International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Neurological Manifestations in Stroke Patients: A Comparative Analysis of COVID-19 and Non-COVID-19 Cases

Sinto Francis[1], K. Sangita[2]

[1]Physiotherapist, Fairlie Health Care Group London, UK
Email: *sintofrancis91[at]gmail.com*

[2]Assistant Professor, Medical Trust, Institute of Medical Science
Email: *sangikey[at]gmail.com*

Abstract: ***Background: Millions of individuals are being affected by the 2019 corona virus disease (COVID-19), which has spread globally. Although there is uncertainty regarding the origin and pattern of this association, certain neurological abnormalities, including stroke, have been reported in individuals with corona virus infection 2019 (COVID-19). Stroke and COVID-19 may be related; however, the exact nature of this connection is unknown. Aims: The aim of my study is to analyze and compare the neurological impairment between stroke patients with COVID-19 and those who are not. Methods: For this study, I followed PRISMA criteria to search published literature for data demonstrating clinical manifestations of stroke with and without COVID-19 reports. For published studies, the following databases were evaluated: PubMed, Google Scholar, Springerlink and Medline. Data were manually retrieved from research that qualified. Results & Conclusions: This narrative review explores the neurological manifestations in stroke patients affected by COVID-19 compared to those unaffected. Utilizing data from 30 studies, this review highlights the prevalence of ischemic strokes in COVID-19 patients, associated risk factors, and clinical symptoms. Findings suggest that COVID-19 intensifies the risk of cerebrovascular events through hypercoagulation and systemic inflammation, emphasizing the need for continuous monitoring and targeted interventions for stroke prevention in COVID-19 patients.***

Keywords: COVID-19, stroke, neurological manifestations, ischemic stroke, cerebrovascular disease

1. Introduction

Severe acute respiratory syndrome Corona Virus 2 was first discovered in Wuhan, China and it was considered as an epidemic of Pneumonia during January 2020. (WHO, Accessed October 26, 2020.) It was found to be highly contagious and very soon it was declared as global pandemic during March 2020. (WHO, Accessed October 26, 2020) Symptoms of Covid-19 varies from person to person ranging from affection in respiratory system (Chen N et al, 2020), special senses like loss of taste, smell (Agyeman AA et al, 2020), myalgia or fatigue, headache, hemoptysis and diarrhoea (Chaolin Huang et al, 2020), fever. (Islam MA et al, 2021) Studies has shown some critical symptoms like respiratory failure, shock or multi organ dysfunction. (7) COVID-19 has also impacted mental health, leading to symptoms like depression, anxiety, and insomnia, while exacerbating pre-existing conditions (Betty Pfefferbaum et al, 2020), post-traumatic stress disorder and stress. (JiaqiXiong et al, 2020)

Many neurological symptoms were also shown by many Covid 19 affected individuals. The symptoms include agitation, dysexecutive syndromes like inattention, disorientation, poorly organised movement in response to command. (Helms J et al, 2020) Impaired consciousness was seen in severely ill subjects. (Mao L et al, 2020) Ischemic stroke is also a complication in severely ill Covid 19 patients.

SARS-CoV-2 is potentially a higher precipitating factor for acute ischemic stroke compared to other classic respiratory infection such as influenza, particularly systemic upper respiratory illness is an important precipitating risk factor. (Lodigiani C et al, 2020) Boehme et al. also reported that risk of acute stroke increases 9 times in young population aged 18-45 within 15 days from onset of influenza-like illness. Another cause of ischemic stroke can be through hypercoagulative state, endothelial injury and cardiogenic embolism. (Markus Hugh S and Brainin Michael, 2020)

Recurrent stroke was defined as any new stroke occurring with an onset separate from that of the index stroke. If a recurrent stroke occurred within 21 days of the index stroke, and was in the same vascular territory, then it was only included if it additionally fulfilled at least one of the following two criteria: (1) there was a new area of acute infarction on neuroimaging or (2) there was a new intracerebral haemorrhage anatomically separate from the infarct or haemorrhage of the index stroke. (Richard J Perry et al, 2021)

The motive of my study is to make a review in comparing the neurological impairment among stroke patients affected with Covid 19 and those without affected with Covid 19.

Definition and Types of Strokes

The first recorded use of ‘stroke’ as a lay term was in 1599. (Coupland et al, 2017) Transient ischemic attacks were previously defined as ‘a sudden, focal neurologic deficit that lasts for less than 24 hours, is presumed to be of vascular origin, and is confined to an area of the brain or eye perfused by a specific artery’. (Albers GW et al, 2002) In 2009 a new definition of transient ischemic attack was endorsed: ‘a transient episode of neurological dysfunction caused by focal brain, spinal cord or retinal ischemia, without acute infarction’. (Easton JD et al, 2009) In 1970, the World Health

Organization defined stroke as 'rapidly developed clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than of vascular origin'. (Aho K et al,) Even though the 'traditional' clinical definition of stroke is still included, a small change has been introduced by the American Heart Association/American Stroke Association, that is the inclusion of 'silent' pathology which is a significant addition. The rationale behind such a change was to move towards a radiological demonstration (tissue-based definition) of infarction or haemorrhage. (Coupland et al, 2017)

Stroke has been estimated to be second leading cause of death world-wide. Approximately 87% of stroke type is ischemic in variety and whose prevalence has subsequently increased since 1990 to 2016. Primary haemorrhage (first time) comprises of the majority of stroke in hemorrhagic variety, with secondary hemorrhagic (second time) constituting an estimated range of 10-25%. (Kuriakose et al, 2020)

Incidence and Epidemiology

One of the main neurological complications of Covid 19 is acute ischemic stroke. (Merkler AE et al, 2020) The incidence of stroke following covid 19 ranges from 0.9% – 3.3%, which was found from a group of retrospective cohort studies. (Aisha Elfasi et al, 2021) When comparing covid 19 and influenza, patients with influenza were less likely to be admitted to an ICU or receive mechanical ventilator and had a lower D dimer and erythrocyte sedimentation rate. Patients with Covid 19 were more likely to have an acute ischemic stroke. A 7•6-fold increase in the odds of stroke with COVID-19 compared with influenza has been reported. (Merkler AE et al, 2020) The morbidity of stroke in Covid 19 patients ranged from 0 to 5%. A pooled prevalence of ischemic stroke in Covid 19 is 2%. On comparing male and female, females were found to have a pooled proportion of 36%. (Luo et al, 2022) Compared with females, males had higher mortality (38% vs.13%; $p = 0.02$) and were less likely to be discharged home. (Trifan G et al, 2020)

Incidence of Types of Stroke in COVID 19

When divided by stroke subtype, there were 77% ischemic, 19% intracerebral hemorrhage and 3% subarachnoid hemorrhage. The most common ischemic stroke etiologies were cryptogenic (39%) and cardio embolic (27%). (Trifan G et al, 2020)

Risk Factors Associated with Stroke in COVID 19

Risk factors in stroke can be divided as modifiable and non-modifiable risk factors. Those risks that can be treated or controlled are termed as modifiable risk and those risks that cannot be changed is termed as non-modifiable risk factors. The modifiable types of risk factor are smoking, high blood pressure, carotid or other artery disease, history of transient ischemic attack (TIA), diabetes, high blood cholesterol, physical inactivity and obesity. The non-modifiable type of risk is age (older age group), gender (males more affected than female), hereditary and race, prior stroke or heart attack. The risk factors associated with acute ischemic stroke includes hypertension, diabetes, hyperlipidaemia, atrial fibrillation, and congestive heart failure. (Adnan I. Qureshi, 2021) Patients with COVID-19 infection are at heightened risk for medical complications, such as atrial arrhythmias, myocardial infarction, heart failure, myocarditis, and venous thrombosis, all of which likely contribute to the risk of ischemic stroke. (Merkler AE et al, 2020)

Difference in Risk Factors between Haemorrhagicand Ischemic Stroke

Majority of the risk factors remain similar in both ischemic and haemorrhagic type of stroke but some differences has been found among both the types. Even though hypertension is a risk factor for both the types, haemorrhagic variety is more prone for it whereas hyperlipidemia is more important risk factor ischemic variety as it can produce atherosclerotic plaque formation of extra cranial and intra cranial blood vessels. (Tirschwell DL et al, 2004) Smoking and alcohol intake has been found to favour Haemorrhagic stroke. Other risk factors that favours Ischemic stroke more are diabetes, atrial fibrillation, previous myocardial infarction, previous stroke and intermittent arterial claudication. (Klaus Kaae Andersen et al, 2009)

Pathology of General Stroke and Stroke Associated with COVID 19

Usually, stroke occurs due to two main causes-ischemic or hemorrhagic. Ischemic type of stroke occurs due to deficient blood and oxygen supply to the brain structure and hemorrhagic variety occurs due to rupture or leaking of any blood vessels.

Ischemic variety accounts for 85% of stroke and occurs mainly due to thrombosis or embolism. Interruption of blood flow brings about a sequel of cellular alteration which mainly depends on the time, topography, severity and duration of ischemia. The most sensitive brain cells are neurons followed by oligodendrocytes, astrocytes and vascular cells. The most vulnerable brain region are hippocampal subfield CA1, neocortical layer 3, 5, 6, the outer segments of striate nucleus and the purkinje and cerebellar cortex.

When brain arteries are occluded, cell injury occurs in the core area of the territory causing swelling or shrinkage. These changes are reversible if blood flow is restored before mitochondrial membrane begins to rupture.1 or 2 hours after the onset of ischemia, the neurons undergo several irreversible necrotic alterations. With ongoing ischemia, neuron gradually loss their sustainability and after 2 – 4 days, transforms to ghost cells. The most prominent alteration during the initial 1 – 2 hours is perivascular and perineuronal astrocytic swelling, after 4 – 6 hours blood brain barrier breaks down resulting in the formation of vasogenic edema, after 1 – 2 days inflammatory transformation of the necrotic tissue occurs together with the development of a peri infarct astroglial scar. (Hossmann, K and Heiss, W, 2019)

Stroke is the result of ischemia in an area of the brain. The Na^+/K^+ ATPase pumps fail mainly because of the poor production of adenosine triphosphate (ATP) and failure of the aerobic mechanism. Ischemia leads to depolarization of cells which results in calcium influx into cells, elevated lactic acid, acidosis, and free radicals. Cell death increases glutamate and leads to a cascade of chemicals (excitotoxicity). (Xing C et al, 2012)

ACE2 was identified as the functional receptor for SARS-CoV-2, which is present in multiple human organs, including nervous system and skeletal muscles. (Mao L et al, 2019) SARS CoV2 binds to angiotensin – converting enzyme 2 (ACE2) receptor with viral surface spike (S) protein and by this way it gains entry to host cell. (Hoffmann Markus et al, 2020) ACE2 has a wide expression in human body, specifically in the neurons, glial cells, endothelial cells, and arterial smooth muscles in the central nervous system. (Baig Abdul Mannan et al, 2020) This makes the central nervous system to get vulnerable targets.

Coagulopathy attributes to thrombotic events and has been widely observed in COVID-19 patients regardless of severity. More than 95% of severe COVID-19 patients have elevated levels of Ddimer and fibrinogen. (Helms Julie et al, 2020) Hypercoagulability as well has been reported in both severe and mild COVID-19 patients. Clot waveform analysis (CWA) demonstrated hypercoagulability that precedes or coincides with severe illness. (Tan CW et al, 2020) Hypercoagulability, along with a systemic inflammatory response to the viral infection, could lead to macro-and micro thrombi formation, ultimately eliciting cerebrovascular incidents. (Panigada Mauro et al, 2020)

Clinical Features of Stroke

In a study conducted by Rauk Soto Camara et al, the knowledge of signs and risk factors were assessed. The study was a cross-sectional descriptive study and the age of the patients selected was 18 years and above over a period of 12 months, diagnosed with stroke. A total of 583 patients were eligible for the study out of which 54 patients were excluded due to various reasons in between the study period. The mean age was 75.36.84.31% of subjects were encountered with ischemic variety of stroke and 15.69% were affected with hemorrhagic type of stroke. High blood pressure, cardio vascular disease and overweight / obesity were the most frequent risk factors reported by the patients. The common clinical symptoms reported were loss of strength / weakness, speech and language disturbance. (Soto-Cámara et al, 2020)

In a study on the risk factors, clinical presentation and predictors of stroke among adult patients admitted to stroke unit of Jimma University Medical Center, South West Ethiopia, conducted by Fekadu, G et al, the most common clinical presentations were headache followed by aphasia and hemiparesis. Atrial fibrillation was an independent predictor of hemorrhagic stroke. Most of the ischemic stroke patients presented with headache, aphasia and facial palsy. Similarly, among the hemorrhagic stroke patients, the common clinical manifestations were headache followed by aphasia and vomiting. Hemorrhagic stroke patient was more likely to be presented with coma, vomiting and neck stiffness but ischemic stroke patients were more likely to be presented with chest pain. The average clinical presentation per patients was found to be 6 that ranged from 2 to 12. (Fekadu et al, 2019)
A study was conducted by Anna M Pietroboni et al to find the clinical features and disease course of patients with acute ischemic stroke just before the first reporting case of covid 19 in Italy. Here they divided the patients into 2 groups. The first group of patients consisted with those who encountered stroke from December 15, 2018 to February 20, 2019 and the second group from December 15, 2019 to February 20, 2020 (till 1 day before the first reporting case of covid 19). No significant differences were found among both the groups in terms of demographical characteristics and comorbidities including hypertension, diabetes, hyper cholesterolemia and coronary heart disease. But a major difference found was that the frequency of cryptogenic stroke was increased during 2019 and 2020 and group 2 had a longer hospitalisation day. (Pietroboni et al, 2021)

In another study conducted by Saif S Rathore et al, on the clinical characterisation of incident stroke and signs and symptoms. Potential stroke events in ARIC Atherosclerosis Risk in Community were identified from cohort of 15792 individual aged between 45 – 64 years. More than 25% of subjects hospitalised with a confirmed stroke presented with a headache at admission, while vertigo, convulsion and gait disturbance were less frequent. The most common presented signs were speech deficit, followed by hemianopia and diplopia. More than 80% of subjects presented with some paresis, most often in the upper limb and face than the lower limb. Many subjects also experienced deficit in sensation. (Saif S. Rathore et al, 2002)

2. Methodology

This systematic review utilized the PRISMA (Preferred Reporting Items for Systemic review) statement in conjunction with the PRISMA checklist and flow diagram for manuscript format development (Liberati A et al, 2009).

Literature Search

In this study, I searched published literature that provided evidence of clinical manifestation manifestations of stroke affected by with COVID-19 and without COVID-19. The following databases were reviewed for published studies prior to May 01, 2022: PubMed, Google Scholar, Springerlink and Medline. The following search strategy was adopted: COVID-19 OR SARS-CoV-2, Stroke or cerebrovascular accident, Neurological manifestation and COVID-19, stroke and Covid 19. AND neurological OR neurologic OR CNS OR nervous AND manifestation OR symptoms OR presentation. Titles, abstracts, and full text were screened to ensure whether they met eligibility criteria.

Eligibility criteria

Included any study, (1) published in English language, (2) which reported neurological manifestations in patients infected by SARS-CoV-2. (3) Articles that focused on ischemic stroke or hemorrhagic stroke associated with COVID-19. (4) Diagnosis of all patients with stroke was based on imaging and clinical symptoms, (5) Studies or articles published from December 2019 to May 2022. This included case reports and pre-print publications, (6) Literatures through database Google scholar, Pubmed, Medline, Springerlink. (7) Publications of cohort studies, case series, case report were assessed. Both male and female were included.

Excluded studies that were reported as (1) abstract-only (with no full-texts available), (2) non-English articles, (3) studies conducted on animal subjects, (4) studies on pediatric populations, and (5) repeat publications on the same patient cohorts, excluded all review articles and hypotheses papers.

Data extraction
Data were manually gathered from research that qualified. First author, study site, study design, year of publication, journal or pre-print server, sample size, and reported neurological signs were among the criteria that were taken into consideration.

Characteristics and outcome assessment
The data was examined to determine mortality, vascular risk factors, TOAST categorization of IS, stroke types, clinical status severity, demographics, and stroke types. I compared the clinical manifestation of (1) patients who had symptoms of COVID-19 at the time of stroke and those who did not; (2) patients who were critically ill and those who were not; and (3) survivors and non-survivors.

3. Result

30 articles out of the 1000 that were found in the initial search were used in my study (Figure 1). The methodology part of the research includes a list of the various type of sets of keyword that were utilized in the search of literature.16 reports related to the case, 8 cases series, 5 studies of retrospective observational, and one prospective observational research were among the 30 records that made up the final analysis. Since the majority of the studies are the case reports, series, and retrospective observational studies, the bias risk was not according to the system evaluated but expected to significant for all of them.

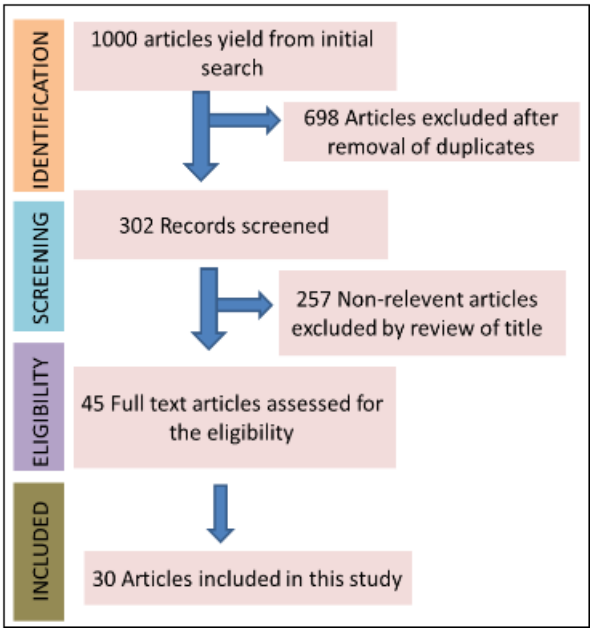

Figure 2: Flow chart of study selection

This review included data from 30 trials that comprised 115 individuals are acute and subacute stroke who were infected with SARS-2. There are many variables that have the missing data and they are not included the variable's analysis in which patient data are missing. The patient's specialty is mentioned in table 1 which is given below.

Neurological Manifestations Seen in Stroke Patients Associated with COVID 19
In a study conducted by Xiaoming Qi et al, it has been conveyed that stroke is much associated with severe covid 19 patients when compared to moderate to mild affection with covid 19. (Aggarwal Gaurav et al, 2020) According to Gaurav Nepal et al While COVID-19 typically presents as a self-limiting respiratory disease, it has been reported in up to 20% of patients to progress to severe illness with multi-organ involvement. Some neurological manifestations were also seen in patients affected with covid 19 which can be divided into 3 subgroups: central nervous system manifestations (e. g., headache, encephalopathy, and stroke), peripheral nervous system impairment (e. g., dysfunction of taste, dysfunction of smell, neuropathy), and skeletal muscle manifestations (e. g., myalgia). (Gaurav Nepal et al, 2020)

Ling Mao et al conducted a retrospective observational case series during January 16, 2020 to February 19, 2020. In this study they tried to study the neurologic manifestation of patients with covid 19. The study included 214 consecutive hospitalised patients with laboratory confirmed diagnosis of severe Corona Virus 2 infection. Out of 214 patients, 126 patients (58.9%) had non severe infection and 88 patients (41.4%) had severe infection according to their respiratory status. Among those, 78 patients (36.4%) had neurological manifestations. Neurologic manifestations fell into 3 categories: central nervous system manifestations (dizziness, headache, impaired consciousness, acute cerebrovascular disease, ataxia, and seizure), peripheral nervous system manifestations (taste impairment, smell impairment, vision impairment, and nerve pain), and skeletal muscular injury manifestations. Patients with more severe infection had neurologic manifestations, such as acute cerebrovascular diseases (5 [5.7%] vs.1 [0.8%]), impaired consciousness (13 [14.8%] vs.3 [2.4%]), and skeletal muscle injury (17 [19.3%] vs.6 [4.8%]). In patients with CNS manifestations, the most common reported symptoms were dizziness (36 [16.8%]) and headache (28 [13.1%]). In patients with PNS symptoms, the most common reported symptoms were taste impairment (12 [5.6%]) and smell impairment (11 [5.1%]). (Mao et al, 2020)

Asma Rahman et al (2020) conducted a study on the neurological manifestation in Covid 19 based on two large Cohort based studies of neurological manifestations. One study done in Wuhan, China, Mao et al (2020) noted neurological manifestation in 36.4% of 214 Covid 19 patients. Bit in another study done by Helms et al, 84%of 58 covid patients admitted in the intensive care unit had neurological signs. In this study only severely affected Covid 19 patients were considered which can explain the difference in mean percentage among both the studies. The main central nervous system manifestation observed were headache, dizziness, cerebrovascular disease (CVD), encephalopathy, delirium and other related manifestation like encephalitis and meningitis. Mao et al had reported seizures and hemiplegia in some patients prior to the onset of respiratory symptoms. But in another study conducted by Lu et al (2020), no risks of seizures were found in Covid 19 patients. Peripheral nervous system manifestation included Guillain-Barre syndrome (GBS) and other related variants and loss of the smell and taste. (Mao et al, 2020) In patients with skeletal muscle injury Creatinine Kinase, D dimer, C Reactive protein and lactate dehydrogenase level were found to be elevated.

Daniele Orsucci et al (2020) conducted a review study on the neurological features of Covid 19. He studied that delirium

and septic encephalopathy are common in severely ill patients. Smell dysfunction and headache were seen in mild cases especially in younger people. Muscle pain is seen in both mild and severe cases. Ischemic stroke has been reported as a possible complication of hypercoaguability associated with severe SARS CoV2 infection. In this study also the same neurological manifestations have been cited as the previous article, with an add on symptoms of headache, that are seen in mild cases of covid 19. ischemic stroke has been rarely found and those found are in severely affected cases. Some rare neurological features has also been described here like intracerebral hemorrhage, cerebral venous thrombosis, slight neck stiffness (with no SARS-Cov-2 genomes in the CSF), generalized myoclonus, seizures, status epilepticus and acute epileptic encephalopathy, hemorrhagic posterior reversible encephalopathy syndrome, acute necrotizing encephalopathy, white matter and globus pallidum inflammatory lesions, diffuse leukoencephalopathy with microhemorrhages, 'steroid-responsive encephalitis', neuroleptic malignant syndrome, and post-infectious acute transverse myelitis. A 6-week-old term male infant was reported with episodes characterized by sustained upward gaze, dystonic bilateral leg extension, and altered responsiveness in the setting of COVID-19 and rhinovirus coinfection. (Dugue R et al, 2020)

In a study conducted by Ademola S Ojo et al it was found that 65% of cases of stroke was cryptogenic. When compared with stroke patients without Covid 19, patients with covid 19 were older (median age 70 Vs.63 years) and had higher National Institute of Health Stroke Score (NIHSS) at admission with elevated peak D dimer. (Ademola S. Ojo et al, 2020)

Alberto Vogrig et al conducted a study on Stroke in patients with COVID-19: Clinical and neuroimaging characteristics, and concluded that Covid 19 appeared to be prone to (a) large vessel occlusion (including internal carotid artery, M1 and M2 segments of the middle cerebral artery [MCA], and the basilar artery); (b) multi-territory involvement; (c) involvement of otherwise uncommonly affected vessels, including like the occlusion of the pericallosal artery, or the presence of multiple focal stenoses in the V4 segment of the vertebral artery. Severe neurological features were seen where the National Institutes of Health Stroke Scale, NIHSS, ranged from 19 to21), and about one quarter of the cases had evidence of systemicthrombosis, including venous thrombosis, pulmonary, and spleen embolism. (Vogrig A et al, 2020)

A case series was studied by Beyrouti R et al, and they concluded that severe covid 19 is associated with proinflammatory cytokines which induced endothelial and mononuclear cell activation which leads to coagulation activation and thrombin generation. Circulation of the free thrombin can activate platelet and lead to thrombosis. In their case study, they found that all the patients had large vessel occlusion. In five of six patient's ischemic stroke developed 8 – 24 days after covid 19 symptoms onset and the remaining one had stroke during the presymptomatic phase of Covid 19. The clinical features revealed that all the patients had difficulty in either speech (dysarthria) or language (aphasia).4 patients had one sided weakness out of which one had an associated same sided sensory inattention (left side). Facial droops were also associated with one sided weakness. Confusion. In coordination, homonymous hemianopia and reduced consciousness were fewer common symptoms seen. (Beyrouti R et al, 2020)

A review study on Covid 19 and stroke was conducted by Xiaoming Qi et al. they collected cohort studies, case series and case report of stroke (both ischemic and hemorrhagic variety) complicated with Covid 19. They studied the presentation of stroke in Covid 19 patients.48.8% of neurological involvement in Covid 19 patients were cerebro vascular incident, which consisted of 87.5% ischemic stroke, 5% cerebral venous thrombosis, 5% intra parenchymal haemorrhage and 2.5% subarachnoid haemorrhage. (Ghannam M et al, 2020) On reviewing the articles they could find that hemiplegia, hypoesthesia, aphasia and facial droops were almost a common clinical feature among the patients. (Qi, X et al, 2020)

A case report on an ischemic stroke in a 29-year-old patient diagnosed with Covid 19 was submitted by Avvantaggiato C et al. The young 29-year-old woman was diagnosed with stroke during her ICU hospitalisation for Covid 19 related pneumonia. The stroke was an ischemic variety. The left sided hemiplegia was reported after she was suspended from medications for sedation in ICU. The computed tomography examination of the head showed areas of hypodensity in the right hemisphere due to recent cerebral ischemia. The patient exhibited signs of facial palsy on the left side, dysarthria with complete paralysis of ipsilateral upper and lower limbs. (Avvantaggiato C et al, 2021)

Neurological Manifestations seen in General Stroke Not Associated with COVID 19

Khaku AS and Tadi P has summarised the risk factors for cerebrovascular accident, presentation of a CVA patient, about their treatment and management, in their updated study on cerebrovascular disease. They explained about the various stroke syndromes and its related clinical manifestations seen. Anterior cerebral artery infarction involves Broca's area, primary motor and sensory area and prefrontal cortex, the clinical features of which can be shown as aphasia, personality issues and contralateral leg weakness and numbness with sparing of hands and face. The Middle cerebral artery supplies basal ganglia (with M1 branch) and parietal, frontal and temporal lobes (by M2 branch). The main clinical features are contralateral arm and facial numbness, gaze deviation towards affected side, aphasia in left sided lesion and neglect in right sided lesion. The posterior cerebral artery supplies occipital lobe, thalamus and some portions of temporal lobe. The classical presentation of PCA stroke is homonymous hemianopia. Bilateral involvement of distal PCA can cause cortical blindness with denial of his deficit (Anton Babinski Syndrome). Patients with cerebellar infarction presents with ataxia, dysarthria, nausea, vomiting and vertigo. (Khaku AS et al, 2022)

Christian Weimar et al in their study on Neurological worsening during acute phase of ischemic stroke, has explained some of the neurological manifestations seen in stroke.11 neurologic departments were recruited for the study. The severity of stroke was assessed using the National Institutes of Health Stroke Scale (NIH-SS) at admission to hospital and 48 – 72 hours later. Neurologic worsening on the

NIH-SS score after 48 – 72 hours were observed in 13% of the patients. The other patients had mostly arm and leg paresis, decreased level of consciousness, sensory deficit and dysarthria.17.2% of patients with neurologic worsening died before hospital discharge. (Weimar C et al, 2005)

Stephen JX Murphy and David J Werring, in their article on Stroke: causes and clinical features, has explained in detail about the various clinical manifestation seen in a stroke patient. They have also explained the various associated risk factors. They divided the clinical manifestation according to the area in the brain. (a) The anterior circulation comprises of anterior and middle cerebral artery which are the branch of internal carotid artery (ICA). If the carotid thrombo embolic disease occurs in the first branch of ICA, then it can lead to 'amaurosis fugax' (transient monooccular loss of vision) in the affected eye. A full proximal occlusion of the middle cerebral artery (often from a cardiac embolus) typically causes contralateral hemiparesis and hemi sensory loss, visual field defect, hemineglect and (if in the dominant hemisphere) aphasia. Involvement of the superior division of the middle cerebral artery produces contralateral hemiplegia, hemi sensory loss and, on the dominant side, a non-fluent (Broca's) aphasia. Involvement of the inferior division often produces a contralateral hemianopia and, if left-sided, a fluent (Wernicke's) aphasia. If more distal branches are involved the territory of neurological deficit becomes more limited (the extreme of this being a 'cortical hand' syndrome due to infarction of primary sensorimotor cortex). (b) Vertebrobasilar circulation: the right and left vertebral arteries join to form the basilar artery, which divides to form the posterior cerebral arteries. These supply the occipital cortex, so that infarction leads to hemianopia. Strokes in the vertebrobasilar territory are a bit difficult as there are a lot of clinical symptoms happening. For example, brainstem ischemia can lead to 'crossed' signs, while basilar ischemia can result in bilateral hemiparesis, sensory loss, visual disturbance and 'locked-in' syndrome. (c) Small vessel occlusions (small subcortical infarcts): Small subcortical infarcts caused by occlusion of small perforating arteries are probably often asymptomatic but when they occur in eloquent brain areas produce 'lacunar syndromes'. The most common lacunar syndromes (and corresponding infarct locations) are pure motor stroke (posterior limb of the internal capsule), pure sensory stroke (lateral thalamus), sensorimotor stroke (thalamo-capsular region), dysarthria–clumsy hand syndrome (usually pons) and ataxic hemiparesis (posterior internal capsule, pons, centrum semiovale). The progression of CSVD with accumulation of small subcortical infarcts and progressive white matter damage causes a typical clinical syndrome of progressive cognitive impairment (typically executive dysfunction) and gait disturbance with reduced stride length and falls. (Murphy et al, 2020)

4. Conclusion

Patients with Covid-19 have shown up with a variety of neurological disorders, many of which can be incredibly harmful, such as stroke. SARS-CoV-2 virus causes coagulopathy, disrupts endothelial function, and lead to hyperco agulative state. Serious COVID-19 infection renders patients bedridden. Collectively, it may lead individuals to cerebrovascular events. Due to the unparalleled strain on the healthcare system, stroke care has been certainly compromised from initial encounter, treatment, to rehabilitation. Research on the fundamental mechanism linking COVID-19 to stroke is still needed, as is the creation of potent therapeutic or preventive measures. From the research conducted we could understand that young adults are more likely to be affected with stroke who has been infected with Covid-19. In a very younger age itself when a person becomes disabled it becomes a devastating event.

According to the research, about 1.4 percentage of the Patients with COVID-19 undergo acute CVD. Those with the most severe infections and those who already had vascular risk factors were at higher risk. A non-COVID-19 stroke population's stroke pattern was different from this population's. Numerous ischemic strokes, a surge in major artery blockage, and numerous territorial infarcts all point to heightened thrombosis and thromboembolism as potential risk factors. The review provided a thorough explanation of the COVID-19 neurological symptoms that are currently known. Given that neurological symptoms have been noted to occasionally precede respiratory symptoms in the course of COVID-19, respiratory symptoms continue to be the hallmark of early diagnosis, cohorting, and therapy of the disease. Hence keeping in mind, the risk factors for stroke in covid 19 patients and all the initial clinical features exhibited, a person if affected with covid-19 can be monitored continuously for preventing the development of stroke. This review highlights the significant impact of COVID-19 on stroke patients, emphasizing the need for continuous monitoring and targeted interventions. Further research is essential to understand the mechanisms linking COVID-19 to cerebrovascular events and to develop effective preventive and therapeutic strategies

5. Future Scope

Limitations

- Samplesizetakenforthestudyissmallandbiggersamplemighthaveledtosomedifferences in the result.
- Only short term effects were being evaluated
- Influence of drug, nutritional factors and climate could not be controlled
- Study only conducted in MCA stroke patients
- As the measurement were taken manually, this may introduce human error, which could treat the study's reliability

Suggestion

- To examine whether these benefits are maintained for along erduration.
- A large sample size should be taken to improve the consistency of results
- More parameters of outcome measurement study more valuable.
- To make the result more generalized, the study can be done in acute and chronic stroke patients
- Blinding of procedure could improve the reliability of the outcome

References

[1] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y. (2020), Epidemiological and clinical characteristics of

99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study, NEngl J Med: 10.1016/S0140-6736 (20) 30211-7.
[2] Agyeman AA, Chin KL, Landersdorfer CB, Liew D, Ofori-AsensoR. (2020), "Smell and Taste Dysfunction in Patients With COVID-19: A Systematic Review and Meta-analysis". Mayo Clin. Proc.95 (8), pp1621–1631.
[3] Chaolin Huang, Yeming Wang, Xingwang Li. (2020), Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China, Epub 15; 395 (10223), pp497-506.
[4] Islam MA. (2021). "Prevalence and characteristics of fever in adult and paediatric patients with coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis of 17515 patients". PLOSONE.16 (4).
[5] Betty P fefferbaum, M. D., J. D., and Carol S. North, M. D. (2020), Mental Health and the Covid-19 Pandemic, M. P. E N Engl J Med, DOI: 10, pp510-512.
[6] JiaqiXiong et al. (2020), Impact of COVID-19 pandemic on mental health in the general population: A systematic review., Journal of Affective DisordersVolume 277, pp 55-64.
[7] Helms J, Kremer S, Merdji H, et al. (2020). Neurologic features in severe SARS-CoV-2 infection. New England Journal of Medicine, DOI: 10.1056/NEJMoa2008597.
[8] Mao L, Jin H, Wang M, et al, (2020), Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China, JAMANeurol, doi: 10.1001.
[9] Boehme A. K., Luna J., Kulick E. R., Kamel H., Elkind M. S. V. (2018), Influenza-like illness as a trigger for ischemic stroke. Ann ClinTransl Neurol; 5, pp456–463.
[10] Lodigiani C, Iapichino G, CarenzoL. (2020), Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy, Thromb Res, Vol: 191, pp9–14.
[11] Markus Hugh S, BraininMichael. (2020), COVID-19 and stroke—A global world stroke organization perspective, Int J Stroke, Vol: 15 (4), pp361–364.
[12] Richard J Perry et al. (2020), Characteristics and outcomes of COVID-19 associated stroke: a UK multicentre case-control study. J NeurolNeurosurg Psychiatry; 92, pp242–248.
[13] Coupland, Alexander P et al. (2017), "The definition of stroke. " Journal of the Royal Society of Medicine vol.110, pp 9-12.
[14] Albers GW, Caplan LR, Easton JD, Fayad PB, Mohr JP, Saver JL, et al. (2002), Transient ischemic attack – proposal for a new definition. N Engl J Med; 347, pp 1713–1716.
[15] Easton JD, Saver JL, Albers GW, Alberts MJ, Chaturvedi S, Feldmann E, et al. (2009), Definition and evaluation of transient ischemic attack: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association Stroke Council; Council on Cardiovascular Surgery and Anesthesia; Council on Cardiovascular Radiology and Intervention; Council on Cardiovascular Nursing; and the Interdisciplinary Council on Peripheral Vascular Disease. The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists. Stroke; 40, pp2276–2293.
[16] Aho K, Harmsen P, Hatano S, Marquardsen J, Smirnov VE, Strasser T. Cerebrovascular disease in the community: results of a WHO collaborative study. Bull World Health Organ 1980; 58, pp113–130.
[17] Kuriakose, Diji, and Zhicheng Xiao. (2020), "Pathophysiology and Treatment of Stroke: Present Status and Future Perspectives. " International journal of molecular sciences vol.21.
[18] Merkler AE, Parikh NS, Mir S, et al. (2020), Risk of ischemic stroke in patients with coronavirus disease 2019 (COVID-19) vs patients with influenza. JAMA Neurol; 77 (11), pp1366-1372.
[19] Aisha Elfasi et al. (2021), Impact of COVID-19 on Future Ischemic Stroke Incidence. eNeurologicalSci, Volume 23, pp100342.
[20] Luo, Wenzhang et al. (2022), "Ischemic stroke associated with COVID-19: a systematic review and meta-analysis. " Journal of neurology vol.269, pp1731-1740.
[21] Trifan G, et al. (2020), Characteristics of a Diverse Cohort of Stroke Patients with SARS-CoV-2 and Outcome by Sex. J Stroke Cerebrovasc Dis. N; 29 (11), pp105314.
[22] Adnan I. Qureshi. (2021), Acute Ischemic Stroke and COVID-19An Analysis of 27 676 Patients. Volume 52, pp 905-912.
[23] Tirschwell DL, Smith NL, Heckbert SR, Lemaitre RN, Longstreth WT Jr. (2004), Association of cholesterol with stroke risk varies in stroke subtypes and patient subgroups. Psaty BM Neurology.63 (10), pp1868-75.
[24] Klaus Kaae Andersen, Tom Skyhøj Olsen, Christian Dehlendorff and Lars Peter Kammersgaard. (2009), Hemorrhagic and Ischemic Strokes Compared; Stroke Severity, Mortality, and Risk Factors. STROKEAHA, Volume 40, pp 2068-2072.
[25] Hossmann, K., &Heiss, W. (2019). Neuropathology and Pathophysiology of Stroke. In M. Brainin& W. Heiss (Eds.), Textbook of Stroke Medicine, pp.1-37.
[26] Xing C, Arai K, Lo EH, HommelM. (2012), Pathophysiologic cascades in ischemic stroke, Int J Stroke, Vol: 7 (5), pp378-85.
[27] Hoffmann Markus, Kleine-Weber Hannah, Schroeder Simon, et al. (2020), SARS-CoV-2 Cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell, 181 (2), pp271–280.
[28] Baig Abdul Mannan, KhaleeqAreeba, Ali Usman, SyedaHira. (2020), Evidence of the COVID-19 virus targeting the CNS: tissue distribution, host–virus interaction, and proposed neurotropic mechanisms. ACS ChemNeurosci; 11 (7), pp995–998.
[29] Helms Julie, Tacquard Charles, Severac François et al. (2020), High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study. Intensive Care Med, Vol: 46 (6), pp1089–1098.
[30] Tan CW, Low JGH, Wong WH, Chua YY, Goh SL, Ng HJ. (2020), Critically ill COVID-19 infected patients exhibit increased clot waveform analysis parameters consistent with hypercoagulability. Am J Hematol; 95 (7), pp156–158.
[31] Panigada Mauro, Bottino Nicola, Tagliabue Paola, GrasselliGiacomo, Novembrino Cristina, et al. Hypercoagulability of COVID-19 patients in intensive

care unit: a report of thromboelastography findings and other parameters of hemostasis. J ThrombHaemost.2020; 18 (7), pp1738–1742.
[32] Soto-Cámara, R.; González-Bernal, J. J.; González-Santos, J.; Aguilar-Parra, J. M.; Trigueros, R.; López-Liria, R. (2020), Knowledge on Signs and Risk Factors in Stroke Patients. J. Clin. Med, 9, pp2557.
[33] Fekadu, G., Chelkeba, L. &Kebede, (2019), A. Risk factors, clinical presentations and predictors of stroke among adult patients admitted to stroke unit of Jimma university medical center, south west Ethiopia: prospective observational study. BMC Neurol 19, pp 187.
[34] Pietroboni, A. M., Lanfranconi, S., Novella, A. et al. (2021), Clinical features and disease course of patients with acute ischaemic stroke just before the Italian index case: Was COVID-19 already there?. Intern Emerg Med 16, pp 1247–1252.
[35] Saif S. Rathore, MPH et al. (2002), Characterization of Incident Stroke Signs and Symptoms, Findings From the Atherosclerosis Risk in Communities Study Stroke Volume 33, pp 2718-2721.
[36] Aggarwal Gaurav, Lippi Giuseppe, Michael Henry Brandon. (2020), Cerebrovascular disease is associated with an increased disease severity in patients with Coronavirus Disease 2019 (COVID-19): A pooled analysis of published literature. Int J Stroke; 15 (4), pp385–389.
[37] Gaurav Nepal et al (2020), Neurological manifestations of COVID-19: a systematic review. Nepal et al. Critical Care; 24, pp421.
[38] Asma Rahman et al. (2020), Neurological manifestations in COVID-19: A narrative review. SAGE Open Medicine Volume 8, pp1–10.
[39] Khaku AS, Tadi P. Cerebrovascular Disease. [Updated 2021 Sep 29]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https: //www.ncbi. nlm. nih. gov/books/NBK430927.
[40] Lu L, Xiong W, Liu D, et al. (2020), New onset acute symptomatic seizure and risk factors in coronavirus disease 2019: a retrospective multicenter study. Epilepsia; 61, pp49-53.
[41] Orsucci, Daniele et al. (2020), "Neurological features of COVID-19 and their treatment: a review. " Drugs in context vol.9, pp 2020.
[42] Dugue R, Cay-Martinez KC, Thakur K, et al. (2020), Neurologic manifestations in an infant with COVID-19. Neurology; 10, pp1212.
[43] Ademola S. Ojo, Simon A. Balogun, and Ahmed O. Idowu. (2020), Acute Ischemic Stroke in COVID-19: Putative Mechanisms, Clinical Characteristics, and Management. Hindawi Neurology Research International. Volume 7, pp 2005.
[44] Beyrouti R, Adams ME, Benjamin L, Cohen H, Farmer SF, Goh YY, Humphries F, Jäger HR, Losseff NA, Perry RJ, Shah S, Simister RJ, Turner D, Chandratheva A, Werring DJ. (2020), Characteristics of ischaemic stroke associated with COVID-19. J NeurolNeurosurg Psychiatry.8, pp889-891.
[45] Ghannam M, Alshaer Q, Al-Chalabi M, Zakarna L, Robertson J, Manousakis G. (2020), Neurological involvement of coronavirus disease 2019: a systematic. Review.
[46] Qi, X., Keith, K. A., & Huang, J. H. (2021). COVID-19 and stroke: A review. Brain hemorrhages, 2 (2), pp 76–83.
[47] Avvantaggiato C, Amoruso L, Lo Muzio M, P, Mimmo M, A, DelliBergoli M, Cinone N, Santoro L, Stuppiello L, Turitto A, Ciritella C, Fiore P, Santamato A. (2021), Ischemic Stroke in a 29-Year-Old Patient with COVID-19: A Case Report. Case Rep Neurol; 13, pp334-340.
[48] Weimar C, Mieck T, Buchthal J, et al. (2005), Neurologic Worsening During the Acute Phase of Ischemic Stroke. Arch Neurol; 62 (3), pp393–397.
[49] Murphy, Stephen Jx, and David J Werring. (2020), "Stroke: causes and clinical features." Medicine, Abingdon, England: UK ed. vol.48, pp 561-566.

Web sites

[50] Coronavirus disease (COVID 19) pandemic: World Health Organisation. Accessed October 26, 2020.
[51] WHO. Coronavirus disease 2019 (COVID-19) Weekly Epidemiological Update. October 23, 2020. Available at: https: //www.who. int/emergencies/diseases/novel-coronavirus-2019/situation-reports. Accessed October 26, 2020.

Author Profile

Sinto Francis, Physiotherapist, Fairlie Health Care Group London, UK
Email: sintofrancis91[at]gmail.com

K Sangita, Assistant Professor, Medical Trust, Institute of Medical Science
Email: *sangikey[at]gmail.com*