ORIGINAL ARTICLE

Rate of Recombinant Tissue Plasminogen Activator (rtPA) Administration for Acute Ischemic Stroke Treatment during the COVID-19 Pandemic in Thailand

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Background: Coronavirus disease 2019 (COVID-19) has become a global pandemic. Preventive policy during this outbreak possibly leads to a negative influence on the highly time-sensitive diseases such as acute ischemic stroke (AIS).

Objective: The present study was to determine the impact of the pandemic on rate of recombinant tissue plasminogen activator (rtPA) administration for AIS in Thailand.

Materials and Methods: A cross-sectional descriptive study. The magnitude of COVID-19 pandemic in each province of Thailand was reviewed from the website of the Ministry of Public Health. The number of patients with AIS who received rtPA was taken from the National Health Security Office, from 1st October 2019 to 21st August 2021. The authors demonstrate the correlation between the pandemic severity and the rate of rtPA administration for patients with AIS.

Results: During the COVID-19 pandemic, there were 37 provinces (48%) in year 2020 and 50 provinces (64.9%) in year 2021 had a reduction in rate of rtPA administration, 40 provinces (51.9%) in year 2020 and 27 provinces (35%) in year 2021 had increase in rate of rtPA administration. Over a period of two years, 25 provinces (32.5%) had only decreased rate (mean=1.12% and 1.63% in year 2020 and 2021 respectively), 15 provinces (19.5%) had only increased rate (mean=1.71% and 1.17% in year 2020 and 2021 respectively), and 37 provinces (48%) had diverse in rate of rtPA administration among both years.

Conclusion: The present study demonstrated that the COVID-19 pandemic does not cause a significant impact on the rate of rtPA administration for AIS in Thailand.

Keywords: COVID-19 pandemic; rtPA administration; Acute ischemic stroke

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The COVID-19 pandemic started in December 2019 in Wuhan (China) and spread worldwide, which had drawn attention and panic around the world as it is an emerging global health threat which had spread rapidly and transmitted from person to person. Moreover, currently there is no effective treatment or preventive method[1-3]. The World Health Organization classified the novel coronavirus (COVID-19) outbreak as a pandemic on March 11, 2020[4].

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As a result, many countries had created different policies aimed at slowing the spread of the virus such as social distancing and travel restrictions[5-8]. As for healthcare service, there are many new guidelines created to prevent the spread, for example, separation of patients, quarantine if suspected of infection in highly endemic areas, performing screening test or wearing personal protective equipment before examine or give treatments to patients[9,10].

Thailand declared COVID-19 as an epidemic according to the Emergency Decree on Public Administration in Emergency Situations with the approval of the Cabinet, which was in effect since 26th March 2020 and the lockdown and social distancing policy had been announced in April 2020 and onwards, which created some restrictions and difficulty in traveling out of home and across provinces[11].

In addition, Thailand has also begun zoning and dividing the area according to the severity of the epidemic based on the number of infected people following the announcement of the COVID-19 Situation Administration Center on 3rd January 2021.

Regarding to the restrictions, zoning, and social distancing policy, it may delay medical procedures for various medical conditions, especially time-sensitive conditions which required immediate medical attention and treatment such as acute ischemic stroke (AIS) which needed emergency brain CT scan and administration of thrombolytic therapy, recombinant tissue plasminogen activator (rtPA), within 270 minutes after the onset of symptoms and if not treated properly and in timely manner, it may result in disabilities and death[12-17].

In various countries, the outbreak of COVID-19 had an impact, while some countries had found that the outbreak does not affect the treatment of AIS[13,18-29]. Consequently, each country had tried to create guidelines for better stroke management[30-32]. Objective of the present study was to determine whether the COVID-19 pandemic has an impact on rtPA administration rate in patients with acute ischemic stroke (AIS) in Thailand during the pandemic.

Materials and Methods

This is a cross sectional descriptive study that gathers data of rate of rtPA administration in patients diagnosed with acute ischemic stroke during COVID-19 pandemic in the fiscal year of 2020 and 2021 (between 1st October 2019 and 21st August 2021) in 77 provinces of Thailand. Data on the numbers of patients diagnosed with acute ischemic stroke and patients who received rtPA administration was obtained from the National Health Security Office and information on the outbreak of COVID-19 was obtained from the website of Ministry of public health.

Rate of rtPA administration was presented as percentage of the total number of stroke patients in each province. Data of number of provinces with percentage reduction in rate of rtPA administration compared to previous fiscal year was also collected and presented.

In terms of information indicating the severity of the COVID-19 outbreak in each province were shown in the form of the ratio of the number of infections per 100,000 population in that area.

The relationship between severity of COVID-19 outbreak and rate of rtPA administration in each year was analyzed using Spearman's rank correlation coefficient. The authors also analyze in different epidemic zones in reference to the zoning of the epidemic provinces and the maximum strictly controlled areas according to announcement of COVID-19 Situation Administration Center, which has a total of 7 times.

The present study was approved by the regional Research Ethics Committee, Faculty of Medicine, Khon Kaen University, No. HE631574.

Results

From the epidemic of COVID-19 in Thailand, the correlation between the number of COVID-19 cases in each year and rate of rtPA administration was shown in Figure 1. It was found that the higher number of COVID-19 cases were related to decrease in rate of rtPA administration, R=-0.119 (p-value=0.301) and -0.114 (p-value=0.322) in fiscal year of 2020 and 2021 respectively. That correlation was found to be insignificant.

Out of all 77 provinces of Thailand, there were 37 provinces in fiscal year of 2020 and 50 provinces in fiscal year of 2021 had a decreased in rate of rtPA administration, which accounted for 48% and 64.9% respectively, and there were 40 provinces in fiscal year of 2020 and 27 provinces in fiscal year of 2021 had increased in rate of rtPA

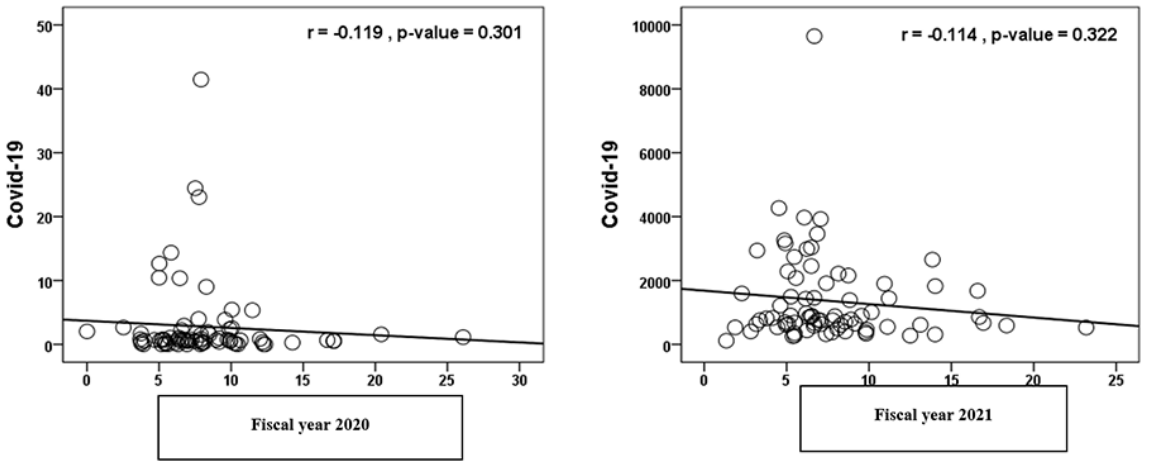

Figure 1. Spearman's rank correlation between number of COVID-19 cases (per 100,000 population) and rate of rtPA administration in each fiscal year.
R-value (correlation): The - sign indicates that the data is inverse. If one increases, one decreases. The + sign indicates that the data goes together. If one is added, one will be added. If one decreases, one decreases. The R-value is 0 - 1. The closer to 1, the higher correlation of the data.

administration, accounted for 51.9% and 35% respectively. This result shown in the table divided by healthy area in 13 districts (Table 1).

In addition, the authors analyzed over a period of two years together, there were 25 provinces (32.5%) had only decreased rate of rtPA administration in both years (mean=1.12% and 1.63% in year 2020 and 2021 respectively), 15 provinces (19.5%) had only increased rate (mean=1.71% and 1.17% in year 2020 and 2021 respectively), and 37 provinces (48%) had diverse in rate of rtPA administration among both years.

According to the announcement of the COVID-19 Situation Administration Center, there has been zoning as the maximum strictly controlled area during fiscal year of 2021, with a total of 7 announcements issued. There are 34 provinces were classified as the maximum strictly controlled areas. It was found that 19 provinces had decreased rate of rtPA administration compared to the fiscal year of 2020. Moreover, most of them were classified as the maximum strictly controlled areas at least two times. However, another 12 provinces were classified in this manner more than two times, but the rate of rtPA administration did not decreased. In addition, 1 province was classified in this way only once, but there was the reduction rate of rtPA administration.

The rate of rtPA administration in each fiscal year, percentage reduction between fiscal year of 2020 and 2021, and number of COVID-19 cases in each province that classified as maximum strictly controlled area were shown in Table 2.

Discussion

In the present study, the number of AIS patients in each province for the most part, the rate of rtPA administration actually decreased during 2020 to 2021 outbreak. More evident in 2021, which the outbreak was more severe and widespread. The authors hypothesized that the decline in the total number of patients receiving rtPA administration is likely related to government control policies during COVID-19 outbreak such as city lockdowns, traveling restrictions, and social distancing which could make access to medical services difficulty for stroke patients. Physical distancing measures may prevent the patient from being promptly rescued in timely at the onset of acute stroke.

Another plausible explanation is that local hospital policies during the outbreak that became more stringent, for instance, screening of patients to ensure they are not contaminated with COVID-19 prior to receiving medical services. It also includes the processes involving personal protective equipment for healthcare professional before examine the patient, which may require additional time than usual. Due to such safety measures, this may prevent us from submitting an investigation such as CT scan in timely manner. Finally, another reason might be related to the patient's fear of not being able to leave their home during the outbreak, resulting in a delay in stroke management.

However, there are still several queries in terms of some areas with high outbreaks, but there is no reduction in the rate of rtPA administration. It may be that the outbreak has caused the number of people suffering from other diseases did not come to the hospital, this makes the diagnosis and treatment of AIS faster than usual. Another possible cause may be that COVID-19 patient themselves are at risk of developing acute thrombosis, resulting in an increase in the number of AIS cases and an increase in the rate of rtPA administration. Alternatively, creating a new stroke guideline during the epidemic to shorten the door to needle time may lead to an increased in the rate of rtPA administration.

The benefit of the present study is that provincial stroke service systems that have increased rtPA rates despite the coronavirus outbreak should be studied and also to be adapted to the service system of each hospital. And should study other factors that enhance more stroke patients to enter the stroke fast track service during the coronavirus outbreak.

The limitation of the present study is the authors cannot prove the hypothesis such that relationship may cause by other confounding factors. This is just a personal assumption that attempts to explain such results. More studies are needed to explore this hypothesis.

Conclusion

The present study suggests that the COVID-19 pandemic may have an impact on rtPA administration in AIS patients in Thailand, but the severity of the outbreak may not be the main factor to explaining, as the decline in rate of rtPA administration was seen in area with few COVID-19 cases and some area that highly in outbreak but the rtPA administration rate was not reduced. Further studies on this issue are still needed.

What is already known on this topic?

COVID-19 pandemic may have an impact on rtPA administration in acute ischemic stroke.

What this study adds?

Rate of thrombolytic treatment in Thailand was not decreased in outbreak of COVID-19.

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Conflicts of interest

The authors declare no conflict of interest.

Table 1. Number of COVID-19 cases and rate of rtPA administration in each fiscal years

Province	Fiscal year of 2019	Fiscal year of 2020			Fiscal year of 2021		
	rtPA administration rate (%)	No. COVID cases (per 100,000 population)	rtPA administration rate (%)	% change (compare with fiscal year of 2019)	No. COVID cases (per 100,000 population)	rtPA administration rate (%)	% change (compare with fiscal year of 2020)
Healthy area 1							
Chiang Mai	7.85	2.37	9.89	+2.04	626.88	9.14	-0.75
Lamphun	10.3	0.96	9.18	-1.12	234.89	12.5	+3.32
Lampang	6.98	0.55	6.84	-0.14	261.22	5.49	-1.35
Phrae	9.86	0.23	10.19	+0.33	283.47	14.01	+3.82
Nan	12.88	0.00	10.46	-2.42	418.95	9.85	-0.61
Phayao	11.3	0.64	9.92	-1.38	307.07	9.82	-0.1
Chiang Rai	7.21	0.77	6.63	-0.58	226.67	5.37	-1.26
Mae Hong Son	2.46	2.03	0	-2.46	102.94	1.34	+1.34
Healthy area 2							
Uttaradit	14.29	0.66	16.67	+2.38	607.35	16.94	+0.27
Tak	19.19	0.51	17.1	-2.09	1513.14	14.02	-3.08
Sukhothai	6.06	0.50	7.03	+0.97	679.84	7.05	+0.02
Phitsanulok	8.76	0.57	7.87	-0.89	314.10	5.48	-2.39
Phetchabun	6.82	0.30	7.99	+1.17	463.74	8.29	+0.3
Healthy area 3							
Chai Nat	14.57	0.00	12.36	-2.21	510.37	6.66	-5.7
Nakhon Sawan	11.82	0.85	12.0	+0.18	677.26	8.91	-3.09
Uthai Thani	7.44	0.30	8.0	+0.56	694.05	6.47	-1.53
Kamphaeng Phet	4.15	0.00	3.91	-0.24	715.14	4.14	+0.23
Phichit	6.86	0.00	6.93	+0.07	546.63	5.1	-1.83
Healthy area 4							
Nonthaburi	4.3	10.44	5.0	+0.7	2939.86	4.86	-0.14
Pathum Thani	11.35	2.54	10.05	-1.3	2004.72	8.14	-1.91
Phra Nakhon Si Ayutthaya	4.32	0.43	3.79	-0.53	1876.23	5.07	+1.28
Ang Thong	8.1	0.00	6.31	-1.79	2494.53	3.21	-3.1
Lop Buri	5.95	0.26	5.48	-0.47	1208.58	6.67	+1.19
Sing Buri	4.71	0.00	5.19	+0.48	830.60	6.19	+1.0
Saraburi	5.29	0.69	5.39	+0.1	2318.98	5.47	+0.08
Nakhon Nayok	9.0	0.74	6.35	-2.65	2541.78	6.23	-0.12
Healthy area 5							
Ratchaburi	7.88	0.76	9.76	+1.88	1328.11	7.41	-2.35
Kanchanaburi	5.53	1.06	5.77	+0.24	1126.05	5.26	-0.51
Suphan Buri	3.34	0.71	5.24	+1.9	1084.04	4.62	-0.62
Nakhon Pathom	8.55	1.95	8.39	-0.16	2126.27	6.49	-1.9
Samut Sakhon	7.71	1.47	7.91	+0.2	8499.56	6.68	-1.23
Samut Songkhram	8.65	0.49	9.93	+1.28	3193.84	7.06	-2.87
Petchaburi	9.62	0.40	9.17	-0.45	2836.56	6.49	-2.68
Prachuap Khiri Khan	8.58	2.94	6.73	-1.85	1210.70	11.21	+4.48
Healthy area 6							
Samut Prakan	7.2	10.35	6.44	-0.76	3542.32	4.53	-1.91
Chonburi	8.69	14.36	5.83	-2.86	2706.85	4.92	-0.91
Rayong	9.15	0.62	10.65	+1.5	1519.55	10.94	+0.29
Chanthaburi	8.76	0.51	7.53	-1.23	840.96	10.15	+2.62
Trat	4.19	0.00	5.61	+1.42	608.52	5.24	-0.37
Chachoengsao	4.62	2.26	6.55	+1.93	2964.90	6.86	+0.31

Table 1. Cont.

Province	Fiscal year of 2019		Fiscal year of 2020		Fiscal year of 2021		
	rtPA administration rate (%)	No. COVID cases (per 100,000 population)	rtPA administration rate (%)	% change (compare with fiscal year of 2019)	No. COVID cases (per 100,000 population)	rtPA administration rate (%)	% change (compare with fiscal year of 2020)
Prachinburi	8.03	1.55	8.48	+0.45	1144.14	6.16	-2.32
Sa Kaeo	3.93	1.71	3.74	-0.19	1343.54	2.28	-1.46
Healthy area 7							
Khon Kaen	10.36	0.33	12.18	+1.82	485.52	11.12	-1.06
Maha Sarakham	6.49	0.10	10.31	+3.82	820.48	9.55	-0.76
Roi Et	5.99	0.23	7.97	+1.98	745.59	7.93	-0.04
Kalasin	7.36	0.31	8.12	+0.76	636.10	8.54	+0.42
Healthy area 8							
Bueng Kan	8.56	0.00	7.87	-0.69	346.71	9.79	+1.92
Nong Bua Lamphu	8.46	0.57	6.51	-1.95	538.88	3.16	-3.35
Udon Thani	6.6	0.64	5.07	-1.53	531.06	4.97	-0.1
Loei	5.27	0.78	5.24	-0.03	357.81	2.82	-2.42
Nong Khai	3.26	0.58	3.99	+0.73	390.15	6.23	+2.24
Sakon Nakhon	5.79	0.09	5.44	-0.35	483.83	4.44	-1.0
Nakhon Phanom	15.74	0.28	14.25	-1.49	559.56	13.12	-1.13
Healthy area 9							
Nakhon Ratchasima	5.3	0.71	4.69	-0.61	512.09	5.48	+0.79
Buriram	6.65	0.88	7.92	+1.27	629.47	6.35	-1.57
Surin	6.07	0.65	6.76	+0.69	707.46	6.54	-0.22
Chaiyaphum	6.62	0.26	6.13	-0.49	605.53	4.91	-1.22
Healthy area10							
Sisaket	14.9	0.55	17.14	+2.24	735.94	16.69	-0.45
Ubon Ratchathani	3.77	0.80	3.71	-0.06	660.05	3.37	-0.34
Yasothon	8.71	0.19	3.76	-4.95	731.26	3.78	+0.02
Amnat Charoen	7.26	0.71	6.98	-0.28	580.53	6.68	-0.3
Mukdahan	19.08	0.88	26.09	+7.01	480.56	23.18	-2.91
Healthy area 11							
Nakhon Si Thammarat	6.93	0.76	7.25	+0.32	392.92	8.08	+0.83
Krabi	9.11	3.97	7.74	-1.37	276.84	7.39	-0.35
Phang Nga	8.77	0.70	8.98	+0.21	332.82	7.74	-1.24
Phuket	7.47	41.45	7.91	+0.44	453.81	6.9	-1.01
Surat Thani	21.02	1.57	20.41	-0.61	464.04	18.35	-2.06
Ranong	3.17	0.00	12.24	+9.07	2019.63	13.85	+1.61
Chumphon	5.0	3.86	9.58	+4.58	546.09	7.79	-1.79
Healthy area 12							
Songkhla	9.87	9.01	8.28	-1.59	1208.08	8.83	+0.55
Satun	5.63	5.44	10.05	+4.42	326.83	8.56	-1.49
Trang	4.63	1.06	6.38	+1.75	554.40	7.09	+0.71
Phatthalung	1.58	2.65	2.53	+0.95	431.84	1.88	-0.65
Pattani	4.19	12.65	5.02	+0.83	1856.39	5.57	+0.55
Yala	7.7	24.45	7.51	-0.19	1875.94	8.74	+1.23
Narathiwat	8.11	5.34	11.47	+3.36	1360.76	16.59	+5.12
Healthy area 13							
Bangkok	6.93	23.05	7.77	+0.84	3440.54	6.07	-1.7

Total 77 provinces

No. COVID cases mean number of COVID-19 detected cases (per 100,000 population in that area). % change mean percentage difference of rtPA administration rate compared to the previous year. The mark (-) mean decrease rate of rtPA administration compared to the previous year. The mark (+) mean increase rate of rtPA administration compared to the previous year

Table 2. Number of COVID-19 cases with the rate of rtPA administration in the maximum strictly controlled province in fiscal year 2021.

Provinces	No. of times announced as a maximum strictly controlled area	No. of COVID-19 cases (per 100,000 population)	Rate of rtPA administration (%)		% Difference between the fiscal year 2020 to 2021
			Fiscal year 2020	Fiscal year 2021	
Bangkok	6	3,440.54	7.77	6.07	-1.7
Kanchanaburi	3	1,126.05	5.77	5.26	-1.51
Chanthaburi	2	840.96	7.53	10.15	+2.62
Chachoengsao	4	2,964.90	6.55	6.86	+0.31
Chumphon	1	546.09	9.58	7.79	-1.79
Chonburi	4	2,706.85	5.83	4.92	-0.91
Trat	2	608.52	5.61	5.24	-0.37
Tak	4	1,513.14	17.1	14.02	-3.08
Nakhon Nayok	3	2,541.78	6.35	6.23	-0.12
Nakhon Pathom	7	2,126.27	8.39	6.49	-1.9
Nonthaburi	6	2,939.86	5.0	4.86	-0.14
Pathum Thani	6	2,004.72	10.05	8.14	-1.91
Prachuap Khiri Khan	2	1,210.70	6.73	11.21	+4.48
Prachinburi	3	1,144.14	8.48	6.16	-2.32
Phra Nakhon Si Ayutthaya	4	1,876.23	3.79	5.07	+1.28
Phetchaburi	3	2,836.56	9.17	6.49	-2.68
Ratchaburi	4	1,328.11	9.76	7.41	-2.35
Ranong	1	2,019.63	12.24	13.85	+1.61
Rayong	3	1,519.55	10.65	10.94	+0.29
Lopburi	3	1,208.58	5.48	6.67	+1.19
Sing Buri	3	830.60	5.19	6.19	+1.0
Samut Prakan	6	3,542.32	6.44	4.53	-1.91
Samut Songkhram	4	3,193.84	9.93	7.06	-2.87
Samut Sakhon	5	8,499.56	7.91	6.68	-1.23
Suphan Buri	2	1,084.04	5.24	4.62	-0.62
Sa Kaeo	2	1,343.54	3.74	2.28	-1.46
Saraburi	3	2,318.98	5.39	5.47	+0.08
Ang Thong	2	2,494.53	6.31	3.21	-3.1
Narathiwat	4	1,360.76	11.47	16.59	+5.12
Pattani	4	1,856.39	5.02	5.57	+0.55
Yala	4	1,875.94	7.51	8.74	+1.23
Songkhla	4	1,208.08	8.28	8.83	+0.55
Nakhon Ratchasima	1	512.09	4.69	5.48	+0.79
Phetchabun	1	463.74	7.99	8.29	+0.3

Total 34 provinces

The mark (-) mean decrease rate of rtPA administration compared to the previous year.The mark (+) mean increase rate of rtPA administration compared to the previous year

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