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Exploring the Relationship Between Air Quality and Ischemic Stroke Admissions During the COVID-19 Pandemic

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Objectives: Amongst all the global catastrophe due to Coronavirus disease 2019, a significant bright spot is a reduction in air pollution as countries undergo lockdowns to limit the spread of infection. Another reduction that has been reported is in the number of strokes presenting to hospitals, despite the virus implicated in causing a hypercoagulable state. Acute exposure to air pollution has been linked to increase in stroke incidence and the improvement in air quality may be responsible for the decrease in stroke presentations. Materials and Methods: To explore this hypothesis, we compared the air quality index (AQI) of Karachi, the largest cosmopolitan city of Pakistan, during the lockdown period in 2020 to the same period in the previous year. Results: We found a significant drop in AQI depicting an improvement in air quality. Simultaneously, we identified a drop in number of stroke admissions to less than half from 2019 to 2020 at one of the largest tertiary care hospitals of the city, during this period of interest. Conclusion: We hypothesize that one important reason for this drop in stroke admissions, may be an actual reduction in stroke incidence brought about by an improvement in air quality.

Key Words: Stroke—Air pollution—Covid—Air quality index—South Asia—Pandemic

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Corresponding author. E-mail: Mohammad.wasay@aku.edu. 1052-3057/\$ - see front matter © 2021 Elsevier Inc. All rights reserved. https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.105860 Coronavirus disease 2019 (COVID-19) is an unprecedented and the deadliest pandemic of our times. It has been just over a year that the first case was detected in Wuhan, China, and the virus has afflicted over a hundred million people and taken more than 2.5 million lives.¹ To limit the spread of coronavirus, global lockdown measures have been implemented that include decreased mobility of the general population with a focus on staying at home, closure of international borders, schools, small businesses, and industries. Among a multitude of economic and health devastations due to the COVID-19 pandemic, a significant bright spot is a reduction in air pollution² as factories remain closed and exhaust from vehicles is down to a minimum.

Air pollution has been ranked as the fifth global risk factor accounting for 7.6% of total global mortality in 2015.³ Stroke amongst other cardiovascular diseases has a special link to air pollution and according to the GBD study 2013, 29.2% of the global stroke burden was attributable to it.⁴ The ill effects of chronic exposure to air pollution are well documented and studied. However, the acute exposure (up to seven days) to air pollution also has a marked association with increased stroke incidence and mortality.⁵ Chen et al have shown this association between air quality index (AQI) as a predictor of emergency visits for ischemic strokes.⁶

Globally a number of countries have reported a drop in the stroke admissions and several reasons are being suggested for this. We hypothesized that a drop in air pollution that is expected to accompany lockdowns in many countries may partly be responsible for this decrease. The objectives of our study were; to evaluate improvement in air quality during the lockdown period in Karachi, Pakistan, which ranks amongst the top ten most polluted cities of the world; and to correlate this with the number of stroke admissions at one of the largest tertiary care hospitals in the city.

Methods

The Air Quality Index (AQI) is an indicator developed by United States Environment Protection Agency (US EPA) as a measure for overall assessment of air quality. Raw concentrations of PM 2.5 (particulates less than or equal to 2.5 microns) are converted into AQI values. These range from 0 to 500 μ g/m³, and values below 50 are considered generally satisfactory. AQI data for Karachi was

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taken from the US EPA at the U.S. Embassy and Consulates in Pakistan⁷. This is an online repository available for public use. We focused on data that was available for both 2019 and 2020 to keep the comparison bias free. Data from May to July 2019 (pre-pandemic period) was extracted and compared to data from May to July 2020 (lockdown period). Independent sample t-test was done to evaluate the difference between the mean AQI indices of the two years. $p \leq 0.05$ was considered significant.

Data of all ischemic stroke admissions in the Department of Neurology of the Aga Khan University Hospital, Karachi, Pakistan during the three-month period of lockdown from May to July 2020 was obtained from the medical record section and compared with the stroke admissions during the same three-month period in the previous year, i.e. 2019. Although the lockdown spanned from mid-March to July 2020, these three months were chosen for comparison and correlation as AQI data was available for both years, 2019 and 2020, for this period only. Study protocol was approved by Ethics review committee of Aga Khan University, Karachi

Results

From May to July 2020 (entire lockdown period), a total number of 53 ischemic stroke patients were admitted; 74% (n = 39) were male and the mean age was 60 years. The ischemic stroke admissions were significantly decreased during the same three-month period in 2019 (n = 141). No significant gender or stroke type differences were noticed. However, a difference in the mortality rate was seen. In 2020, mortality rate was zero, while the mortality rate was 2.8% (n = 4) in 2019. Baseline demographic factors as well as stroke type and severity of the patients admitted from May to July in 2019 and 2020 are summarized in Table 1.

We also collected the online PM2.5 AQI data of Karachi, Pakistan. We could only access the last 20 months of AQI data that included our focused lockdown period of May-July 2019 and 2020. There was a significant decrease in AQI between the two years. The mean AQI from May to July 2019 was 93.7 (SD 17.74) and this dropped significantly to 73.31 (SD 21.05) (p < 0.001) in May to July 2020. To further establish that the lockdown was responsible for this drop in AQI, we also compared the pre-lockdown values from the same year of 2020 to the post-lockdown values. In Karachi, the lockdown commenced on March 15, 2020. The average AQI pre-lockdown from 1–14 March 2020 is recorded to be 126.15 (SD 70.85), which dropped to 90.26 (SD 66.32) in the last half of March (p < 0.001).

We plotted the AQI for the three months in 2019 and 2020 along with the stroke admissions for the two years to assess this relationship (Fig. 1) and found a positive correlation with increasing air pollution (suggested by a higher AQI) and number of stroke admissions.

 Table 1. Baseline demographic factors and stroke severity of the patients admitted from May to July 2019 and 2020

1		
	2019	2020
No. of Patients	141	53
Age [years] (mean \pm SD)	62 ± 12	60 ± 13.9
Gender:		
Male	74% (105)	74% (39)
Female	26% (36)	26% (14)
Co-morbids:		
HTN	80% (112)	70% (37)
DM	62% (87)	42% (22)
Dyslipidemia	30% (42)	23% (12)
AF	3.5% (5)	7.5% (4)
Stroke Territory:		
MCA	62% (87)	62% (33)
PCA	29% (41)	25% (13)
ACA	4% (6)	2% (1)
≥ 2	5% (7)	11% (6)
Stroke Type		
Small-vessel	47% (66)	51% (27)
Large-vessel	35% (50)	26% (14)
Cardioembolic	14% (19)	17% (9)
Unknown/Idiopathic	4% (6)	6% (3)
Treatment:		
tPA	3.5% (5)	7.5% (4)
Single AP only	46% (65)	36% (19)
Dual AP only	40% (57)	38% (20)
AC only	3.5% (5)	15% (8)
AC + AP	8% (12)	6% (3)
mRS (mean)	2.31	2.34
Complications:		
Pneumonia	13% (19)	26% (14)
UTI	7% (10)	15% (8)
Mortality	2.8% (4)	0

Abbreviations: AC = Anti-coagulation; ACA = Anterior cerebral artery; AF = Atrial fibrillation; AP = Antiplatelet; DM = Diabetesmellitus; HTN = Hypertension; MCA = Middle cerebral artery; PCA = Posterior cerebral artery; SD = Standard deviation; tPA = tissue plasminogen activator; UTI = Urinary tract infection.

Discussion

We report a decrease in stroke admissions during the pandemic at one of the largest tertiary care hospitals in Karachi, Pakistan. We have simultaneously demonstrated an improvement in air quality as evidenced by a drop in AQI compared to pre-pandemic period in the preceding year as well as pre-lockdown period of the same year. This AQI drop is secondary to the strict lockdown that resulted in this large cosmopolitan city to control the spread of the pandemic. We believe, the reduction in strokes may partly be explained by improvement in the air quality.

A number of countries have reported decreased number of stroke admissions during the COVID-19 period⁸. In Italy, Morelli et al. reported only six stroke admissions in a month during the COVID-19 lockdown in their hospital

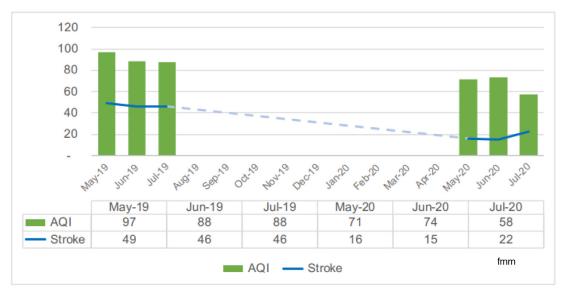


Fig. 1. AQI and stroke admissions.

compared to the monthly average of 51 stroke admissions.⁹ Another study from Italy reported a 45% reduction in stroke admissions during the lockdown compared to the same period in 2019 with similar mortality rates. However, they reported higher admission National Institutes of Health Stroke Scale (NIHSS) scores among their stroke patients.¹⁰ Two Egyptian stroke centers also reported a reduction in the stroke admissions in the COVID period as compared to the pre-COVID period (n = 93 vs n = 151).¹¹ This reduction in stroke admissions is puzzling considering COVID-19 reportedly causes a systemic pro-thrombotic state and has been associated with large artery strokes.

Various studies explain this decline to result from milder strokes and Transient Ischemic Attacks (TIA) not reaching stroke services due to these facilities being overwhelmed by COVID patients or the patients themselves avoiding hospital visits. This explanation is supported by several studies from England,¹² Germany,¹³ Brazil¹⁴ and the United States.¹⁵

We hypothesize that an alternative explanation for this drop in stroke admissions may be related to an actual decrease in the incidence of stroke during the lockdown period. This reduction may be resulting from an improvement in air quality resulting from the lockdowns in various major cities.^{16,17} During the COVID-19 pandemic, a recent study obtained PM2.5 levels before and during the lockdown from the four major cities of Pakistan and reported a mean PM2.5 reduction of 38.03%. This PM2.5 reduction was estimated to reduce all-cause mortality by 28-32% and stroke mortality by 19-21% using the AirQ+ model [Fayyaz, Mahmood, Khan, Safdar, Fatmi. Fine particulate matter and potential mortality in major cities of Pakistan: AirQ+ model. Journal of social and policy sciences (JSAPS); manuscript under review]. Another study reported an average reduction of 31% of the global

population-weighted PM2.5 during the lockdown.¹⁸ NASA satellites have also documented a significant reduction in air pollution, 20% - 30% in many major cities globally.

Short-term and long-term effects of air pollution on stroke incidence, morbidity, and mortality are well-documented.⁵ One study from China evaluated the association between short-term exposure to air pollution and ischemic stroke admission on the same day, and found a positive correlation.¹⁹ A meta-analysis reported that for every 10 μ g/m³ increase in PM2.5, there is a pooled excess risk of 11% (95% CI, 5% to 16%) for cardiovascular mortality.²⁰ Carotid artery stenosis, one of the risk factors for ischemic stroke, is also reported to be independently associated with increasing PM2.5 concentration.²¹ Population attributable risk factor for PM2.5 was highest for stroke (19.6%) as compared to other cardiovascular diseases in a large multinational cohort study.²²

Therefore, one possible explanation for a reduction in stroke admissions may be an actual decrease in incidence of stroke during the lockdown months when the air pollution had significantly reduced. In addition, there was a significant reduction in mortality rates among stroke patients in our center during the lockdown and this may also be attributed in part to the reduction in the air pollution. Other possible explanation may include population shifts and limited movement of patients from out of city to our center. The population of the city of Karachi is growing at a rate of 7% per year. However, due to lockdown this rate must have slowed down substantially and we do not expect a major difference in population during the years. There were also no indications of huge population exodus from Karachi during lockdown which may have some implications on hospital admissions. The major difference in these two periods was absence of vehicles on the roads and major industries which were not operating to its full

potential. The population health seeking might be affected for health conditions which do not need urgent attention, however, we assume that most stroke patients would have sought health care during the lockdown period.

This study has several limitations. Firstly, the stroke data is a single center data and a wider sampling frame would have provided us with more reliable statistics. Also, the AQI data is only for PM2.5 and measurements of other pollutants would have validated this improvement further. Thirdly, this is merely a correlational study where a number of individual factors that can confound this finding, could not be evaluated.

However, we believe our findings are enough to recommend that the current COVID-19 pandemic situation be used as a useful lens to visualize the impact of air pollution on our health in general, and stroke in particular. These findings warrant further exploration and research. Raising public awareness as well as advising and implementing interventions to limit air pollution is the need of the hour.

References

- WHO Coronavirus Disease (COVID-19) Dashboard: World Health Organization; 2021 updated January 24, 2021. Available from: https://covid19.who.int/.
- 2. Nelson B. The positive effects of COVID-19. BMJ 2020:369.
- **3.** Cohen AJ, Brauer M, Burnett R, Anderson HR, Frostad J, Estep K, et al. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. The Lancet 2017;389(10082):1907-1918.
- Feigin VL, Roth GA, Naghavi M, Parmar P, Krishnamurthi R, Chugh S, et al. Global burden of stroke and risk factors in 188 countries, during 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet Neurol 2016;15(9):913-924.
- Shah AS, Lee KK, McAllister DA, Hunter A, Nair H, Whiteley W, et al. Short term exposure to air pollution and stroke: systematic review and meta-analysis. BMJ 2015:350.
- Chen L, Villeneuve PJ, Rowe BH, Liu L, Stieb DM. The Air Quality Health Index as a predictor of emergency department visits for ischemic stroke in Edmonton, Canada. J Expo Sci Environ Epidemiol 2014;24(4):358-364.
- US EPA, US Embassy and Consulates in Pakistan. Air Quality Data 2020 2021. Available from: https://pk. usembassy.gov/embassy-consulates/air-quality-data/.
- 8. Kim JS. Coronavirus Disease 2019 and Stroke. J Stroke 2020;22(2):157-158.

- 9. Morelli N, Rota E, Terracciano C, Immovilli P, Spallazzi M, Colombi D, et al. The baffling case of ischemic stroke disappearance from the casualty department in the COVID-19 Era. Eur Neurol 2020;83(2):213-215.
- Naccarato M, Scali I, Olivo S, Ajcevic M, Buoite Stella A, Furlanis G, et al. Has COVID-19 played an unexpected "stroke" on the chain of survival? J Neurol Sci 2020;414:116889.
- Roushdy TM, Nahas NME, Aref HM, Georgy SS, Zaki AS, Bedros RY, et al. Stroke in the time of Coronavirus disease 2019: experience of two University Stroke Centers in Egypt. J Stroke 2020;22(2):275-277.
- 12. Perry R, Banaras A, Werring DJ, Simister R. What has caused the fall in stroke admissions during the COVID-19 pandemic? J Neurol 2020;267(12):3457-3458.
- Hoyer C, Ebert A, Huttner HB, Puetz V, Kallmunzer B, Barlinn K, et al. Acute stroke in times of the COVID-19 pandemic: a multicenter study. Stroke 2020;51(7):2224-2227.
- 14. Diegoli H, Magalhaes PSC, Martins SCO, Moro CHC, Franca PHC, Safanelli J, et al. Decrease in Hospital Admissions for Transient Ischemic Attack, mild, and moderate stroke during the COVID-19 era. Stroke 2020;51(8):2315-2321.
- Siegler JE, Heslin ME, Thau L, Smith A, Jovin TG. Falling stroke rates during COVID-19 pandemic at a comprehensive stroke center. J Stroke Cerebrovasc Dis 2020;29 (8):104953.
- Shrestha AM, Shrestha UB, Sharma R, Bhattarai S, Tran HNT, Rupakheti M. Lockdown caused by COVID-19 pandemic reduces air pollution in cities worldwide. 2020.
- Fu F, Purvis-Roberts KL, Williams B. Impact of the covid-19 pandemic lockdown on air pollution in 20 major cities around the world. Atmosphere 2020;11(11):1189.
- Venter ZS, Aunan K, Chowdhury S, Lelieveld J. Air pollution declines during COVID-19 lockdowns mitigate the global health burden. Environ Res 2021;192:110403.
- Tian Y, Liu H, Zhao Z, Xiang X, Li M, Juan J, et al. Association between ambient air pollution and daily hospital admissions for ischemic stroke: a nationwide time-series analysis. PLoS Med 2018;15(10):e1002668.
- Hoek G, Krishnan RM, Beelen R, Peters A, Ostro B, Brunekreef B, et al. Long-term air pollution exposure and cardio- respiratory mortality: a review. Environ Health 2013;12(1):43.
- 21. Newman JD, Thurston GD, Cromar K, Guo Y, Rockman CB, Fisher EA, et al. Particulate air pollution and carotid artery stenosis. J Am Coll Cardiol 2015;65(11):1150-1151.
- 22. Hystad P, Larkin A, Rangarajan S, AlHabib KF, Avezum A, Calik KBT, et al. Associations of outdoor fine particulate air pollution and cardiovascular disease in 157 436 individuals from 21 high-income, middle-income, and low-income countries (PURE): a prospective cohort study. Lancet Planet Health 2020;4(6):e235-ee45.