and lifestyle recommendations are crucial for all patients, although their relative contribution to the outcome of stroke differs between studies and populations [6,8].

Studying stroke prevention strategies would be preferable due to the rapidly rising burden of stroke in the years to come and the death of stroke care in India. Preventive measures will lower the incidence of stroke [9]. Our study focused to discover the significant risk factors, leading to the result of a stroke in light of the rising incidence, and high healthcare expenditures for the potential prevention of stroke.

METHODS

This was a prospective and observational study with 100 patients with ischemic stroke getting admitted to the Department of Medicine in Sri Venkateswara Ramnarain Ruia Hospital, Tirupati, AP.

This study was approved by the Institutional Ethics Committee (Lr No.19/2017) of S.V. Medical College, Tirupati. Before the subject Enrollment, all the subjects were briefed about the purpose of the study and written informed consent was obtained. If the patient could not give consent, informed written consent was taken from the legally authorized representative of the patient. All investigations were done free of cost and no financial burden was imposed on the patient.

The objectives of this study were to evaluate the risk factors in patients with ischemic stroke, to find out the prognosis of ischemic stroke regarding risk factors, and to identify the patients having modifiable risk factors so that care can be taken to prevent recurrences.

Patients were recruited from November 2017 to October 2018. The study population included patients of either gender aged about ≥18 years with evidence of ischemic stroke, that is, signs and symptoms suggestive of acute loss of focal or global cerebral function and evidence

of ischemia on a computed tomography (CT) scan of the brain. Patients with focal epilepsy, structural brain lesions (such as tumors), evidence of hemorrhage on a CT scan of the brain, stroke secondary to an infection, and connective tissue disorders were excluded. Patients who did not give informed written consent were also excluded from the study.

The risk factors assessed in our study were age, sex, hypertension, diabetes mellitus, smoking, alcohol intake, dyslipidemia, heart disease, TIA, migraine, hypercoagulable states, hormone therapy, and family history.

Patients with ischemic stroke as evident on CT scan who met the inclusion criteria were evaluated with a comprehensive clinical history, detailed physical examination, and relevant investigations include complete blood count, serum creatinine, fasting and postprandial blood sugar, lipid profile, urine analysis, electrocardiography (ECG), 2D ECHO with carotid Doppler CT scan as routine investigations, and other investigations such as chest X-ray, serum electrolytes, coagulation profile, MRI scan, and serum homocysteine levels in young patients were done when needed. All the modifiable and non-modifiable risk factors attributed for ischemic stroke were evaluated.

While evaluating the risk factors, hypertension was considered in the patient with a BP of systolic and diastolic of >140/90 mmHg on three separate occasions, taken on 3 different days. Patients who are already on antihypertensive medications were also taken as hypertensive. The dyslipidemia was considered when the patient's serum cholesterol was >200 mg/dL, LDL cholesterol was >130 mg/dL, and high-density lipoprotein HDL cholesterol in female patients was <35 mg/dL and male patients was <40 mg/dL. The patients were considered as suffering from heart diseases if they had ischemic heart disease, congestive heart failure, rheumatic heart disease, atrial fibrillation, or evidence of the left ventricular hypertrophy on ECG or echocardiography. The smoking, tobacco chewing, and alcohol intake of the patients were based on the clinical history of past and present consumption of these substances. Diabetes was considered that the patients were diagnosed as per the American diabetic association guidelines. Patients on antidiabetic medications were also considered diabetics.

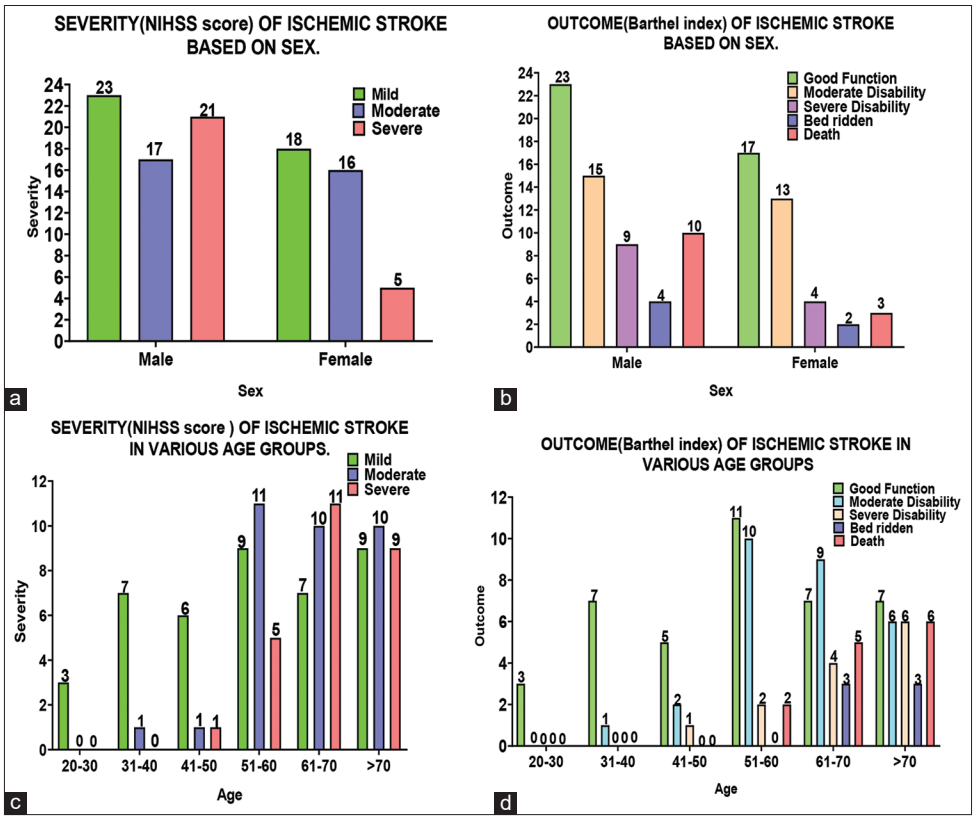

Fig. 1: (a) Severity of ischemic stroke based on sex. (b) Outcome of ischemic stroke based on sex. (c) Severity of ischemic stroke in various age groups. (d) Outcome of ischemic stroke in various age groups

Table 1: Age, sex, and risk factor distribution in ischemic stroke

Age (years)	20–30				31–40				41–50				51–60				61–70				>70				Total patients
RR	M		F		M		F		M		F		M		F		M		F		M		F		
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	
0-RF	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	1	1	1	1	2	2	0	0	5%
1-RF	2	2	1	1	1	1	2	2	3	3	1	1	7	7	5	5	2	2	2	2	4	4	6	6	36%
2-RF	0	0	0	0	0	0	1	1	2	2	0	0	3	3	0	0	1	1	7	7	1	1	5	5	20%
3-RF	0	0	0	0	0	0	0	0	1	1	0	0	3	3	1	1	2	2	3	3	7	7	0	0	17%
4-RF	0	0	0	0	0	0	3	3	1	1	0	0	6	6	1	1	7	7	0	0	2	2	0	0	20%
5-RF	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	1	0	0	2%

RF: Risk factor, M: Male, F:Female, N: Number of patients, %: Percentage of patients

NIHSS score was used to classify the severity of the stroke. A score of 0–5 indicates mild stroke, 6–15 denotes moderate stroke, and a score of more than 15 is suggestive of severe stroke. The Barthel index was used to assess prognosis at the time of discharge. A Barthel index score of 76–100 points denotes a good function, 51–75 points denotes moderate disability, and a score under 50 denotes severe disability. A score of 0 represents a dependent bedridden state.

Statistical analysis for the association between risk factors and stroke was done using ANOVA and relative risk was calculated. $p<0.05$ was taken as significant. Severity and outcome between the genders were assessed by Z-test. ANOVA was done to estimate the difference in severity (within each age group) and outcome (within each age group). The statistical software, namely, SPSS 25, Stata 15, Systat 13.2, Medcalc 18.11, and Effect Size calculator was used for the analysis of the data. GraphPad Prism 8.0.1 has been used to generate graphs and Microsoft Word and Excel have been used to generate tables.

RESULTS

In the present study, 100 patients of acute ischemic stroke who met inclusion criteria were assessed with regard to each risk factor, individually and in combination and they were correlated with the outcome**.** The age and sex distribution among the single and multiple risk factors (two, three, four, and five risk factors) of ischemic stroke is depicted in Table 1. The 51–60 age group, the majority were male (19 patients) and possessed a single risk factor.

The mean age of the study population was 61.4±13.7 years which is comparable to the study done by Biswas *et al*. shows 64±10 years (Indians) versus 71±13 years (Americans) [10] and the study done by Sylaja *et al*. showed that the mean age of presentation of stroke was 58.3±4 years [11].

There was no statistically significant (p=0.28) difference in the outcome of the patients with respect to gender which differs from results in a study by Irie *et al*., female sex was independently associated with poor functional outcome at discharge [12] and a study by Sylaja *et al*. showed that female sex was associated with poor prognosis [11]. There was a statistically significant (p=0.04) difference in the severity of the patients respective to gender which differs from the results of a study by Kevin *et al*. which found no sex difference in stroke severity, stroke subtype, or infarct size, and location in patients with incident ischemic stroke [13] Whereas in a study by Fahimfar *et al*., it was shown that the male gender was independently associated with an increased risk of stroke events in the total population [14]. Thirteen out of 100 patients did not survive in the present study. The mean age of the surviving population was 63±13 years, whereas that of the non-surviving patients was 72±8.5years, similar to the study by Wei *et al*. in which the mean age of the surviving population was 68.78±11.22 years, whereas that of the non-surviving patients was 76.42±7.692 years [15].

The severity (NIHSS score) and outcome (Barthel index) of the ischemic stroke patients based on age and sex are represented in Fig. 1.

There was a statistically significant difference between severity of stroke within age (years) groups 20–30 (p=0.013), 61–70 (p=0.0001), and >70 (p=0.00008)) irrespective of gender and there was a statistically significant difference between outcome of stroke within age (years) groups 20–30 (p=0.015), 61–70 (p=0.009), and >70 (p=0.01) irrespective of gender (Table 2). There was a statistically significant difference in severity and outcome between the age groups, in which the increase in age leads to the increase in severity and less outcome of the ischemic stroke in patients. This result was similar to the previous studies such as the study by Sylaja *et al*. shows old age is an independent risk of poor prognosis [11] and a study by Hernández *et al*. reported that 55.7% of patients older than 80 years and 73.8% of

Table 2: Severity, outcome, gender, and age distribution in ischemic stroke

Age (Years)	Gender	NIHSS score (mean)			p-value	BARTHELINDEX (mean)			p-value
		Mild	Moderate	Severe		GF	MD	SD	
20–30	Male	3	0	0	**0.013**	62.3	0	0	**0.015**
	Female	2	0	0		95	0	0	
31–40	Male	3	0	0	0.544	92.3	0	0	0.121
	Female	3.2	12	0		93	75	0	
41–50	Male	3	8	16	0.759	91.67	62.5	45	0.199
	Female	2	0	0		92.5	0	0	
51–60	Male	2.86	9.714	16.8	0.683	88.125	64.28	45	0.077
	Female	3	7.5	0		91.67	70	0	
61–70	Male	3.33	10.5	20	**0.0001**	90	65	30	**0.009**
	Female	2.5	9.67	19.33		91.25	71	45	
>70	Male	2	10.8	20.28	**0.00008**	93	60	45	**0.01**
	Female	3	10.4	20		82.5	67.5	47.5	

GF: Good function, MD: Moderate disability, SD: Severe disability

Table 3: The relative risk of risk factors in terms of severity and outcome

Risk factor	With risk factor			Without risk factor			RR	With risk factor					Without risk factor					RR
	M	Mo	S	M	Mo	S		GF	MD	SD	BR	D	GF	MD	SD	BR	D	
Hypertension	10	25	20	31	8	6	**1.2**	9	20	11	3	12	31	8	2	3	1	**1.2**
Diabetes mellitus	5	14	21	36	19	5	0.67	5	13	10	4	8	35	15	3	2	5	0.67
Smoking	8	9	17	33	24	9	0.52	8	9	5	3	9	32	19	8	3	4	0.52
Alcohol intake	3	8	15	38	25	11	0.35	4	8	3	2	9	36	20	10	4	4	0.35
Dyslipidemia	4	13	6	37	20	20	0.3	4	12	3	2	2	36	16	10	4	11	0.3
Heart disease	2	7	4	39	26	22	0.15	2	4	3	2	2	38	24	10	4	11	0.15
Tia	6	2	2	35	31	24	0.11	6	2	0	1	1	34	26	13	5	12	0.11
Migraine	5	1	0	36	32	26	0.06	5	1	0	0	0	35	27	13	6	13	0.06
Hypercoagulable states	5	1	0	36	32	26	0.06	5	1	0	0	0	35	27	13	6	13	0.06
Hormone therapy	2	1	0	39	32	26	0.03	1	1	0	0	1	39	27	13	6	12	0.03
Family history	1	0	1	40	33	25	0.02	1	0	0	1	0	39	28	13	5	13	0.02

M: Mild, Mo: Moderate, S: Severe, GF: Good function, MD: Moderate disability, SD: Severe disability, BR: Bedridden, D; Death, RR: Relative risk

patients < 80 years were discharged with a modified rank in the score of ≤2 after ischemic stroke [16].

Among 100 patients, 55 had hypertension and the relative risk of hypertension was found to be 1.22, indicating hypertension is the most predominant risk factor and there was an association between hypertension and the incidence of ischemic stroke. A similar observation was found in the previous studies, that is, the study by Renjen *et al*. showed 56.9% of ischemic stroke patients have hypertension [17] and the study by Dalal showed about 88.5% of the patients have hypertension [18]. In our study, we found that patients with hypertension had a moderate stroke and moderate disability. The relative risk of all the risk factors is depicted in Table 3. The risk factors observed in ischemic stroke patients were represented in Fig. 2. There was a statistically (p=0.00) significant difference between the patients with no risk factor, single, and multiple risk factors with respect to the NIHSS score. There was a statistically (p=0.00) significant difference between the patients with no risk factor, single, and multiple risk factors with respect to the Barthel index score. There was no statistically (p=0.504) significant difference in severity between the patients with no risk factor, single, and multiple risk factors. There was no statistically (p=0.32) significant difference in outcome between the patients with no risk factor, single, and multiple risk factors.

Among 100 patients in the study, 40% of the patients had diabetes mellitus which is higher when compared to other studies. The relative risk of diabetes was 0.67 which demonstrates that there was no association between the diabetes and incidence of stroke and it was found that patients with diabetes mellitus had severe strokes and moderate disabilities this result differs from the study by Nayak *et al*. which showed that diabetes increases the risk of dependent/expired outcomes in acute ischemic stroke patients [19].

In the present study, 34% of the patients had a history of smoking which is comparable with a study by Sylaja *et al*. in which 32.2% of the patients with ischemic stroke had a history of smoking. The relative risk of smoking was 0.52, demonstrating that there was no association between smoking and ischemic stroke. This differs from the findings in the study by Lee *et al*., showed that smoking was independently associated with severe stroke [20]. In our study, it was noted that smokers had a severe stroke and poor prognosis which is similar to the study by Ovbiagele *et al*. showed that current or recent smokers experience poorer functional outcomes than non-smokers 3 months after acute ischemic stroke [21].

Among 100 patients, 26 had a history of alcohol consumption. It is lower when compared to a study by Sylaja *et al*. [11]. The relative risk of alcohol consumption was found to be 0.35. It was found that patients with alcohol intake had severe strokes and moderate disabilities. The previous studies did not show a strong association between alcohol consumption and functional outcome after stroke [22,23].

In the present study, 23% of patients had dyslipidemia which is more when compared to a study by Nayak *et al*. was 18% [19]. The role of dyslipidemia in the pathogenesis of cerebrovascular diseases is less certain than for CAD, a more consistent association has been noted with low, HDL cholesterol, and high total cholesterol to HDL cholesterol ratio than with total cholesterol, low-density lipoprotein cholesterol, and triglycerides [24]. The relative risk of dyslipidemia was 0.3, indicating that there was no association between dyslipidemia and stroke.

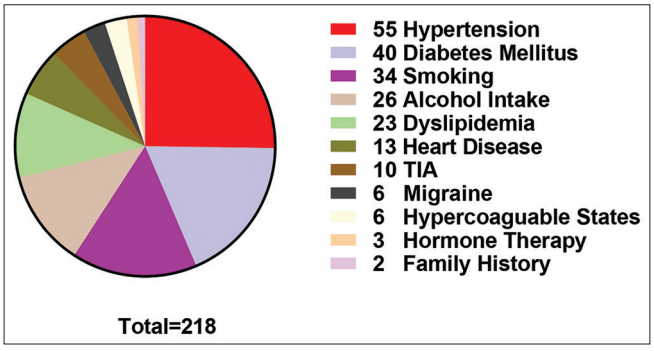

Fig. 2: Risk factors observed in ischemic stroke patients

In the present study out of 100 patients, 13 had heart disease, 10 had a history of TIA and six patients had migraines, five of them had mild strokes, and one of them had moderate strokes differs from the results of population-based studies and prospective studies which consistently reported a two-fold increased risk of ischemic stroke in patients with overall migraine [25]. In the present study, three out of 100 patients had a history of using oral contraceptives pills. In which two of them are having migraine as corisk factor differs to the findings of the study by Champaloux *et al*., the joint effect of combined hormonal contraceptives and migraine with aura was associated with a 6-fold increased risk of ischemic stroke compared with neither risk factor [26]. In the present study, six patients had hypercoagulable states, out of them five had elevated homocysteine levels and one had protein C deficiency. All of these patients were < 45 years of age and noted mild stroke and good functional outcome, these findings differ from the findings in the study by Shi *et al*. in which elevated homocysteine levels in the acute phase of an ischemic stroke can lead to mortality, especially in stroke patients with the large-vessel atherosclerosis subtype [27].

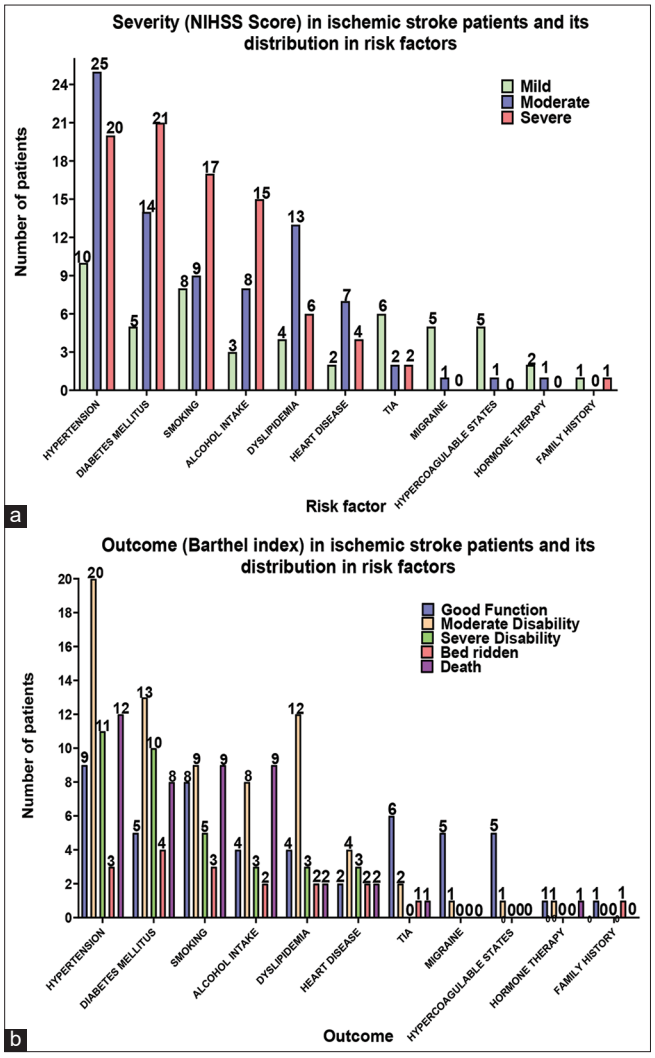

Fig. 3: (a) Severity (NIHSS Score) in ischemic stroke patients and its distribution in risk factors. (b) Outcome (Barthel index) in ischemic stroke patients and its distribution in risk factors

The 20–30 (p=0.0520), 31–40 (p=0.0144), and 41–50 (p=0.0315) age groups show a statistically significant reduction of severity (NIHSS Score) with 61–70 age group and also there was a statistically (p=0.0499) significant reduction between age group 31–40 and >70 of Severity (NIHSS Score). The 20–30 age group shows a statistically significant reduction with respect to outcome (Barthel index) with the 61–70 age group and 70 age group (Table 4). The severity (NIHSS Score) in ischemic stroke patients' distribution of risk factors and the outcome (Barthel index) in ischemic stroke patients and its distribution in risk factors is illustrated in Fig. 3. The severity of ischemic stroke in patients with no risk factor, single, and multiple risk factors and outcome in patients with no risk factor, single, and multiple risk factors are represented in Fig. 4. Regression analysis of risk factors and severity of stroke based on NIHSS score and risk factors and outcome of stroke based on Barthel index score are depicted in Table 5.

DISCUSSION

The impact of risk factors with respect to severity and outcome of patients was analysed. The 61 were male and 39 were female in the study. The severity of the ischemic was more in the male patients when compared with the female patients. The main risk factors for stroke as per the WHO were high blood pressure, tobacco use, physical inactivity, unhealthy diet, use of alcohol, atrial fibrillation, raised blood lipid levels, obesity, genetic disposition, stress, and depression [28]. In our study, we have explored a greater number of risk factors that include age, sex, diabetes, heart disease, migraine, family history of stroke, dyslipidemia, hormonal replacement, and TIA.

We observed that the increase in the age of the patients leads to increase in the severity and poor prognosis. The patients of age 20–30 years showed mild stroke and good function whereas patients of

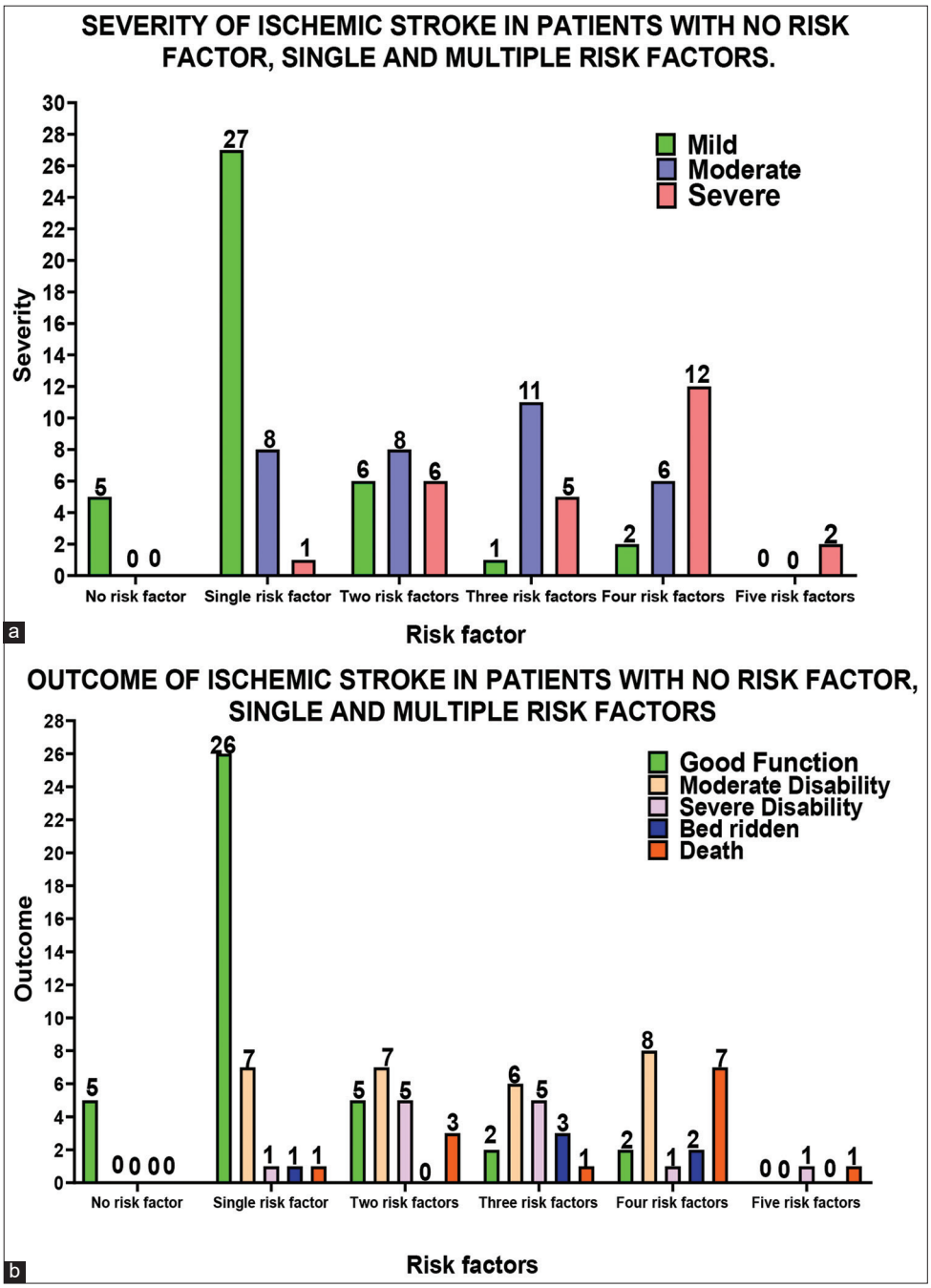

Fig. 4: (a) Severity of ischemic stroke in patients with no risk factor, single, and multiple risk factors. (b) Outcome of ischemic stroke in patients with no risk factor, single, and multiple risk factors

Table 4: Age-wise severity and outcome assessment

Age (Years)	Severity (NIHSS Score) (p-value)						Outcome (Barthel index) (p-value)					
	20–30	**31–40**	**41–50**	**51–60**	**61–70**	**>70**	**20–30**	**31–40**	**41–50**	**51–60**	**61–70**	**>70**
20–30	-	0.9786	0.9117	0.3301	**0.0520**	0.0910	-	0.9989	0.6588	0.4302	0.0875	**0.0534**
31–40	0.9938	-	0.9987	0.3665	**0.0144**	**0.0402**	0.9997	-	0.7307	0.3422	**0.0175**	**0.0069**
41–50	0.9668	0.9987	-	0.5480	**0.0315**	0.0800	0.7933	0.7307	-	0.9939	0.2797	0.1503
51–60	0.5358	0.4546	0.6538	-	0.1673	0.4566	0.6556	0.4188	0.9969	-	0.2577	0.1002
61–70	0.0897	0.0174	0.0388	0.1695	-	0.9798	0.1475	**0.0206**	0.3448	0.2577	-	0.9914
>70	0.1588	0.0499	0.1013	0.4625	0.9798	-	0.0888	**0.0080**	0.1848	0.0997	0.9912	-

Table 5: Regression analysis of risk factors and severity of stroke based on NIHSS score and risk factors and outcome of stroke based on Barthel index score

Risk factors	Severity	Outcome
	p-value	**p-value**
Age	0.0031	0.0002
Sex	0.9174	0.551
Hypertension	0.0033	0.0042
Diabetes	0.000000716	0.003
Smoking	0.0620	0.05
Alcohol	0.0271	0.001
Hypercoagulable states	0.0813	0.166
Heart disease	0.2418	0.039
Migraine	0.3331	0.80
Family history of stroke	0.6997	0.52
Dyslipidemia	0.6627	0.88
Hormonal replacement	0.8721	0.08
TIA	0.6270	0.57

age group 61–70 years and >70 years showed severe stroke and poor prognosis.

Out of 100 patients, 26 patients noted severe stroke. Although the relative risk of diabetes mellitus was found to be a little lower for diabetes, the severity and poor prognosis was observed in the patients with risk factor diabetes mellitus.

In our study, patients without risk factors and single risk factors had shown mild stroke and good function and patients with five risk factors showed severe stroke and poor prognosis. The severity and poor prognosis were increased with an increase in a number of risk factors indicating that the presence of several risk factors has an impact on both the severity and outcome of the stroke.

The hypertension was the highest noted single risk factor in the patients. Among the patients with two risk factors, the highest noted combination was hypertension and diabetes mellitus. Hypertension, diabetes mellitus, and dyslipidemia were the highest noted three risk factors combination in the patients. Among the patients with four risk factors, the highest noted combination was hypertension, diabetes mellitus, smoking, and alcohol intake. Hypertension was the most common risk factor noted among the single and multiple risk factors. High blood pressure is common in acute stroke and is independently associated with a poor prognosis [29].

In the present study, patients with severe stroke (NIHSS score >15) had poor functional outcomes when compared to those with NIHSS score of <15 at the time of admission proves that the NIHSS score was found to be a good predictor of functional outcome in patients with ischemic stroke [30]. This finding was similar to the findings of Shi *et al*. showed that the baseline NIH stroke scale is strongly associated with functional outcomes after 1 week of acute ischemic stroke [27]. Our study had limitations that include: It was conducted in a small group of patients, there were confounding factors in the present study, and long-term follow-up of patients was not done.

CONCLUSION

Hypertension is the most prevalent risk factor in the present study. As per our study findings, hypertension, diabetes mellitus, a history of smoking, and a history of alcohol intake were the preventable risk factors leading to severe stroke and poor functional outcome. Ischemic stroke was more prevalent in the male sex and patients with multiple risk factors had severe stroke and poor functional outcome when compared to the patients with single or no risk factors. Patients with severe stroke based on NIHSS score had poor functional outcome. Further studies involving multiple centers and a greater number of patients are required to substantiate the results of the present study.

AUTHORS CONTRIBUTION

Dr. K Chandra Shekar played a crucial role in developing the project's conceptual framework, analyzing data, and making significant contributions to manuscript preparation and review. Ms. Hima Sree Polisetti played a pivotal role in shaping the project's direction, contributing innovative ideas, conducting comprehensive research, and performing data analysis. In addition, she made significant contributions to the manuscript's preparation and organization. Dr. K Karthikeya contributed innovative ideas in the design phase, conducted a literature search, employed techniques to gather study information, and played a significant role in manuscript editing. Dr. K R Vinay Rajan made significant contributions to the research design, experimental protocols, and project structure. He also played a key role in formulating research questions, performing data analysis, and manuscript review.

CONFLICTS OF INTERESTS

The authors declare that there were no conflicts of interest in this research.

AUTHORS FUNDING

Nil.

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