

Characteristics and Outcomes of COVID-19 Related Stroke: A Cohort Study

Kasra Afsahi, Maryam Soheilifar, Omid Seyed Esmaeili

Abstract—Background: Cerebrovascular accident (CVA) is a neurological side effect of COVID-19 disease with high rate in pandemics. Effect of COVID-19 disease on disorder is unclear. In this cohort, patients with COVID-19 disease were assessed. Materials and methods: 60 CVA cases were assessed in a referral hospital in 2020. The major factor was mortality and the cases were those with and without death. The groups were compared for all features about mortality in the patients with COVID-19 and CVA. Results: Totally 23 out of 60 cases (38.3%) were expired. In univariate analysis there was significant association for death by ischemic heart disease ($P = 0.015$), high-severity stroke ($P = 0.012$), high CRP ($P = 0.001$), high ESR ($P = 0.009$), pleural effusion ($P = 0.005$), pericardial effusion ($P = 0.027$), cardiomegaly ($P = 0.005$), ground glass opacity ($P = 0.001$), and consolidation ($P = 0.001$). Among these factors, there was significant association only for C reactive protein (CRP) ($P = 0.001$) and consolidation ($P = 0.003$) in multivariate analysis. Conclusion: Mortality in the cases with COVID-19-related CVA is one-third and it has relationship to elevated CRP and finding the consolidation in the computerized tomography scan of the lungs.

Keywords—COVID-19, stroke, prognosis, mortality

I. INTRODUCTION

COVID-19 infection is a terrible health event leading to a pandemic that resulted in high economic burden due to high mortality and morbidity in affected cases [1], [2]. Despite predominance of respiratory symptoms in patients with COVID-19 infection, the other systems such as kidneys, heart, and brain may be also affected that leads to higher burden of the problem [3]-[5]. The COVID-19 virus can enter to the body cells by ACE2 receptor that is widespread in cells of heart, kidney, lung, gut, brain, etc. [6].

The involvement of cerebral tissue and development of some neurological symptoms such as decreased consciousness, seizure, headache, anosmia, taste sensation disturbance, neuralgia, and musculoskeletal complaints are reported in some patients with COVID-19 infection [7]-[9]. Some proposed etiological mechanisms include direct COVID-19 infection of brain, hypoxia, increased CO₂ pressure, and lung involvement leading to respiratory problems [10]-[12]. Stroke is one of the neurological consequences of COVID-19 infection that has shown

increased rate during current pandemic [13], [14]. But the impact of COVID-19 infection on the course of disease is not completely understood. Accordingly in this study characteristics and outcomes of patients with simultaneous COVID-19 infection were studied.

II. MATERIALS AND METHODS

In this cohort, 60 consecutive stroke cases were enrolled including subjects admitted intensive care unit in a tertiary health care center in Tehran, Iran in 2020. Inclusion criteria were established cases of COVID-19 infection by lung computerized tomography (CT) scan and polymerase chain reaction (PCR), confirmed ischemic/hemorrhagic stroke cases (by brain CT scan), and lack of complex elongated course. Exclusion criteria were history of immunodeficiency, use of immunosuppressor drugs, and death at arrival to the hospital.

This study was approved by local ethical committee. Data including demographic, diagnostic, and clinical findings were gathered by data collection form (checklist) with use the existing medical documents. The main outcome in patients was mortality. According to death occurrence the cases were subdivided into two groups; with and without death. The characteristics in two mentioned groups were compared to determine the contributing factors for mortality in patients with simultaneous COVID-19 and stroke.

Data analysis was done among 60 cases by SPSS (version 19.0) statistical software. The utilized tests for comparative means were Chi-Square, Exact-Fisher, and Logistic-Regression and the P values under 0.05 were considered statistically significant.

III. RESULTS

The cases were mainly older than 50 years (85.0%) and majority of them were male subjects (56.7%). The history of background disease is shown in Table I that showed diabetes mellitus and hyperlipidemia as main background diseases.

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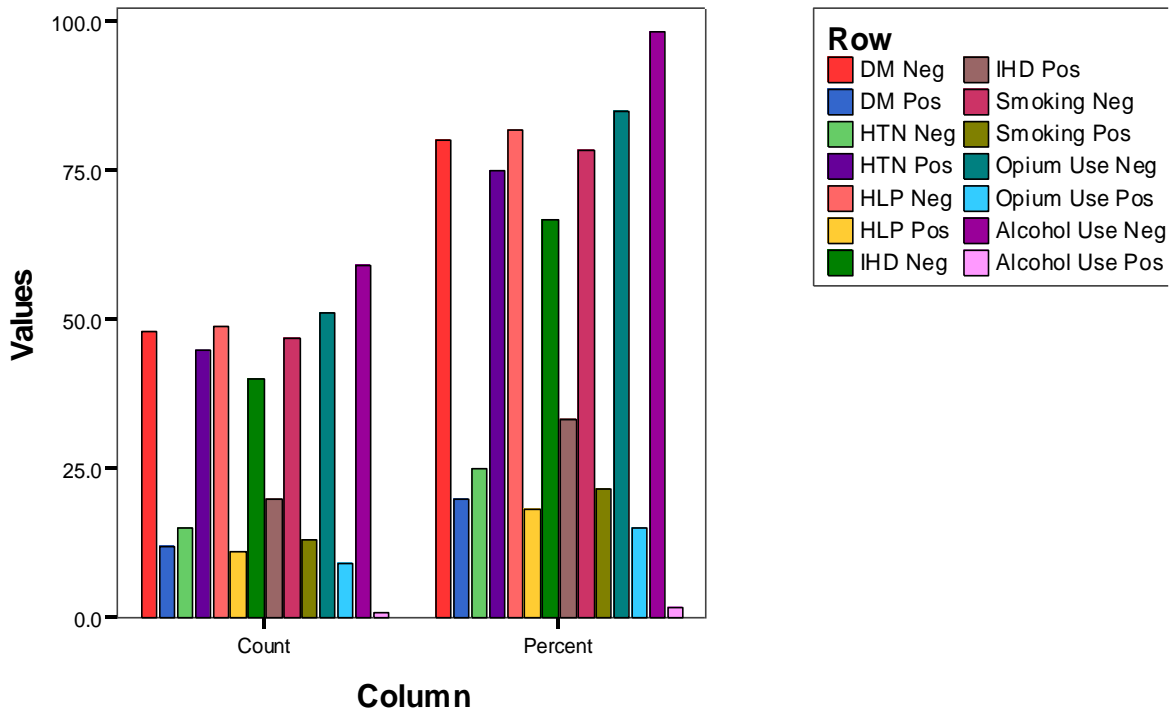


Figure I Frequency distribution of background diseases in patients

The stroke type was ischemic in 43 (71.7%) and it had high severity in 32 patients (53.3%). C reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were high in 36 cases

(60.0%) and 40 patients (66.7%), respectively. The imaging findings in the patients are demonstrated in Figure 2.

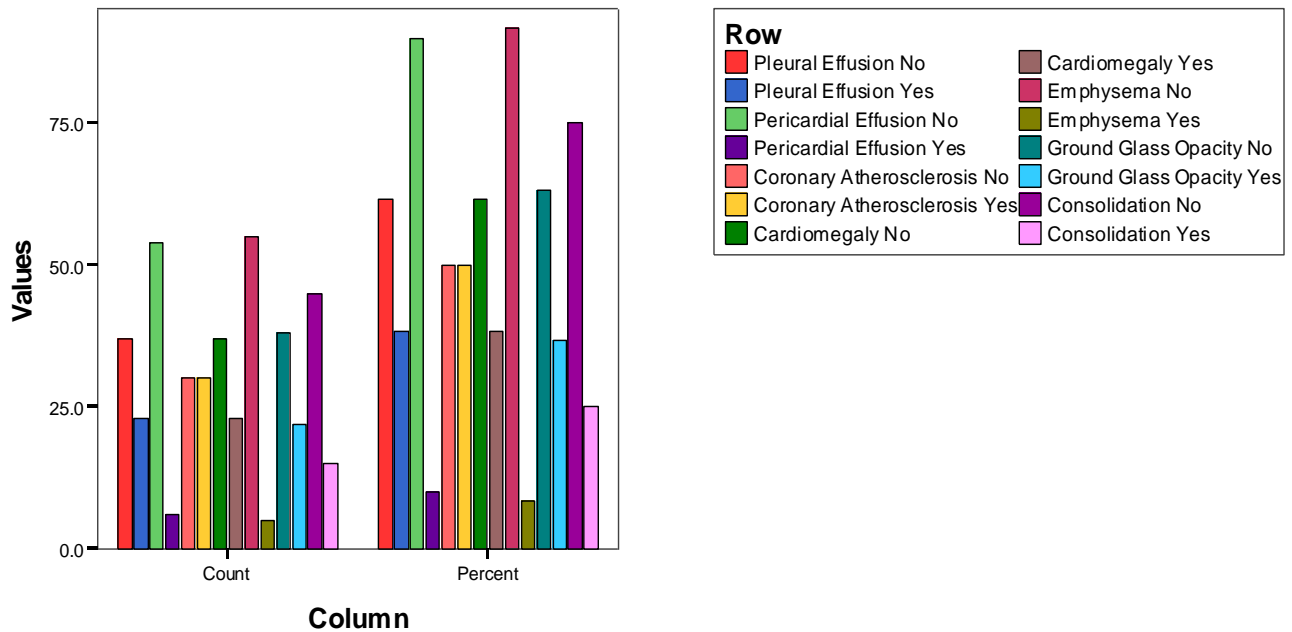


Figure 2- Findings by imaging techniques in the patients

Totally 23 out of 60 cases (38.3%) were expired. In univariate analysis (Table 1) there was significant association for death by ischemic heart disease ($P = 0.015$), high-severity stroke ($P = 0.012$), high CRP ($P = 0.001$), high ESR ($P = 0.009$), pleural effusion ($P = 0.005$), pericardial effusion ($P =$

0.027), cardiomegaly ($P = 0.005$), ground glass opacity ($P = 0.001$), and consolidation ($P = 0.001$). Among these factors, there was significant association only for CRP ($P = 0.001$) and consolidation ($P = 0.003$) in multivariate analysis.

TABLE 1
CONTRIBUTING FACTORS FOR DEATH IN UNIVARIATE ANALYSIS

		Outcome				
		Expired Count	Expired Percent	Survived Count	Survived Percent	P Value
Age	< 50	1	11.1%	8	88.9%	.134
	> 50	22	43.1%	29	56.9%	
Sex	Male	14	41.2%	20	58.8%	.604
	Female	9	34.6%	17	65.4%	
DM		4	33.3%	8	66.7%	.752
HTN		19	42.2%	26	57.8%	.283
HLP		2	18.2%	9	81.8%	.178
IHD		12	60.0%	8	40.0%	.015
Smoking		4	30.8%	9	69.2%	.749
Opium Use		3	33.3%	6	66.7%	1.000
Alcohol Use		1	100.0%	0	.0%	.383
Stroke Type	Hemorrhagic	5	29.4%	12	70.6%	.371
	Ischemic	18	41.9%	25	58.1%	
Stroke Severity	Low	6	21.4%	22	78.6%	.012
	High	17	53.1%	15	46.9%	
CRP	< 10	0	.0%	24	100.0%	.001
	> 10	23	63.9%	13	36.1%	
ESR	< 20	3	15.0%	17	85.0%	.009
	> 20	20	50.0%	20	50.0%	
Pleural Effusion		14	60.9%	9	39.1%	.005
Pericardial Effusion		5	83.3%	1	16.7%	.027
Coronary Atherosclerosis		14	46.7%	16	53.3%	.184
Cardiomegaly		14	60.9%	9	39.1%	.005
Emphysema		3	60.0%	2	40.0%	.362
Ground Glass Opacity		16	72.7%	6	27.3%	.001
Consolidation		13	86.7%	2	13.3%	.001

IV. DISCUSSION

In this study the mortality rate and related factors for death were evaluated and it was found that nearly one-third of cases with simultaneous stroke and COVID-19 infection were expired and the main contributing factors were high CRP levels and consolidation in lung CT scan. In [14] the reported mortality rate was 36%. Similarly in the study the background diseases were not related to the outcome in patients. However, in our study the presence of IHD was related to mortality in univariate analysis there was no association in multivariate analysis.

Ntaios et al. [15] reported that majority of cases with COVID-19 stroke had high-severity involvement as seen in our study that more than half of cases were severe stroke patients. Also, the death was related to Covid-19 infection in less than half of cases in Ntaios et al study [15] that is in line with our report. Mehrpour et al. [16] reported that there was no significant difference between mortality rates in stroke cases in three periods of time including before and during COVID-19 pandemic. But the mortality rate was lower than our report and it was sixteen percent during the pandemic.

The reported mortality rate in COVID-19-related stroke by [17] in a meta-analysis was 31.5% and it was near to our study. Yamakawa et al. [18] published another meta-analysis and reported mortality rate of 44% and it was slightly higher than our rate in current study. Differed mortality rates in some studies may be related to variations in coagulation status in

COVID-19 patients that is rationally related to therapeutic programs for stroke patients in different clinical health settings [19].

As mentioned by [20] presence of COVID-19 in stroke patients can increase the mortality rate by three times. For this prognostic role of COVID-19 in stroke cases in such patients, higher cares and clinical cautions should be considered to reduce the mortality rate and improve the prognosis [21]. Benny et al. [22] reported mortality in nearly one-third of stroke patients with COVID-19 infection and in their study type and severity of stroke were related to death. But in our study, there was no association in multivariate analysis. However, in their study CRP was related to death as seen in our study. Similar to our study, the report [23] demonstrated that two factors including CRP and consolidation were contributing factors with COVID-19 infection either with or without stroke.

V. CONCLUSION

Totally according to the results in this study the mortality rate in cases with COVID-19-related stroke is nearly one-third and it is related to high CRP levels and consolidation in lung CT scan. However further studies with larger sample population and multi-center samplings are required also with enrollment of control non-stroke patients with Covid-19 infection to attain more evidences in this era.

REFERENCES

- [1] Phan L, Chen-Li D, Iacobucci M, Ho R, Majeed A, McIntyre RS. Impact of COVID-19 pandemic on mental health in the general population: A systematic review. *J Affect Disord.* 2020; 277:55-64.
- [2] Mahalmani VM, Mahendru D, Semwal A, Kaur S, Kaur H, Sarma P, et al. COVID-19 pandemic: A review based on current evidence. *Indian J Pharmacol.* 2020; 52(2):117-29.
- [3] Zaim S, Chong JH, Sankaranarayanan V, Harky A. COVID-19 and Multiorgan Response. *Curr Probl Cardiol.* 2020; 45(8):100618.
- [4] Mokhtari T, Hassani F, Ghaffari N, Ebrahimi B, Yarahmadi A, Hassanzadeh G. COVID-19 and multiorgan failure: A narrative review on potential mechanisms. *J Mol Histol.* 2020; 51(6):613-28.
- [5] Wu T, Zuo Z, Kang S, Jiang L, Luo X, Xia Z, et al. Multi-organ Dysfunction in Patients with COVID-19: A Systematic Review and Meta-analysis. *Aging Dis.* 2020; 11(4):874-894.
- [6] Baig AM, Khaleeq A, Ali U, Syeda H. Evidence of the COVID-19 Virus Targeting the CNS: Tissue Distribution, Host-Virus Interaction, and Proposed Neurotropic Mechanisms. *ACS Chem Neurosci.* 2020; 11(7):995-8.
- [7] Renu K, Prasanna PL, Valsala Gopalakrishnan A. Coronaviruses pathogenesis, comorbidities and multi-organ damage - A review. *Life Sci.* 2020; 255:117839.
- [8] Lukiw WJ, Pogue A, Hill JM. SARS-CoV-2 Infectivity and Neurological Targets in the Brain. *Cell Mol Neurobiol.* 2020; 25:1-8.
- [9] Soltani Zangbar H, Gorji A, Ghadiri T. A Review on the Neurological Manifestations of COVID-19 Infection: A Mechanistic View. *Mol Neurobiol.* 2021; 58(2):536-49.
- [10] Solomon T. Neurological infection with SARS-CoV-2 - the story so far. *Nat Rev Neurol.* 2021; 17(2):65-6.
- [11] Wang L, Ren Z, Ma L, Han Y, Wei W, Jiang E, et al. Progress in Research on SARS-CoV-2 Infection Causing Neurological Diseases and Its Infection Mechanism. *Front Neurol.* 2021; 11:592888.
- [12] Reza-Zaldívar EE, Hernández-Sapiéns MA, Minjárez B, Gómez-Pinedo U, Márquez-Aguirre AL, Mateos-Díaz JC, et al. Infection Mechanism of SARS-COV-2 and Its Implication on the Nervous System. *Front Immunol.* 2021 Jan 29; 11:621735.
- [13] Correia AO, Feitosa PWG, Moreira JLS, Nogueira SÁR, Fonseca RB, Nobre MEP. Neurological manifestations of COVID-19 and other coronaviruses: A systematic review. *Neurol Psychiatry Brain Res.* 2020; 37:27-32.
- [14] Requena M, Olivé-Gadea M, Muchada M, García-Tornel Á, Deck M, Juega J, et al. COVID-19 and Stroke: Incidence and Etiological Description in a High-Volume Center. *J Stroke Cerebrovasc Dis.* 2020; 29(11):105225.
- [15] Ntaios G, Michel P, Georgiopoulos G, Guo Y, Li W, Xiong J, et al. Characteristics and Outcomes in Patients With COVID-19 and Acute Ischemic Stroke: The Global COVID-19 Stroke Registry. *Stroke.* 2020; 51(9):254-8.
- [16] Mehrpour M, Shuaib A, Farahani M, Hatamabadi HR, Fatehi Z, Ghaffari M, et al. Coronavirus disease 2019 and stroke in Iran: a case series and effects on stroke admissions. *Int J Stroke.* 2020:1747493020937397.
- [17] Nannoni S, de Groot R, Bell S, Markus HS. Stroke in COVID-19: A systematic review and meta-analysis. *Int J Stroke.* 2021; 16(2):137-49.
- [18] Yamakawa M, Kuno T, Mikami T, Takagi H, Gronseth G. Clinical Characteristics of Stroke with COVID-19: A Systematic Review and Meta-Analysis. *J Stroke Cerebrovasc Dis.* 2020; 29(12):105288.
- [19] Diener HC, Berlitz P, Masjuan J. COVID-19: patients with stroke or risk of stroke. *Eur Heart J Suppl.* 2020; 22(Suppl Pt t):25-8.
- [20] Trejo-Gabriel-Galán JM. Stroke as a complication and prognostic factor of COVID-19. *Neurologia.* 2020; 35(5):318-22.
- [21] Siniscalchi A, Gallelli L. Could COVID-19 represent a negative prognostic factor in patients with stroke? *Infect Control Hosp Epidemiol.* 2020; 41(9):1115-6.
- [22] Benny R, Singh RK, Venkitachalam A, Lalla RS, Pandit RA, Panchal KC, et al. Characteristics and outcomes of 100 consecutive patients with acute stroke and COVID-19. *J Neurol Sci.* 2021; 423:117348.
- [23] Izcovich A, Ragusa MA, Tortosa F, Lavena Marzio MA, Agnoletti C, Bengolea A, et al. Prognostic factors for severity and mortality in patients infected with COVID-19: A systematic review. *PLoS One.* 2020; 15(11):e0241955.