(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 6, Issue 6 , Page No: 155-164
November-December 2023

IJMSCR

A Study Of Dwi And Flair Mismatch In Acute Ischemic Stroke In A Teritary Care Hospital In Andhra Pradesh

[1]Dr. Kristudasu Palaparthi, [2]Dr.T. Sikindar Mohan, [3]Dr. Fahima Begum
[1,3]Assistant Professor, [2] Associate Professor,
Department of General Medicine,
[1,3]Guntur Medical College, Guntur, Andhra Pradesh
[2]Government Medical College, Eluru, Andhra Pradesh

***Corresponding Author:**
Dr. Kristudasu Palaparthi
Assistant Professor, Department of General Medicine,
Guntur Medical College, Guntur, Andhra Pradesh

Type of Publication: Original Research Paper
Conflicts of Interest: Nil

Abstract

Background: Stroke is the second-leading global cause of death behind heart disease in 2013 and is a major cause of permanent disability. The burden of stroke in terms of mortality, morbidity and disability are increasing across the world. Hence the present study was done to identify DWI and FLAIR mismatch in acute ischemic stroke

Methodology: A hospital based observational study was carried out over a period of 12 months among 108 Acute ischemic stroke patients confirmed by MRI, attending the neurology department of Ramesh Cardiac and Multispecialty Pvt Ltd.

Results: A total of 108 participants were included in the study. The mean age was 60.29 ± 14.27 years. Males (61.11%) were predominant. Around 75% of the study population had history of Hypertension,50.93% had Diabetes and 17.59% had hypercholesterolemia as history.

Majority (71.30%) of the participants had middle cerebral artery occlusion. Around 79.63% of eligible participants were thrombolysed. The loading doses of anti-platelets and stains were administered in 20.37% of the participants. In Around 95.29% of the patients, the time from the onset of symptom to Emergency Room time was <4.5 hours were flair negative, and 4.71% of participants were flair positive. Around 38.46% of the patients the time from the onset of symptom to Emergency Room (ER) time was between 4.51 to 9 hours and were flair negative whereas 61.54% of participants were flair positive. The time from the onset of symptom to Emergency Room (ER) time was > 9 hours.

Conclusion: It was observed that most of the patients with acute ischemic stroke were having flair positivity outside the 4.5-hour window.

Keywords: Acute Ischemic Stroke (AIS), DWI (Diffusion-weighted imaging), FLAIR (Fluid-attenuated inversion recovery), WUS (Wake- up stroke), CT (Computerized tomography), MRI (Magnetic resonance imaging), Emergency Room (ER), Neurological Disorders and Stroke (NINDS) and European Cooperative Acute Stroke Study 3 (ECASS3).

Introduction

Worldwide, stroke is the second leading cause of death .[1] Stroke is defined as a neurological deficit attributed to an acute focal injury of the central nervous system by a vascular cause including cerebral infarction, intracerebral haemorrhage, and

subarachnoid hemorrhage.[2] Among all cases of stroke, 87% are of ischemic stroke.[3]

Acute ischemic stroke occurs when a blood vessel is obstructed, leading to an irreversible brain damage and subsequent focal neurological deficits.[4] The strongest risk factors for the early onset of ischemic stroke are atrial fibrillation, cardiovascular diseases, and Diabetes Mellitus.[5]

Thrombolytic therapy is based on the hypothesis that recanalization of the occluded vessels is required for salvageable of ischemic penumbra. Hence, in the treatment of AIS, recanalization is an important indicator of efficacy. An ischemic stroke develops when there is interrupted cerebral blood flow to an area of the brain. It accounts for approximately 80% to 88% of all stroke. Ischemic stroke may result from large-artery atherosclerotic disease resulting in stenosis or occlusion, small vessel or penetrating artery disease (lacunes), cardiogenic or, non-atherosclerotic vasculopathies, hypercoagulable disorders and infarcts of undetermined causes. If the patient meets appropriate criteria, intravenous administration of recombinant tissue plasminogen activator (rtPA) remains the only proven intervention for emergency management of acute ischemic stroke and the only approved therapy for acute ischemic stroke by the FDA. A strong correlation has been shown between arterial recanalization and neurological improvement in acute cerebral ischemia. Understanding how baseline clinical, biological, and imaging variables impact outcome is critical for the subsequent management of patients with acute ischemic stroke. Intravenous thrombolytic therapy rtPA (alteplase) is recommended within 4.5 hours from onset of ischemic symptoms, adhering to the eligibility criteria and therapeutic regimen provided by the National Institute of Neurological Disorders and Stroke (NINDS) and European Cooperative Acute Stroke Study 3 (ECASS3). There are different imaging modalities for the selection of patients for reperfusion therapy [unknown time because of sleep and aphasia and no eye witness].

The onset time of the ischemic event can be indirectly estimated through diffusion-weighted imaging-fluid attenuated inversion recovery [DWI - FLAIR] mismatch concept.[6]

The only evidence-based therapeutic option for improving the outcomes of patients with acute ischemic stroke is the intravenous tissue plasminogen activator.[7] There is a clear benefit when the ischemic stroke patients are treated with intravenous thrombolysis within 4.5 hours of symptom onset.[8,9]

An estimated 25% of ischemic strokes occur during sleep, which means that this large group of patients are precluded from thrombolysis in earlier trials. The risk of harm exceeds potential benefit if intravenous thrombolysis is administered later than 4.5 hours after the onset of symptoms.[10] The DWI-FLAIR mismatch concept is mostly used to identify the patients presenting within 4.5 hours of the ischemic event with a high positive predictive value of 83-87%.[11]The major complication associated with thrombolysis is the intracranial haemorrhage.[12] Advanced age, high blood pressure, diabetes mellitus and stroke severity are the factors influencing the risk of haemorrhage.[13] The practical challenge for the physicians is to understand which imaging technique is to implement and how to optimally use them.

The time urgency for evaluation of patients and the complexity of acute stroke are the factors that influence the choice of imaging techniques.[14]The exact time of symptoms onset is unknown in a large population of patients with ischemic stroke. Around 25% of patients wake from sleep with a neurological deficit and is called wake upstroke,[15] and a patient who are aphasic and no eye witness. According to the present guidelines, the last documented time, the patient was known to be asymptomatic is defined as the symptom onset.[16] As a result, intravenous thrombolysis treatment is precluded in wake-up stroke patients.[17] Selection of optimal treatment, improved survival rate and reduced disability rate can be achieved through an accurate assessment of the progress of ischemic stroke.[18–20]The present study was conducted to study the mismatch of DWI and FLAIR in Acute Ischemic Stroke in various time windows.

Objectives:

To study the risk factors of acute ischemic stroke.

To study for mismatch in DWI and FLAIR IN MRI in all patients with Acute Ischemic Stroke

To estimate the possible time of thrombolysis in wake-up stroke patients within 9

hours of onset.

Volume 6, Issue 6; November-December 2023; Page No 155-164

Methodology:

Study Design: Hospital based Observational study

Study setting: Department of Neurology, Ramesh Cardiac Multispecialty Hospital Pvt Ltd,

Study population: Acute ischemic stroke patients confirmed by MRI, attending the

Neurology department of Ramesh Cardiac and Multispecialty Pvt Ltd.

Sample size: A total of 108 patients admitted with acute ischemic stroke In Ramesh hospital

for 1 year (January 2019 to December 2019 for a period of 1 year.)

Sampling method: All the eligible subjects were recruited into the study consecutively by

convenient sampling till the sample size is reached.

Study duration: The data collection for the study was done between January 2021 to

December 2021 for a period of 1 year.

Inclusion Criteria:

1. All Acute Ischemic stroke patients with age above 18 years. This will include both
2. wake-up strokes and stroke with unknown time of onset.
3. Patients who gave consent and willing to participate in the study
4. Both in patients and out patients were enrolled

Exclusion criteria:

Patients below 18 years of age

Ethical considerations: Study was approved by institutional human ethics committee.

Informed written consent was obtained from all the study participants.The risks and benefits involved in the study and the voluntary nature of participation were explained to the participants before obtaining consent. Confidentiality of the study participants was maintained.

Data collection tools: All the relevant parameters were documented in a structured study proforma.

Methodology:

This is a hospital based observational study, carried out in Department of Neurology of a tertiary care hospital in Andhra Pradesh over a period of 12 months. The study subjects were enrolled after informed consent.

DWI-FLAIR mismatch:

Description:

The diffusion-weighted imaging and fluid attenuated inversion recovery mismatch is a magnetic resonance imaging technique in which the time of the ischemic event is indirectly estimated. The DWI-FLAIR mismatch concept is mostly used to identify the patients presenting within 4-5 hours of the ischemic event with a high positive predictive value of 83-87%.[6,11]

The patients with acute ischemic lesions that are visible on DWI but not in FLAIR images i.e DWI_FLAIR mismatch is likely to be within the therapeutic window (3- 4.5 hours from stroke onset) for thrombolysis.[21] There is a decrease in DWI-FLAIR mismatch as time passes after the stroke onset.[22,23]

The FLAIR signal intensity can be correlated with the time from stroke onset and MRI.

In **clear onset stroke patients (COS),** the time of stroke occurrence is known. Therefore, the serial changes of DWI-FLAIR mismatch in clear onset stroke patients may be used as a time scale for estimating the stroke onset in **unclear stroke onset patients (UnCOS).**

Rationale for TIME DURATION 9 HOURS: Most of the stroke patients will get DWI and FLAIR Positivity by this time so there is a chance for mismatch within this time. [Mismatch can be seen up to 24 hours in a very few numbers of patients]. These was based on two studies by **Thomalla G, et al**[6,24] study. But in the present study it was extended up to 9 hours {**Based on EXTEND Trial**}.

Thrombolysed were considered as primary outcome variable. Difference time (symptom to ER time) (in hours), Combination of DWI positive, flair negative and duration were considered as Secondary outcome variables.

Statistical Analysis:

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency, and proportion for categorical variables.

Volume 6, Issue 6; November-December 2023; Page No 155-164

Non normally distributed quantitative variables were summarized by median and interquartile range (IQR). Categorical outcomes were compared between study groups using Mann-Whitney test. P value < 0.05 and <0.001 was considered statistically significant.

Data was entered into MS Excel spread sheet and analysed using IBM SPSS version 22

Results:

A total of 108 subjects were included in the final analysis.

The mean age was 60.29±14.27 years, Minimum age was 22 years, and the maximum was 87 years in the study population.

Among the study population, 9(8.33%) participants were aged up to 49 years, 45(41.67%) were aged between 41 to 60 years, 49(45.37%) were aged between 61 to 80 years and remaining 5(4.63%) were aged more than 80 years.

Among the study population, 66(61.11%) participants were male and remaining 42(38.49%) participants were female.

Among the study population, 81(75%) participants had a past **history** of hypertension, 55(50.93%) had diabetes, 19(17.59%) had hypercholesterolemia, 20(18.69%) had an old stroke, and 13(12.04%) had Atrial Fibrillation. Among the study population, 45 (41.67%) participants had a combination of hypertension Vs diabetes.

Among the study population 89(82.41%) participants had DWI Positive, Flair Negative and 19(17.59%) participants had DWI Positive, Flair Positive.

Among the study population, 4(3.7 %) participants had Internal carotid artery occlusion,7(6.48%) had anterior cerebral artery occlusion, 77(71.30%) had middle cerebral artery occlusion, 17(15.74%) had Posterior cerebral artery occlusion and 8)7.41%) had extracranial occlusion.

Among the study population, 2(1.85%) participants reason for onset time was night time sleep, and 98.15% onset time was not known [Altered sensorium].

Among the study population, 86(79.6%) were thrombolysed whereas thrombolysis not possible among 20.4%.

The mean NIHSS score at the time of admission was 8.78 ± 5.34. The minimum score was 2 and maximum was 21 in the study population.

Among the people with symptom to ER time, 85 91.80%) participants were up to 4.5 hours, 8(8.64 %) participants were 4.51 to 6 hours, and 5 (5.4%) participants were 6.1 to 9 hours and 10 [10.8 %] above 9 hours.

Among people with symptom to ER time <4.5 hours, 81 (95.29%) participants had flair negative and 4 (4.71%) participants had flair positive. Among people with symptom to ER time 4.51 to 6 hours, 3 (37.5%) participants had flair negative, and 5 (62.5%) participants had flair positive. Among people with symptom to ER time 6.01 to 9 hours, 2 (40%) participants had flair negative, and 3 (60%) participants had flair positive. Among people with symptom to ER time > 9 hours, 3 (30%) participants had flair negative, and 7 (70%) participants had flair positive.

Among people with lesion volume<=20, 73 (82.02%) participants had flair negative and 16 (17.98%) participants had flair positive.

Among the people with thrombolysed, the median MRS score at 3rd month was 1 (IQR 1, 2) and 2 (IQR 1.50, 3) it was people without thrombolysed. The difference between two groups was statistically significant (P value 0.045). Around 84 patients have no significant disability; able to carry out all pre-stroke activities. Remaining 24 patients has slight disability; unable to carry out all pre-stroke activities but able to look after self without daily help.

In this comparative table age group is comparable in both groups and predominantly males in both groups. Risk factors in the Flair negative group was hypertension 66(81.48%), Diabetes mellitus in 43(78.80%). The combination of hypertension and diabetes was observed in 34(74.56%), old ischemic stroke 16(80%) whereas in flair positive group was hypertension in 15 (18.52%), Diabetes mellitus in 12(21.82%) The combination of hypertension and diabetes was observed in 11(24.44%) old ischemic stroke 4(20%).

NIHSS score was comparable in both groups and commonly occluded vessel is middle cerebral artery in both groups and MRS at 3 months is better in flair negative group who were Thrombolysed. Among

Volume 6, Issue 6; November-December 2023; Page No 155-164

people with symptom to ER time <4.5 hours, 95.3% participants had flair negativity and 4.71% participants had flair positivity. Among people with symptom to ER time 4.5 to 9 hours, 38.46% participants had flair negativity and 61.5% participants had flair positivity. Among patients with symptom to ER time > 9 hours, 30% participants had flair negativity and 70% participants had flair positivity. The difference in the proportion of all DWI positive across symptom to ER time was statistically significant (P value <0.001).

Table 1 : Comparison of symptom to ER time between DWI positive, flair negative (N=108)

Symptoms to ER_Time_4 Groups	All DWI Positive	
	Flair Negative	Flair Positive
<=4.5 (N=85)	81 (95.29%)	4 (4.71%)
4.51 To 6 (N=8)	3 (37.5%)	5 (62.5%)
6.01 To 9 (N=5)	2 (40%)	3 (60%)
>9 (N=10)	3 (30%)	7 (70%)
Comparison of lesion volume between all DWI positive (N=108)		
Lesion volume	**Flair Negative**	**Flair Positive**
<=20 (N=89)	73 (82.02%)	16 (17.98%)
>20 (N=19)	16 (84.21%)	3 (15.79%)

Table 2 : Comparison of median Modified Rankin Score (mRS) at 3 months between thrombolysed among flair negative (N=108)

Thrombolysed	MRS score at 3 months Median (IQR)	Mann Whitney (P value)
Yes (N=84)	1 (1, 2)	0.045
No (N=24)	2 (1.50, 3)	

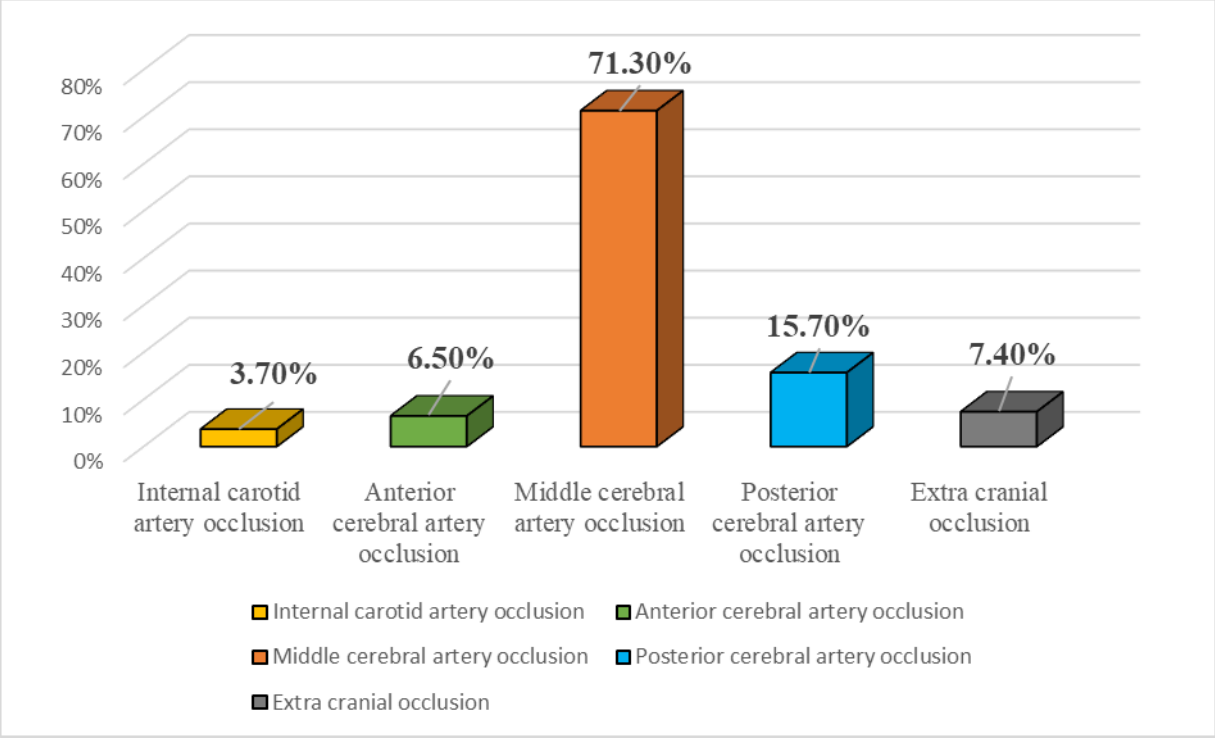
Table 3 : Comparison of parameter between flair negative and flair positive

PARAMETER	FLAIR NEGATIVE	FLAIR POSITIVE	P VALUE
AGE(MEAN)	60.26	60.42	0.964
MALE	54(81.82%)	12(18.8%)	0.840
SYSTEMIC HYPERTENSION	66(81.48%)	15(18.52%)	0.777
DIABETES MELLITUS	43(78.80%)	12(21.82%)	0.240
HYPERTENSION WITH DIABETES	34(74.56%)	11(24.44%)	0.114

Volume 6, Issue 6; November-December 2023; Page No 155-164

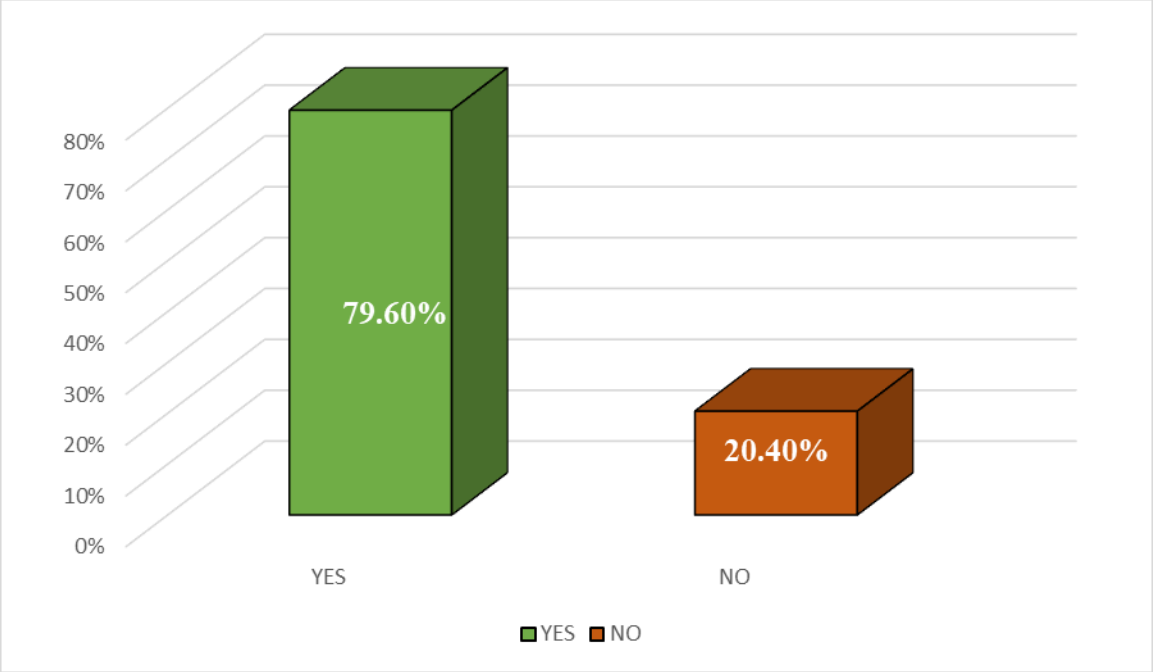
OLD ISCHEMIC STROKE	16(80%)	4(20%)	0.752
NIHSS AT ADMISSION	7	6	0.160
VESSELS OCCULDED ON MRI -ICA	1(25%)	3(75%)	0.017
VESSLES OCCULDED ON MRI-ACA	3(42.86%)	4(57.14%)	0.018
VESSLES OCCULDED ON MRI-MCA	69(89.61%)	8(10.39%)	0.002
VESSLES OCCULDED ON MRI-PCA	15(88.24%)	2(11.76%)	0.732
VESSLES OCCULDED ON MRI- OTHERS [EXTRA CRAINAL]	4(50%)	4(50%)	0.031
DWI VOLUME	15	15	0.470
MRS SCORE AT THREE MONTHS	1	2	0.012
SYMPTOMS TO ER TIME < 4.5 HRS	95.3%	4.7%	<0.001
SYMPTOMS TO ER TIME 4.5 HRS TO 9 HRS	38.4%	61.5%	<0.001
SYMPTOMS TO ER TIME >9 HRS	30%	70%	<0.001

Figure 1 : Distribution of study population based on type of occlusion (N=108)



Volume 6, Issue 6; November-December 2023; Page No 155-164

Figure 2 : Distribution of study population based on of thrombolysis(N=108)



Discussion:

Stroke is the second-leading global cause of death behind heart disease and is a major cause of permanent disability. The burden of stroke in terms of mortality, morbidity and disability is increasing across the world. The present study was conducted to identify DWI and FLAIR mismatch in acute ischemic stroke. A total of 108 participants were enrolled for the final analysis.

In the present study, the mean age was 60.29 ± 14.27 years. Whereas the mean age of study population was68.78 ± 13.62 years in a study done by **Yue Y et al**[25] and 64.4 ± 13.2 years in a study done by **Song Let al**[26].

In the present study, 8.33% of the participants were aged up to 40 years, 41.67% were aged between 41 to 60 years, 45.37% were aged between 61 to 80 years, and 4.63% were aged more than 80 years. Minimum age was 22 years and maximum age was 87 years. Raghuvanshi S et al[69], conducted an observational non-interventional study in 175 participants in which 18.28% of the patients were aged between 20 to 40 years, 52.5% were aged between 41- 60 years, 28% were aged between 61 to 80 years, and 1.15% were aged above 80 years.

In the present study, majority of the participants were males with 61.11% and remaining females with 38.49%. Similar findings were observed in a study done by **Thomalla G et al**[21] where 56.7% were males and 43.3% were females. and in **Fang et al** 54.1% were males and 45.9% were females[27].

In the present study, history of hypertension, diabetes mellitus, hypercholesterolemia, old stroke, and Atrial Fibrillation was seen in 75%, 50.93%,17.59%, 18.69% and12.04% respectively. In a study done by **Raghuvanshi S et al**[28], hypertension, diabetes mellitus, hypercholesterolemia, old stroke, and Atrial Fibrillation were seen among 52.52%, 29.14%, 62.86%, 13.71% and 3.43% of the study population respectively. In a study done by **Aoki, J et al**[11] it was found that significantly less incidence of hypertension, atrial fibrillation, hyperlipidemia, diabetes mellitus and smoking seen in 18% patients, 14 %patients, 7% patients, 6% patients and 6 % patients respectively.

In a study done by **Jeong JY et al.**[29], hypertension, diabetes mellitus, hypercholesterolemia, old stroke, and Atrial Fibrillation were seen among 31%, 11%, 32% 10% and 13% of the study population respectively.

Volume 6, Issue 6; November-December 2023; Page No 155-164

In the present study, up to 4.5-hour group had flair negative in 95.3%, the 4.5 to 6-hour Group Flair Negative was seen in 37.5% and the 6 to 9-hour flair Negative was 40%. **Thomalla G et al[21],** performed a study in 120 participants in which 4.5 hours to 6 hours, flair negative is 56.60%. In a study done by **Emeriau, S et al.**[30] the 3to 4.5-hour flair Negative was 63.40%.

The types of occlusions in the study population were the Internal carotid artery occlusion or stenosis (atherosclerosis), anterior cerebral artery occlusion or stenosis (atherosclerosis),

middle cerebral artery occlusion or stenosis [atherosclerosis], Posterior cerebral artery occlusion or stenosis (atherosclerosis) and extra cranial occlusion or stenosis (atherosclerosis) with 3.7%, 6.48%, 71.30%, 15.74% and 7.41% respectively. **Jeong JY, et al[31]**, conducted a study in 50 participants in which the location of occlusion was anterior in 70%, posterior in 26% whereas, both anterior and posterior were observed in 4% of the participants. **kaul et al[32],** done a study in south India on risk factors and vascular lesion involvement in stroke showing MCA lesions were common in anterior circulation (53/142, 37.3%) followed by ICA (21/142, 14.8%) and ACA (6/142, 4.2%). In posterior circulation PCA (24/142, 16.9%) was frequently involved, followed by VA (18/142, 12.7%) and BA (6/142, 4.2%). Mixed arterial lesions were noted in 14/142 patients.

The mean NIHSS score in the present study was 8.78 ± 5.34. **Prasad J et al[33],** performed a prospective observational study in 26 patients in which 13.5 was the mean NIHSS score. In a population of 364 participants **Fink, JN et al[34]**, performed a study in which the mean NIHSS score in patients with known stroke onset was 7 whereas in those who woke with stroke was 5. **Thomalla, G et al[35]**, conducted a randomized, double-bind study in which the mean NIHSS score was 6 in the study participants.

Risk factor in the study Population was hypertension 75%, Diabetes mellitus 50.9 % The combination of hypertension and diabetes was observed in 41.67% of the participants. Hypercholesterolemia 17.6%, old ischemic stroke 18.7% and atrial fibrillation 12%.

Kaul et al 32done a study in south India on risk factors and vascular lesion involvement in stroke showing Hypertension (HTN), diabetes, alcohol, smoking, hyperlipidemia, and hyper homocysteinemia was present in 82%, 52%, 34%, 33%, 28%, and 23%, respectively.

In the present study, among people with onset of symptom to Emergency Room time <4.5 hours,95.29% of the participants had flair negative while 4.71% participants had flair positive. Among people with symptom to ER time 4.51 to 9 hours, 38.46% of participants had flair negative and remaining 61.54% participants had flair positive. Among people with symptom to ER time > 9 hours, 30% participants had flair negative and 70% participants had flair positive. In our study DWI FLAIR mismatch observed in [38.46%], the number is comparable to **G Thomalla[36]** study stroke with unknown time of symptom onset].

Conclusion:

In the present study, the group with symptom to ER time of up to 4.5 hours, 95.29% had flair negativity and 4.71% participants had flair positivity. Among people with symptom to ER time 4.51 to 9 hours, 38.46% of participants had flair negativity and 61.54% of participants had flair positivity. Whereas, among people with symptom to ER time > 9 hours, 30% of participants had flair negativity, and 70% of participants had flair positivity. Hence there is a possibility of extending the thrombolysis window beyond the present 4.5 hours based on MRI morphology.

References:

1. Musuka TD, Wilton SB, Traboulsi M, Hill MD. Diagnosis and management of acute ischemic stroke: Speed is critical. Cmaj. 2015;187(12):887–93.
2. Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJ, Culebras A, et al. An updated definition of stroke for the 21st century: A statement for healthcare professionals from the American heart association/American stroke association. Stroke. 2013;44(7):2064–89.
3. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, et al. Executive summary: Heart disease and stroke statistics-2013 update: A Report from the American Heart Association. Circulation. 2013;127(1):143–52.

Volume 6, Issue 6; November-December 2023; Page No 155-164

4. Bansal S, Sangha KS, Khatri P. Drug treatment of acute ischemic stroke. Am J Cardiovasc Drugs. 2013;13(1):57–69.
5. Kivioja R, Pietilä A, Martinez-Majander N, Gordin D, Havulinna AS, Salomaa V, et al. Risk factors for early-onset ischemic stroke: A case-control study. J Am Heart Assoc. 2018;7(21).
6. Thomalla G, Cheng B, Ebinger M, Hao Q, Tourdias T, Wu O, et al. DWI-FLAIR mismatch for the identification of patients with acute ischaemic stroke within 4·5 h of symptom onset (PRE-FLAIR): A multicentre observational study. Lancet Neurol. 2011;10(11):978–86.
7. Hasan TF, Rabinstein AA, Middlebrooks EH, Haranhalli N, Silliman SL, Meschia JF, et al. Diagnosis and Management of Acute Ischemic Stroke. Mayo Clin Proc. 2018;93(4):523–38.
8. Marler JR, Tilley BC, Lu M, Brott TG, Lyden PC, Grotta JC, et al. Early stroke treatment associated with better outcome: The NINDS rt-PA Stroke Study. Neurology. 2000;55(11):1649–55.
9. Bluhmki E, Chamorro Á, Dávalos A, Machnig T, Sauce C, Wahlgren N, et al. Stroke treatment with alteplase given 3·0-4·5 h after onset of acute ischaemic stroke (ECASS III): additional outcomes and subgroup analysis of a randomised controlled trial. Lancet Neurol. 2009;8(12):1095–102.
10. Sandercock P, Wardlaw JM, Lindley RI, Dennis M, Cohen G, Murray G, et al. The benefits and harms of intravenous thrombolysis with recombinant tissue plasminogen activator within 6 h of acute ischaemic stroke (the third international stroke trial [IST- 3]): A randomised controlled trial. Lancet. 2012;379(9834):2352–63.
11. Aoki J, Kimura K, Iguchi Y, Shibazaki K, Sakai K, Iwanaga T. FLAIR can estimate the onset time in acute ischemic stroke patients. J Neurol Sci. 2010;293(1–2):39–44.
12. Mishra NK, Davis SM, Kaste M, Lees KR. Comparison of outcomes following thrombolytic therapy among patients with prior stroke and diabetes in the Virtual International Stroke Trials Archive (VISTA). Diabetes Care. 2010;33(12):2531–7.
13. Zaheer Z, Robinson T, Mistri AK. Thrombolysis in acute ischaemic stroke: An update. Ther Adv Chronic Dis. 2011;2(2):119–31.
14. Wintermark M, Sanelli PC, Albers GW, Bello J, Derdeyn C, Hetts SW, et al. Imaging recommendations for acute stroke and transient ischemic attack patients: A joint statement by the American Society of Neuroradiology, the American College of Radiology, and the Society of Neurointerventional Surgery. Am J Neuroradiol. 2013;34(11).
15. Mackey J, Kleindorfer D, Sucharew H, Moomaw CJ, Kissela BM, Alwell K, et al. Population-based study of wake-up strokes. Neurology. 2011;76(19):1662–7.
16. Jauch EC, Saver JL, Adams HP, Bruno A, Connors JJB, Demaerschalk BM, et al. Guidelines for the early management of patients with acute ischemic stroke: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2013;44(3):870–947.
17. Odland A, Særvoll P, Advani R, Kurz MW, Kurz KD. Are the current MRI criteria using the DWI-FLAIR mismatch concept for selection of patients with wake-up stroke to thrombolysis excluding too many patients? Scand J Trauma Resusc Emerg Med. 2015;23(1):22.
18. Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, et al. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. N Engl J Med. 2018;378(8):708–18.
19. Healey JS, Oldgren J, Ezekowitz M, Zhu J, Pais P, Wang J, et al. Occurrence of death and stroke in patients in 47 countries 1 year after presenting with atrial fibrillation: a cohort study. Lancet. 2016;388(10050):1161–9.
20. Von Gadow N, Nikoubashman O, Freiherr J, Block F, Reich A, Fesl G, et al. Endovascular stroke treatment now and then - Procedural and clinical effectiveness and safety of different mechanical thrombectomy techniques over time. Quant Imaging Med Surg. 2017;7(1):1–7.
21. Thomalla G, Rossbach P, Rosenkranz M, Siemonsen S, Krützelmann A, Fiehler J, et al. Negative fluid-attenuated inversion recovery imaging identifies acute ischemic stroke at 3 hours or less. Ann Neurol. 2009;65(6):724–32.

Volume 6, Issue 6; November-December 2023; Page No 155-164

22. Song SS, Latour LL, Ritter CH, Wu O, Tighiouart M, Hernandez DA, et al. A pragmatic approach using magnetic resonance imaging to treat ischemic strokes of unknown onset time in a thrombolytic trial. Stroke. 2012;43(9):2331–5.
23. Petkova M, Rodrigo S, Lamy C, Oppenheim G, Touzé E, Mas JL, et al. MR imaging helps predict time from symptom onset in patients with acute stroke: Implications for patients with unknown onset time. Radiology. 2010;257(3):782–92.
24. Wouters A, Dupont P, Norrving B, Laage R, Thomalla G, Albers GW, et al. Prediction of Stroke Onset is Improved by Relative Fluid-Attenuated Inversion Recovery and Perfusion Imaging Compared to the Visual Diffusion-Weighted Imaging/Fluid- Attenuated Inversion Recovery Mismatch. Stroke. 2016;47(10):2559–64.
25. Yue Y hua, Li Z zhang, Hu L, Zhu X qiong, Xu X shen, Sun H xian, et al. Clinical characteristics and risk score for poor clinical outcome of acute ischemic stroke patients treated with intravenous thrombolysis therapy. Brain Behav. 2019;9(4):e01251.
26. Song L, Lyu C, Shen G, Guo T, Wang J, Wang W, et al. Application of FLAIR vascular hyperintensity-DWI mismatch in ischemic stroke depending on semi- quantitative dwi-alberta stroke program early CT score. Front Neurol. 2019;10(SEP):994.
27. Fang J, Yan W, Jiang GX, Li W, Cheng Q. Time interval between stroke onset and hospital arrival in acute ischemic stroke patients in Shanghai, China. Clin Neurol Neurosurg. 2011;113(2):85–8.
28. Raghuvanshi S. A Study of Clinical Profile and Subtypes of Acute Ischemic Stroke in a Tertiary Care Center. Int J Sci Study. 2016;4(5):128–31.
29. Jeong JY, Han SK, Shin DH, Na JU, Lee HJ, Choi PC, et al. Diffusion-weighted imaging–fluid-attenuated inversion recovery mismatch is associated with better neurologic response to intravenous thrombolytic therapy in acute ischemic stroke patients. Clin Exp Emerg Med. 2015;2(1):31–7.
30. Emeriau S, Serre I, Toubas O, Pombourcq F, Oppenheim C, Pierot L. Can diffusion-weighted imaging-fluid-attenuated inversion recovery mismatch (positive diffusion-weighted imaging/negative fluid-attenuated inversion recovery) at 3 tesla identify patients with stroke at <4.5 hours? Stroke. 2013;44(6):1647–51.
31. Jeong JY, Han SK, Shin DH, Na JU, Lee HJ, Choi PC, et al. Is There a Difference in the Effect of Thrombolytic Therapy according to the Presence of Diffusion-Weighted Imaging (DWI)-Fluid Attenuated Inversion Recovery (FLAIR) Mismatching in Patients with Acute Ischemic Stroke? J Korean Soc Emerg Med. 2015;26(3):225–31.
32. Ram R, Kaul S, Alladi S, Afshan J, Prabha T, Kohat A, et al. Risk factors, vascular lesion distribution, outcome and recurrence of strokes due to intracranial atherosclerosis: One year data from Hyderabad stroke registry. Ann Indian Acad Neurol. 2017;20(4):387–92.
33. Prasad Jagini S, I. S. Clinical profile of patients with acute ischemic stroke receiving intravenous thrombolysis (rtPA-alteplase). Int J Adv Med. 2018;5(1):164.
34. Fink JN, Kumar S, Horkan C, Linfante I, Selim MH, Caplan LR, et al. The stroke patient who woke up clinical and radiological features, including diffusion and perfusion MRI. Stroke. 2002;33(4):988–93.
35. Thomalla G, Boutitie F, Fiebach JB, Simonsen CZ, Nighoghossian N, Pedraza S, et al. Stroke with Unknown Time of Symptom Onset: Baseline Clinical and Magnetic Resonance Imaging Data of the First Thousand Patients in WAKE-UP (Efficacy and Safety of MRI-Based Thrombolysis in Wake-Up Stroke: A Randomized, Doubleblind, Placebo-Controlled Tria. Stroke. 2017;48(3):770–3.
36. Thomalla G, Boutitie F, Fiebach JB, Simonsen CZ, Pedraza S, Lemmens R, et al. Clinical characteristics of unknown symptom onset stroke patients with and without diffusion-weighted imaging and fluid-attenuated inversion recovery mismatch. Int J Stroke. 2018;13(1):66–73.

Volume 6, Issue 6; November-December 2023; Page No 155-164