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Epidemiology of Stroke 2 Years Before and During COVID-19 Pandemic in Kerman (south of Iran): a Hospital-Based Study

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Original Article

Abstract

INTRODUCTION: Stroke is the second leading cause of death worldwide. Recent studies have shown that the COVID-19 pandemic has been associated with a higher frequency of stroke. This study aimed to investigate the epidemiologic aspects of stroke two years before and during the COVID-19 pandemic in Kerman.

METHOD: This cross-sectional study was conducted in Kerman. The participants included all patients with a confirmed diagnosis of stroke. COVID-19 confirmation was based on a positive PCR test. The data was analyzed with SPSS.V24 software.

RESULTS: In this study, 4152 patients with stroke were evaluated. The frequency of stroke before and during the COVID-19 pandemic was the same. The total number of stroke patients with COVID-19 was 298 (8.16%). The frequency of ischemic stroke patients before the COVID-19 pandemic was 1751 and during the pandemic was 1770. Before and after the pandemic, the mean age of ischemic stroke patients was 67.42±14.14 and 64.49±14.46 respectively, which showed a statistically significant difference (P>0.001). Our findings showed a significant difference between the NIHSS of ischemic stroke before and after the pandemic (P<0.001). The mortality rate of stroke patients was 111 before COVID-19 and 115 patients in the first two years of COVID-19. Except for the mortality rate (P<0.001), there was no significant difference in other demographic variables between ischemic stroke patients with and without COVID-19.

CONCLUSION: The patients with ischemic stroke during the COVID-19 pandemic were younger and had more neurological deficits than the ischemic stroke patients before the pandemic. COVID-19 was associated with higher mortality in patients with ischemic stroke.

Keywords: Frequency, Corona, Sex, Mortality, Ischemic

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Introduction

Stroke is one of the most common neurological disorders and is also considered one of the leading causes of disability and mortality [1, 2]. Hypertension, ischemic heart disease, diabetes, smoking, and hyperlipidemia are the main risk factors for stroke [3]. In addition to these known risk factors, several reports have been published about the impact of COVID-19 on the incidence and clinical course of stroke. The recent pandemic has changed the pattern of patient admission and stroke severity [4]. For instance, studies in China, as the first country involved with this disease, suggest a prevalence of ischemic stroke in 5% of COVID-19 patients [5]. Forster et al. also

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showed that 260 deaths among 8,809 patients with a positive COVID-19 test were due to stroke [6]. In a systematic review, Nannoni et al. evaluated 108,571 patients with COVID-19. They observed that 1.4% of these patients had nervous system involvement, with ischemic stroke being the most common neurological manifestation [7]. Also, COVID-19 increases disability and mortality in stroke patients [8, 9]. This effect is not related to the severity of the disease. It can be seen in mild or asymptomatic cases and is associated with radiological abnormality [10-12]. Clinical evidence suggests that the effect of COVID-19 is not exclusive to ischemia and is also found in hemorrhagic cases [13]. Although the pathophysiology of the COVID-19 effect on the stroke process is not fully known, inflammation and coagulation dysfunction are considered the primary factors [14]. To get more information about the effect of COVID-19 on stroke, the authors evaluated epidemiological aspects of stroke two years before and during the COVID-19 pandemic in Kerman.

Materials and Methods

This cross-sectional study was conducted on patients with a clinical diagnosis of stroke two years before the COVID-19 pandemic from 2018 to 2019, and during the pandemic period from 2020 to 2021 at Shafa Hospital in Kerman (south of Iran). Shafa Hospital is the main center for the admission of stroke patients in Kerman city. The definitive diagnosis was confirmed by neuroimaging studies (CT scan, MRI). Patients diagnosed with transient ischemic attack (TIA) and cerebral vein thrombosis (CVT) were excluded. COVID-19 infection was confirmed by a positive PCR test. The study was approved by the Ethics Committee of Kerman University of Medical Sciences (IR.KMU.REC.1401.057). Data were collected from the national stroke registration system and hospital medical records. It should be noted that in Iran, there is a national stroke registry system that provides a computerized report of all cases of stroke hospitalized in main hospitals. Demographic information, clinical, and paraclinical findings are recorded in the national stroke registry system.

Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences, 24th version (SPSS.V24) software. The mean and standard deviation were used to describe the quantitative variables. Frequency and percentage indices were used to describe the qualitative variables. For continuous variables, a normality test was checked. If the normality assumption was satisfied, parametric tests were used (Independent samples T test, ANOVA). Nonparametric tests (Mann-Whitney or Kruskal-Wallis tests) were used when the normality assumption was not met. The Chi-square test was used for calculating the relation between discrete variables. Also, the independent t-test or ANOVA was used for the quantitative variables. In this study, P-values less than 0.05 were considered statistically significant.

Results

The findings of this study were extracted from 4264 medical records of stroke patients, including ischemic and hemorrhagic patients, before and during the COVID-19 pandemic. 112 (47 before the pandemic and the rest during the pandemic) were excluded from the study due to incomplete records. During the pandemic, 298 patients (16.8%) had a positive COVID-19 test. The stroke frequency two years before and during the pandemic was similar (Table 1). The Mann-Whitney U test revealed a statistically significant difference in the mean ages of people diagnosed with ischemic stroke before and during the COVID-19 pandemic ($P<0.001$). Data regarding gender, history of underlying diseases, and the territory of vascular involvement before and during the COVID-19 pandemic showed no statistically significant difference between the ischemic stroke patients (Table 2). Also, NIHSS scores before and during the COVID-19 pandemic revealed a significant difference in the ischemic patients ($P < 0.01$) (Chart 1).

Table 1. Comparing the frequency of stroke before and during the Covid-19 pandemy

	Before pandemy	Pandemy	Total	P-value
Ischemic stroke	1751(84.9%)	1770(84.6%)	3521(84.8%)	0.964
Hemorrhagic stroke	310(15.1%)	321(15.4%)	631(15.2%)	
Total	2061	2091	4152	

*Chi-square test was used

Table 2. Comparison of demographic characteristics of ischemic stroke patients before and during the Covid pandemy

	Before pandemy	Pandemy	P-value
Number of patients	1751	1770	
Number of Covid positive (N%)	----	298 (16.8%)	----
Age (Mean ± SD)	67.42±14.24	64.49±14.46	<0.001
Female (N%)	855(48.9)	863 (48.8)	0.953
Male (N%)	895(51.1)	907 (51.2)	
Hypertension	885(50.5%)	834(47.1%)	0.051
Diabetes mellitus	608(34.7%)	590(33.3%)	0.384
Smoking	324(18.5%)	402(22.7%)	0.435
Coronary artery disease	288(16.4%)	309 (17.5%)	0.226
Chronic heart failure	152 (8.7%)	158(8.9%)	0.797
AF	208 (11.9%)	210 (11.9%)	0.989
Renal failure	37 (2.1%)	33 (1.9%)	0.597
Cancer	17 (1%)	25 (1.4%)	0.228
Types of ischemic stroke			0.256
Cardio embolic	382(21.8%)	392(22.1%)	
Small vessels	641 (39.9%)	628 (35.5%)	
Large vessels	240 (13.7%)	284 (16%)	
Other	487 (27.8%)	466 (26.3%)	
(NIHSS)			
0-4	698 (39.9%)	597 (33.7%)	
5 – 8	555 (31.7%)	538 (30.4%)	<0.001
9 -14	261 (14.9%)	274 (15.5%)	
14 <	236 (13.5%)	361 (20.4%)	
Anterior circulation	1357 (77.5)	1365 (77.1)	0.788
Posterior circulation	394 (22.5)	405 (22.9)	
Mortality rate	109(6.2%)	114(6.4%)	0.976
Thrombolysis	151(8.6%)	168(9.4%)	0.498

*Chi-square test and Independent samples test were used

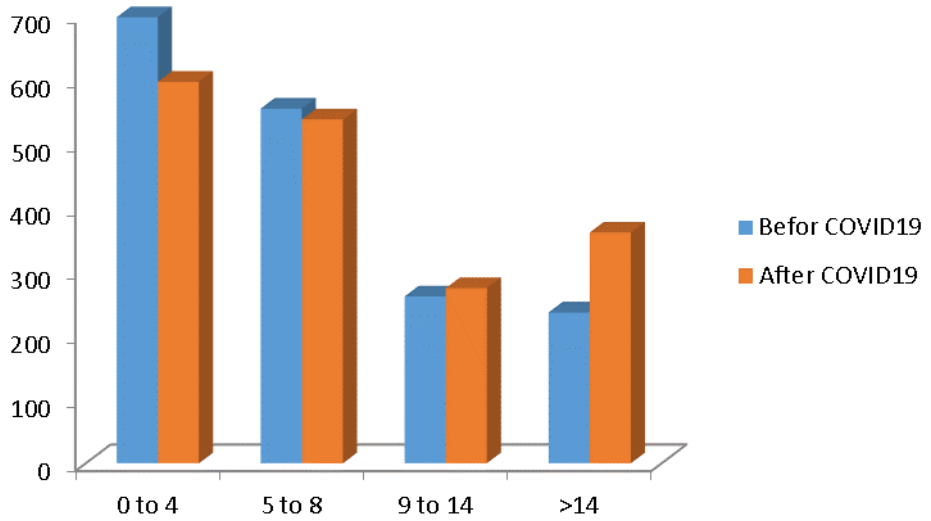

Chart 1. NIHSS before and during the Covid pandemy in ischemic stroke patients.

The Mann-Whitney test shows a significant difference between the times of referring stroke patients to the emergency department before and during the COVID-19 pandemic (P=0.001). The patients were referred to the hospital significantly faster after the COVID-19 pandemic (Table 3). Also, the Mann-Whitney test shows no significant difference in the patients with and without COVID-19 regarding the demographic variables and underlying diseases during the pandemic. However, the mortality rate was significantly different in patients with positive and negative COVID-19 tests (Table 4). No significant difference was found before and during the pandemic period regarding the demographic factors, type of stroke, and mortality.

Table 3. Comparing the referral time of ischemic stroke patients to the emergency department before and during the covid pandemy

Variable		Mean ± SD	Z	P-Value
Referral time (Minute)	Before	11.32±8.09	-9.41	<0.001
	Pandemy	9.12±7.11		

*Man Whitney U test was used

Table 4. Comparison of variables between two groups of non-covid and covid stroke patients during the covid pandemic

	Covid +	Covid -	P-value
Number	298	1472	
Age (Mean ± SD)	15.08±64.34	14.33±64.53	0.838
Woman N%	144(48.3%)	719(48.8%)	
Man N%	154(51.7%)	753 (51.2%)	0.869
Hypertension	139(46.6%)	695(47.2%)	0.437
Diabetes mellitus	92(30.9%)	498(33.8%)	0.323
Coronary artery disease	44(14.8%)	265 (18%)	0.179
Chronic heart failure	27 (9.1%)	131(8.9%)	0.929

	Covid +	Covid -	P-value
AF	40 (13.4%)	170 (11.5%)	0.362
Renal failure	4 (1.3%)	29 (2%)	0.465
Cancer	2 (0.7%)	23 (1.6%)	0.234
Types of ischemic stroke			
cardio embolic	60 (20.1%)	332 (22.6%)	
small vessels	107 (35.9%)	521 (35.4%)	0.803
large vessels	48 (16.1%)	236 (16%))	
other	83 (27.9%)	383 (26%)	
NIHSS			
0-4	103 (34.6%)	494 (33.6%)	
5-8	90 (30.2%)	448 (30.4%)	
9-14	57 (19.1%)	217 (14.7%)	0.094
>14	48 (16.1%)	313 (21.3%)	
Mortality rate	37(12%)	77(%5)	<0.001

*Chi-square test and Independent samples test were used

Discussion

The current study compared the demographic aspects of stroke patients two years before and during the COVID-19 pandemic in Kerman city. The results revealed no difference in the frequency of stroke before and during the pandemic. Also, the ratio of ischemic to hemorrhagic stroke did not show any change before and during the pandemic. The lack of increase in stroke cases in our study, and even a reduction in some studies, may be due to the lack of referral to medical centers due to the fear of COVID-19 infection in mild stroke cases [10, 15]. Nagraj et al. published a systematic review in 2022. They found that the overall incidence of stroke in patients with COVID-19 is low and appears to be lower than that reported in previous reports [16]. However, some studies have reported an increase in stroke incidence during the pandemic period [10, 17]. In our study, 298 patients (16.8%) had a positive COVID-19 test during the COVID-19 pandemic. This is similar to another study in Iran (18.6%) [18]. Studies in other countries indicate an incidence of 0.1% to 6.9% of ischemic stroke in hospitalized COVID-19 patients [19]. Also, studies suggest that COVID-19 increases the risk of ischemic stroke by 5 times [7]. A multicenter study showed that among 26,175 patients with COVID-19, the overall stroke risk was 5%, and 79% of them had ischemic stroke [20]. The mean age of admitted patients decreased from 67 years before the pandemic to 64 years during the pandemic, indicating a statistically significant difference between the two periods. Osley et al. found similar results [10]. Yaghi et al. also observed that stroke patients were younger during the COVID-19 pandemic. They also found that men are at higher risk of stroke [21]. Some other studies have also achieved the same results [19, 22-24], but there are some studies that have reported opposite results [7, 25]. We found an increase in NIHSS in severe cases (9-14 and more than 14) during the COVID-19 pandemic. In line with the results of this study, Tavanaei et al. reported an NIHSS increase in severe stroke patients after the COVID-19 pandemic [4].

Zini et al. also reported an increase in moderate-to-severe stroke cases after the COVID-19 pandemic [26]. A study by Yaghi et al. showed the same results [21]. Consistent with our results, Ntaios observed that the severity of symptoms is higher in COVID-19 patients with stroke [27] and is associated with increased mortality in COVID-19 patients. Our findings showed higher mortality in positive COVID-19 stroke patients (P<0.001). Other studies have confirmed this result [9, 10, 18, 22, 27-30]. Mild stroke patients may have refused to receive emergency care due to the fear of COVID-19 infection.

Regarding the stroke types, including cardio embolic, small or large vessels atherosclerotic infarction, and the other cases, the patients did not show any significant difference before and during the pandemic. Thus, the COVID-19 infection did not have any effect on the type of ischemic stroke. Some studies that evaluated the ischemic stroke type showed that large vessels were more involved [10, 24, 31, 32]. It might be related to the difference between the kind of vessel involvement and the type of ischemic stroke in western and eastern countries. Intracranial and small vessel involvement is more common in some eastern countries [33]. Our findings showed that the patients' time of referring to the hospital during the COVID-19 pandemic decreased significantly. In line with these results, Tavanaei's study also reported a significant reduction in the time of stroke onset till hospital admission in ischemic stroke patients. This time was reduced from 12 hours before the COVID-19 pandemic to 6 hours during the COVID-19 pandemic [4]. Although it was expected that the fear of COVID-19 might decrease the admission rate and increase the delay in referring to the hospital, the referring time decreased. However, its main reason is not known. It might be due to the increased public knowledge about the golden time in stroke management. No difference was observed regarding stroke risk factors in patients with COVID-19 and non-COVID in this study. However, some studies, including the study by Nannoni et al., have reported that these factors were significantly higher in COVID-19 patients [7]. Many studies have been reported concerning the pathophysiology of the effect of COVID-19 on stroke occurrence and course [34]. It seems that COVID-19 infection predisposes patients to arterial and venous thromboembolic events by inflammation, hypoxia, immobility, and disseminated intravascular coagulation. Also, hypercoagulopathy, increased levels of antiphospholipid antibodies, and disturbance of angiotensin 2 plasma level are other causes of stroke in COVID-19 patients [7, 14, 19, 22, 35, 36]. It should be noted that the role of race in infection with COVID-19 has been proven [37]. Some epidemiological differences in the studies may be secondary to this point. One of the limitations of the study is that the data of this study were obtained from hospitalized patients, so the results should be interpreted with caution. Also, it should be noted that in our study, COVID-19 infection was confirmed by a positive PCR test. In general, the results revealed that ischemic stroke patients during the COVID-19 pandemic were younger and had more neurological deficits. COVID-19 was associated with higher mortality in patients with ischemic stroke.

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Declarations

Ethics approval and consent to participate: This study had been approved by the ethics committee of Kerman University of Medical Sciences.

Consent for publication: Written informed consent was obtained from participants.

Availability of data and materials: All data generated or analyzed during this study are included in this published article.

Competing interests: The authors have no example conflicts of interest to disclose.

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