

## Original Research Article

## Clinical audit of intravenous recombinant tissue plasminogen activator (r-tPA) recipients in ischemic stroke patients presenting at a tertiary Care hospital, in Islamabad Pakistan

Salman Mansoor<sup>1</sup>, Mujtaba Shahbaz<sup>2</sup>, Raja Farhat Shoaib<sup>3</sup>, Maimoona Siddiqui<sup>4</sup>

<sup>1</sup>FCPS Trainee Neurology, Department of Neurology, Shifa International Hospital, Islamabad, Pakistan

<sup>2</sup>Research Associate, Department of Neurology, Shifa International Hospital, Islamabad, Pakistan

<sup>3</sup>Consultant Stroke Medicine, Department of Neurology, Shifa International Hospital, Islamabad, Pakistan

<sup>4</sup>Consultant Neurologist, Department of Neurology, Shifa International Hospital, Islamabad, Pakistan

### \*Corresponding author

Dr Salman Mansoor

Email: [salmanmansoor.dr@gmail.com](mailto:salmanmansoor.dr@gmail.com)

**Abstract:** The objective of this clinical audit was to report initial experience with the use of intravenous recombinant tissue plasminogen activator (r-tPA) to treat acute ischemic stroke at a tertiary care hospital in Pakistan from the hospital's prospective stroke registry was taken for analysis. All patients with acute ischemic stroke treated with intravenous r-tPA from January 2015 to February 2016 were included in this audit. Time from stroke onset to arrival at the emergency department (ED), door to needle time, rates of symptomatic intracerebral hemorrhage (ICH), clinical outcomes at 2 and 24 hours as assessed by National Institute of Health Stroke Scale (NIHSS) scores were reported. Among the 312 patients admitted with ischemic stroke, 13 received intravenous r-tPA. Median time from stroke onset to arrival in emergency department was 80 minutes, and median door-to-needle time was 43 minutes. Median times for National Institutes of Health Stroke Scale (NIHSS) recorded at baseline, 2 hours post r-tPA, and 24 hours post r-tPA were 15, 11 and 7 respectively. No patient had symptomatic ICH at 24 hours. No patient received r-tPA 60 minutes after arrival. Rates of favorable outcomes were similar to the ones reported at other specialized centers, and there were no symptomatic ICH at our hospital. However only 13 patients out of a total of 312 were thrombolysed owing to delay in presentation to our facility. Identification and addressing factors and issues related to delay in presentation at a stroke facility equipped with intravenous r-tPA.

**Keywords:** Ischemic stroke, Intravenous Alteplase, Door to needle time, Pakistan.

### INTRODUCTION

Stroke poses a significant disease burden in Pakistani population. A community based survey conducted in Karachi concluded the prevalence of stroke to be 19.1% [1]. Thrombolytic therapy for acute ischemic stroke has been approached cautiously because there were high rates of intracerebral hemorrhage (ICH) in early clinical trials. This is an audit from our prospective stroke registry of intravenous r-tPA recipients with ischemic stroke. The objectives of this audit was to analyze the intravenous Alteplase administration at a tertiary care hospital with no prior experience in administering intravenous r-tPA and comparing our services with recommended international standards. The main outcomes were measured.

### MATERIALS & METHODS

This clinical audit is from the ongoing prospective stroke registry at a tertiary care hospital in Islamabad, Pakistan. This is a 1 year data of 13 patients

with stroke who received intravenous r-tPA in the emergency department and stroke unit, during the period from 13th January 2015 to 21st February 2016.

Intravenous Alteplase in a dose of 0.9mg/kg was used in these patients with initial 10% of the dose given in 1 minute and the rest over 1 hour.

Inclusion criteria included all those with clinical presentation consistent with acute ischemic stroke, within 3 hours of hospital arrival, and a CT scan brain negative for any sort of intracranial bleed.

Exclusion criteria included patients who didn't consent to intravenous r-tPA administration, intracranial bleed on the initial CT-scan brain, high blood pressures in the ranges above 185/110mmHg not responsive to antihypertensives, those on anticoagulation with a deranged INR >1.8, previously a high modified Rankin score of >3 with multiple co-morbidities, low platelet count <100,000, National Institute of Health Stroke

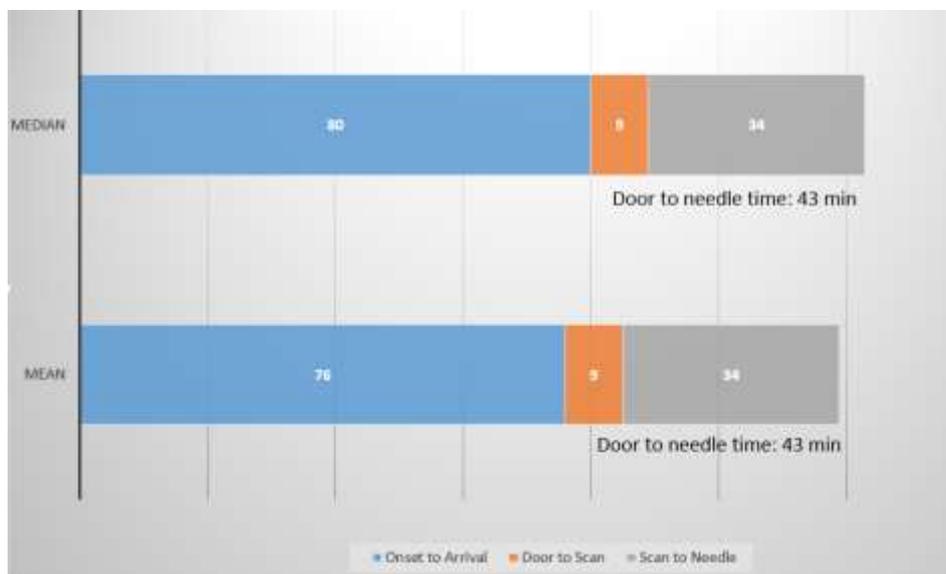
Scale (NIHSS) score of >25, improving neurological deficit, seizures at onset, a recent surgery, active bleeding, history of hemorrhagic stroke, and pregnancy.

Collected information was summarized for demographic variables, territory of stroke with the help of clinical presentation, The quality parameters in this audit included: (1) Onset to arrival time (2) Door to needle time (3) Arrival to neuroimaging time, (4) Outcomes at 2 hours and 24 hours from baseline were measured by NIHSS and (5) Incidence of ICH by computed tomography (CT) scan brain. The data was entered and analyzed using SPSS version 20 software.

**RESULTS**

We received a total of 312 patients with ischemic stroke from January 2015 to February 2016. Out of these 13 ischemic stroke patients received

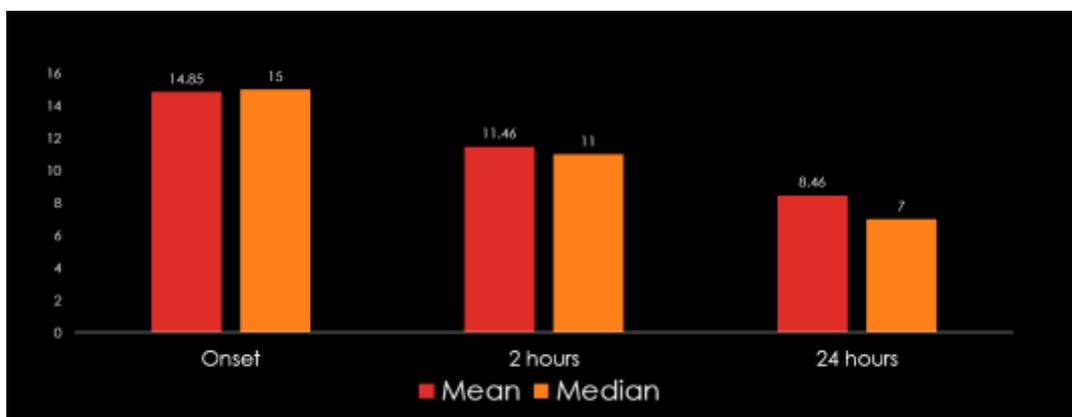
intravenous r-tPA there were 6 males (46.2%) and 7 females (53.8%). The mean age at presentation was 65 years (SD ± 13.76) with a median of 68 years. The age range varied from a minimum of 42 years to a maximum of 82 years. There were 8 patients who had left middle cerebral artery (MCA) stroke while 5 had right MCA stroke. The mean time to stroke symptoms onset to arrival in emergency department was 76 minutes (SD ± 41.129) and the median time was 80 minutes; the minimum time from symptom onset to arrival was 18 minutes to a maximum of 135 minutes. The mean time to CT scan brain plain was 9 minutes (SD ± 6.371) with minimum time to scan 3 minutes to the maximum time 25 minutes. The mean door to needle time for administration of r-tPa was 43 minutes (SD ± 11.927) and the median was also 43 minutes with the range from 20 minutes minimum to 60 minutes maximum. These are depicted in Figure 1.



**Fig-1: Door to needle time for administration in Stroke Patients**

The mean NIHSS at presentation was 14.85 (SD ± 5.289) with a median of 15. The minimum NIHSS was 6 and the maximum was 25. The NIHSS was checked subsequently at 2 hour and 24 hours intervals after receiving the r-tPa. The mean for NIHSS

2 hours after receiving r-tPa was 11.46 (SD ± 6.267) with a median score of 11.00; the range was from 2-23. The NIHSS at 24 hours was 8.46 (SD ± 6.118) with a median of 7.00; the range was from 0-19. These scores are shown in Figure 2.



**Fig-2: NIHSS presentation**

These differences in mean values were found statistically significant on the paired sample t-test with p-values of 0.042 and 0.002 respectively with a low degree of freedom due to the small number of cases.

## DISCUSSION

Despite the fact that our center only recently started administering r-tPA, we have been able to achieve very satisfactory goals in regards to the administration of r-tPA. We have been able to achieve a door to CT brain time of 9 minutes, in comparison to 60 minutes reported by Brewer *et al.* [2].

Moreover, every patient received r-tPA within 60 minutes after arrival, in comparison to a door-to-needle time of 97 minutes reported by Lau *et al.* [3] and 75 minutes reported Joshi *et al.* [4]. The fact that not a single patient had symptomatic intracerebral hemorrhage (ICH) (in comparison to ICH in 28.1% of patients reported by Lau *et al.*, 4.4% reported by Joshi *et al.* [4], 4.3-5.8% reported by Fonarow *et al.* [5] and 4.7% reported by a National Stroke Foundation [6]) indicates to a very strict safety protocol implemented at our center for the administration of r-tPA.

The reason that only 2.5% of stroke patients received thrombolytics, even though they arrived to hospital within 60 minutes (much within the 3-hour-window for thrombolytics according to AAN's class I recommendations (level of evidence A)) was most probably because of unaffordability. This thrombolysis rate is less than the 6.4% rate reported by Joshi *et al.* [4], 7% reported by Campbell *et al.* [7] and 9.1% reported by Fonarow *et al.* [5].

One of the reasons for our center's good performance includes the fact that we have a dedicated stroke unit, and a neurology resident dedicated for the stroke unit. Also, we have a bed on the stroke unit dedicated for r-tPA administration. In essence, our focus has been on following the protocols as set by the guidelines [8]. This has helped markedly reduce door-to-needle time.

One of the limitations of our study includes the fact that only 13 patients receive thrombolytics. It is therefore difficult to say if we would achieve the same success with a larger number of patients receiving thrombolytics.

In an acute ischemic stroke, time is brain, and so we at our center have remarkably achieved a door to needle time of <60 minutes. Based on our preliminary findings we recommend: (1) ensuring timely and appropriate referrals from nearby healthcare facilities, (2) organizing a more detailed audit to identify the reasons for delaying the administration of r-tPA and to minimize those delays, (3) to create guideline-based algorithms, order sets and dosing charts [9-11], (4) to set up educational programs via print media, social media and television [12], (5) to hold workshops for

healthcare providers, especially paramedical staff, in identifying eligible patients and timely notifying a stroke care facility by phone and transferring patients there [13-16], and (6) setting up online exchange forums to share best practices, challenges, and successes.

## CONCLUSIONS

Rates of favorable outcomes were similar to the ones reported at other specialized centers, and there were no symptomatic ICH at our hospital. However only 13 patients out of a total of 312 were thrombolysed owing to delay in presentation to our facility. We recommend identification and addressing factors and issues related to delay in presentation at a stroke facility equipped with intravenous r-tPA.

## REFERENCES

1. Kamal AK, Itrat A, Murtaza M, Khan M, Rasheed A, Ali A, Akber A, Akber Z, Iqbal N, Shoukat S, Majeed F. The burden of stroke and transient ischemic attack in Pakistan: a community-based prevalence study. *BMC neurology*. 2009 Dec 1;9(1):1.
2. Brewer L, Arize C, Williams D. Delays in the stroke thrombolysis pathway-identifying areas for improvement. *Irish medical journal*. 2014 May 1.
3. Lau AH, Hall G, Scott IA, Williams M. Thrombolysis in acute stroke: ongoing challenges based on a tertiary hospital audit and comparisons with other Australian studies. *Australian Health Review*. 2016 Feb 22;40(1):43-53.
4. Joshi P, Fink J, Barber PA, Davis A, Lanford J, Seymour A, Wright P, Busby W, Abernethy G, Ranta AA. Stroke thrombolysis in New Zealand: data from the first 6 months of the New Zealand Thrombolysis Register. *The New Zealand medical journal*. 2016 Jul 15;129(1438):44.
5. Bray BD, Campbell J, Hoffman A, Tyrrell PJ, Wolfe CD, Rudd AG. Stroke thrombolysis in England: an age stratified analysis of practice and outcome. *Age and ageing*. 2013 Mar 1;42(2):240-5.
6. Fonarow GC, Zhao X, Smith EE, Saver JL, Reeves MJ, Bhatt DL, Xian Y, Hernandez AF, Peterson ED, Schwamm LH. Door-to-needle times for tissue plasminogen activator administration and clinical outcomes in acute ischemic stroke before and after a quality improvement initiative. *Jama*. 2014 Apr 23;311(16):1632-40.
7. Party IS. National clinical guideline for stroke.
8. Campbell BC, Meretoja A, Donnan GA, Davis SM. Twenty-year history of the evolution of stroke thrombolysis with intravenous alteplase to reduce long-term disability. *Stroke*. 2015 Aug 1;46(8):2341-6.
9. Batmanian JJ, Lam M, Matthews C, Finckh A, Duffy M, Wright R, Brew BJ, Markus R. A protocol-driven model for the rapid initiation of stroke thrombolysis in the emergency department.

- Medical Journal of Australia. 2007 Nov 19;187(10):567-70.
10. Meretoja A, Strbian D, Mustanoja S, Tatlisumak T, Lindsberg PJ, Kaste M. Reducing in-hospital delay to 20 minutes in stroke thrombolysis. *Neurology*. 2012 Jul 24;79(4):306-13.
  11. Meretoja A, Strbian D, Mustanoja S, Tatlisumak T, Lindsberg PJ, Kaste M. Reducing in-hospital delay to 20 minutes in stroke thrombolysis. *Neurology*. 2012 Jul 24;79(4):306-13.
  12. Bray JE, Mosley I, Bailey M, Barger B, Bladin C. Stroke public awareness campaigns have increased ambulance dispatches for stroke in Melbourne, Australia. *Stroke*. 2011 Aug 1;42(8):2154-7.
  13. Audebert HJ, Saver JL, Starkman S, Lees KR, Endres M. Prehospital stroke care New prospects for treatment and clinical research. *Neurology*. 2013 Jul 30;81(5):501-8.
  14. O'Brien W, Crimmins D, Donaldson W, Risti R, Clarke TA, Whyte S, Sturm J. FASTER (Face, Arm, Speech, Time, Emergency Response): experience of Central Coast Stroke Services implementation of a pre-hospital notification system for expedient management of acute stroke. *Journal of Clinical Neuroscience*. 2012 Feb 29;19(2):241-5.
  15. Tai YJ, Weir L, Hand P, Davis S, Yan B. Does a 'code stroke' rapid access protocol decrease door-to-needle time for thrombolysis?. *Internal medicine journal*. 2012 Dec 1;42(12):1316-24.
  16. Quain DA, Parsons MW, Loudfoot AR, Spratt NJ, Evans MK, Russell ML, Royan AT, Moore AG, Miteff F, Hullick C, Attia J. Improving access to acute stroke therapies: a controlled trial of organised pre-hospital and emergency care. *Med J Aust*. 2008 Oct 20;189(8):429-33.