Journal of Research in Medical and Dental Science
2022, Volume 10, Issue 8, Page No: 208-212

Available Online at: www.jrmds.in
eISSN No.: pISSN No.2347-2545

Cognitive as Well as Functional Deficits in Individuals with COVID-19 Infection: A Review

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ABSTRACT

Background: Given instances of 'Extended COVID' symptoms extending into to the persistent phase and case studies demonstrating brain dysfunction in severely afflicted people, there is rising worry regarding the potential cognitive repercussions of COVID-19. However, nothing is known about the type and general occurrence of cognitive difficulties following infection, or about the whole range of illness severity. It is uncertain if cognitive symptoms are connected with the severity of a new coronavirus (COVID-19) illness. Clinical studies have indicated neurological issues in COVID-19 individuals who have been significantly afflicted. However, nothing is known about the nature and overall prevalence of cognitive difficulties following illness, or the whole range of severity. Early identification of neurocognitive symptoms may reduce the likelihood of permanent damage and continued neurocognitive deterioration. The present COVID outbreak is unprecedented in terms of spread and intensity in human society. The consequences for cognitive performance might be just as catastrophic. Although the current focus is on immediate illness treatment, in the near future, attention will need to shift to the lengthy consequences of COVID infection and how to decrease them. When age, gender, educational status, wealth, race of people, and well before medical conditions were all controlled for, people who had cured displayed severe cognitive abnormalities. They exhibited a significant impact size not just for patients who were institutionalized, but also for moderate yet medically proven instances with no breathing trouble. Performance assessments at a higher level back up the concept that COVID-19 has a multi-system influence on human intelligence.

Aim: The purpose of this study is to analyse the real outline of cognitive and functional impairment found in COVID by examining all published case studies and publications to create a thorough evaluation.

Methods: Search strategy we searched Google scholar, Scopus, Research gate, Medline, PubMed and WHO sites to understand and throw light on the cognitive manifestations of novel coronavirus disease to prepare a review. We limited our search to relevant English language publications from recent years. For MEDLINE the search terms used were COVID-19, delirium, neurological manifestations, cognitive impairment and found numerous articles related to the topic. References from linked reviews and collected papers were also reviewed for potentially relevant literature.

Key Words: COVID-19, Delirium, Neurological manifestations, Cognitive impairment

HOW TO CITE THIS ARTICLE: Mudit Kerwal, Swarupa Chakole, Cognitive As Well As Functional Deficits in Individuals with COVID-19 Infection: A Review J Res Med Dent Sci, 2022, 10 (8): 208-212.

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Received: 25-May-2022, Manuscript No. JRMDS-22-49555;
Editor assigned: 30-May-2022, Pre QC No. JRMDS-22-49555 (PQ);
Reviewed: 13-Jun-2022, QC No. JRMDS-22-49555;
Revised: 26-Jul-2022, Manuscript No. JRMDS-22-49550 (R);
Published: 05-Aug-2022

INTRODUCTION

In the November of 2019 SARSCoV-2 virus was found in Wuhan, China. The human sickness related with it that is COVID-19 spread swiftly and became a global threat [1]. Fever, dry cough, tiredness, and dyspnoea are common symptoms, and respiratory failure and consequent pneumonia commonly necessitate hospitalisation. Neurological symptoms have been seen and are becoming more well-known. The most common are headaches, myalgia's, and fatigue lack of burst and odour [2]. These symptoms may be taken into account as a straight impact of a viral infection on the normal brain, immune–mediated illness that is para-infectious or post-infectious [3]. COVID-19's systemic effects can cause neurological problems. COVID-19 virus, like SARS-CoV, allows angiotensin II to enter inside cells. It emphasises the importance of studying ACE2 expression in the Central Nervous System to assess COVID-19's direct impact on brain tissue provided proof that SARS-CoV-2 host cell entrance is dependent on the SARSCoV receptor. ACE2

provides critical information into the infection's first stages and Virus invasion into cells [4]. Following any severe illness, cognitive abnormalities are prevalent, long-lasting, and devastating. They're becoming better recognised as a COVID-19 problem. The situation is complicated by a number of things. Illness and its treatment may cause cognitive consequences. Hypoxia, ventilation, sedation, delirium, and cerebrovascular disease are among them. Case reports and studies on cognitive functioning are generally restricted. Only a few studies have employed purposeful neurological and psychological tests. The severity and characteristics of cognitive impairment during recovery is variable. A study of 29 outpatients found prolonged attention and reaction time deficiencies, whereas in another study of nine individuals, worldwide cognitive deficits were discovered like in Attention, memory, language, and praxis. Those who have recovered from COVID infections continue to exhibit symptoms. Many patients nevertheless experience weariness, joint pain and bone pain, palpitation, headache, disorientation, and sleeplessness. Long-term lung scarring and dysfunction have also been cited as concerns, particularly in persons with severe pulmonary disease. The virus was discovered 2 years ago, long term and deep research does not exist, and the prognosis for these individuals is unknown. COVID-19 is predicted to have substantial long-term repercussions. The effect of COVID-19 on cognitive performance, especially in persons with moderate symptoms, is one of the long-term repercussions that are becoming more evident [5].

COVID-19 risk factors

Ageing, physiological ailments such as high blood pressure, type 2 diabetes, adiposity, and smoking [6,7]. The most common triggers for serious COVID-19 illness. Many of the risk factors for cognitive decline are shared by this community, including older years, brain trauma, overweight, high blood pressure, smoking habits, and type 2 diabetes [8]. When these lifestyle factors are added together, they create a baseline neurocognitive fragility that may increase susceptibility to perceptual impairments throughout and following inflammatory disorder [9]. Similar to the perioperative neuropsychological abnormalities following surgical intervention and anesthetic medication [10]. As a result, people who are prone to serious COVID-19 illness might be prone to mental impairment in the presence of COVID-19 inflammatory process.

LITERATURE REVIEW

COVID-19 inflammation's multi-systemic function in cognitive decline

Respiratory: In COVID-19, invasion of ciliated epithelium of bronchus and type II pneumocystis produces respiratory impairment. By attaching to the ACE2 receptor, the virus can enter these cells and cause viral endocytosis. The TMPRSS2 then cleaves the virus surface spike glycoprotein, allowing viral contents to be released and the infection to spread. COVID-19 induced respiratory impairment and hypoxia are expected to add to brain damage and ultimate mental impairment [11]. Patients suffering from chronic hypoxemia, such as those suffering from COPD and sleep apnoea [12]. Frequently experience mental impairment. Similarly, individuals with COVID-19 ARDS may have substantial hypoxemia despite otherwise normal lung mechanics [13]. In COVID-19 patients, this 'silent hypoxaemia' has been defined as 'levels of oxygen unsuitable for survival without having any dyspnoea [14]. Tracheal intubation and extended mechanical ventilation have often been necessary to address the resultant chronic hypoxemic condition in extremely unwell COVID-19 patients.

Hypoxia, a primary cause of cognitive impairments in ARD, has been linked to brain shrinkage and ventricle expansion, and the duration of hypoxia has been linked to attentiveness, memory retrieval, and cognitive reasoning scores upon discharging from hospital. Acute respiratory distress syndrome, on the other hand, can result in inflammatory responses, anaemia, and ischaemia, all of which can lead to cardiovascular and liver failure. A chain reaction of neurological and physiological processes like these might exacerbate neurological damage in the early stages, leading to chronic cognitive impairment. Patients, who had the most intrusive respiratory support, were also the youngest. According to the findings, the youngest patients benefitted from the most intrusive respiratory aid and had the highest preserved cognitive capabilities.

Thrombosis and coagulation in the vasculature: The virus has also been observed to infiltrate vascular endothelium, resulting in endothelial dysfunction and an elevated risk of vascular thrombosis [15]. The virus causes a cytokine cascade and generalized vasculitis, which can impact organ systems like the kidneys, liver, skin, and heart. The most severe cardiac consequences of COVID-19 illness range from uncontrollable myocarditis to myocardial failure and arrest [16]. Because both inflammatory response and coagulation are linked with an increased incidence of disorientation and bad results in intensive care units, the hyper coagulation and hyper inflammation reported in serious COVID-19 may lead to delirious and subsequent cognitive impairment [17]. Furthermore, SARSCoV-2 infection can increase the risk of hidden infarction and thrombosis through small emboli.

Neural: Neural concerns include failure of BBB, activation of glial cells, and straight injury to neurons [18]. By interacting with the BBB, neuro inflammation can cause cognitive impairment. Inflammatory shocks in both animals and people can result in an increase in proinflammatory cytokinin and other mediators of inflammation in the blood [19]. 11 Proinflammatory cytokinins from the periphery, likeIL-1 and IL-6, as well as TNF-a, decreases the permeability of BBB by activating COX-2 and MMP. Once the BBB is breached, mediators could infiltrate the Brain, activating microglia and causing oxidative stress, leading to cumulative cognitive impairment. In the near term, the resultant neuro inflammation can cause disorientation, and in the long

run, it can cause cognitive impairments [20]. There have been two basic routes of invasion:

- The BBB which is the first layer of defence to virus is composed of cerebral vascular endothelium, and gap junctions regulating barrier passage tend to be compromised during corona virus infection, presumably as a result of inflammation [21].
- The virus may infect peripheral neurons or sensory neurons of olfaction immediately before entering the CNS *via* axonal transport [22]

Iatrogenic and delirium: Even after established preventable causes of cognitive impairment in COVID-19 patients, many patients were refused normal cognitive health precautions and treatments in the first wave because to viral transmissibility and the increased load of seriously sick patients. In the course of their sickness many patients were ventilated and intubated before time, with little or no family involvement. Because it is usual in ARDS treatment to sustain PaO_2 values up to 55 mmHg or SaO_2 levels up to 88 percent, these intubated patients were exposed to long stretches of iatrogenic hypoxemia [23]. Vented patients were frequently restless, necessitating extended periods of sedative with a variety of medicines in order to protect themselves or personnel. Although alertness and hearing capabilities, such as hearing a patient's name said by a friendly sound, are among the most beneficial treatments for recovery from consciousness impairments, basic therapies such as these are hard to enforce due to global epidemic safeguards. Although long-term investigations are presently underway, both short and long term neural impairments have previously been discovered in both severely ill and non-severely ill survivors. Indeed, disorientation or altered awareness is the fourth most prevalent clinical manifestation of COVID-19, showing both active and passive initial effects on the brain. These results emphasize serious issues about the patients' probable neurocognitive deterioration, considering that mental impairment is generally a gradual process that occurs after some preceding neuronal or cognitive damage. Furthermore, mental impairment doesn't really happen in isolation; instead, it appears as a worse standard of living and a diminished capacity to do Daily duties and technical Aspects of behaviour. Cognitive impairment is frequently misdiagnosed until it has progressed to the point where it is causing moderate to severe functional problems. Thinking about the long effects of COVID-19 when combined with anaesthetics and surgical procedures, which are both well-known causes of inflammatory related neurocognitive impairment. Considering the similar inflammation response to damage in both, we might well be able to predict unfavourable neurocognitive results in COVID-19 patients and attempt to develop preventative medicines or therapies that may ameliorate the long-term implications of COVID-19. Using the vast corpus of research on neurocognitive disorders during operative procedures, which have a similar inflammation aspect, may allow for rapid breakthroughs in treatment for both, as well as other neurologic illnesses. Lifestyle factors, pathophysiology, clinical course, and clinical manifestations all work together to create a cascade of brain damages that are expected to expose individuals to lengthy cognitive problems and functional impairment. COVID-19 survivors must be tested and evaluated for cognitive problems, negative psychosocial results, and functioning deterioration. To reduce or eliminate these deleterious consequences for COVID-19 patients, as well as many other inflammation related brain traumas, further research into the brain sequelae of COVID-19, anaesthesia, surgery, and other inflammatory illnesses is required. The association between COVID-19 and cognitive impairment has never been documented. Given COVID-19's well-documented neurotropic and the fact that cognitive impairments have been observed in other viral infections, we determined that the relationship was quite feasible. We determined that the COVID-19 infection profile matched that of the overall population. As previously stated, the most prevalent clinical manifestation in our sample was fever, following cough, muscle aches, weariness, and headaches. Men had greater D Dimer and ferritin levels than women. A previous study discovered that severe infection was more prevalent in males due to greater ACE2 concentrations. SARS-CoV-2, like other respiratory viruses, can reach the CNS *via* the blood or backward neural pathways, as evidenced by the fact that many of the patients in research exhibited a loss of smell. Headache, loss of odour, and loss of taste were all shown to be highly related to deterioration in a range of assessments, encompassing focus, recall, and cognitive processing domains. Headache was the most common neural complaint related with underperformance in neuropsychological testing. This episode, as previously said, may be symptomatic of COVID-19's potential Brain invading abilities. Individuals who required oxygen therapy during their stay had cognitive impairment, which might be described by the persistent low levels of oxygen in blood caused by COVID related lungs illness. The primary variables that were significantly linked to cognitive impairment were headache and oxygen therapy.

People with these symptoms had a lower global Cognitive Index. Patients who had diarrhoea after an illness fared worse on a cognitive test. We didn't record whether the diarrhoea was caused by the sickness or a side effect of the drug. This information would be valuable to retain for future investigations.

There were no differences in cognition between patients with and without complaints, but they rated themselves far more anxious and depressed. Patients who complained of cognitive problems attributed them on attention decline and nominal aphasia. Perceived perceptual deficiencies may be exacerbated by behavioural discomfort, like worry, depression, and sleeplessness. The results emphasize the importance of detecting worry and sadness in COVID patients early on in order to minimise eventual cognitive impairments. We identified a much greater frequency of cognitive problems many months following individuals were diagnosed with COVID-19 in our research. Cognitive

performance, processing power, categorizing dexterity, recall imprinting, and recall impairments were all frequent in admitted individuals. Memory recognition is marginally spared in the setting of poor encoding and recall, indicating an operational tendency. This trend matches early accounts of a dysexecutional syndrome after COVID-19, and it has substantial consequences for vocational, psychosocial, and functioning outcomes. Certain populations (e.g., the elderly) are known to be more vulnerable to cognitive injury during critical illness, but a high proportion of the fairly young group in the ongoing investigation revealed cognitive impairment months after recovery from COVID. The outcomes of this investigation are mostly similar with previous virus research (e.g., influenza).

Difficulties with cognition as a result of psychological suffering

All mental diseases are characterised by cognitive deficiencies. Independent of viral status, the general population had large rates of psychiatric problems like worry, depression, suicidal tendencies, and posttraumatic stress during prior HCoV epidemics. Studies in individuals isolated for suspected or known MERS found that 70.8 percentages of proven patients who experienced the infection showed mental symptoms such as visions and delusions, with 40 percent receiving a psychiatric illness within their hospitalisation. Surprisingly, either of the probable but unproven MERS patients had any signs, indicating a viral mechanism, a dose-response effect, or a greater mental effect from having a verified respiratory illness diagnoses. The severity of the sickness and impaired functioning were found to be linked to the level of psychiatric problems [24,25]. As a result, since increased levels of psychotic signs may well be anticipated in the overall population as a result of exposure to stressful events in life (lost earnings, worry, fatality of family members and friends). Within this cohort there could be individuals whose psychological and cognitive abnormalities are clearly relevant to Sars-cov brain damage. The issue then becomes whether the latter group will react to traditional treatments such as antidepressants, anxiolytics, and cognitive therapies. The little data from animal research and earlier pulmonary outbreaks shows that HCoV not just damages brain, but the impact on mental function may last a long time after recovery. The consequences are expected to be even worse for infected people that already have Brain problems.

DISCUSSION

Patients diagnosed with COVID can experience neurocognitive impairment soon after leaving the hospital. The presence of neurological symptoms like headaches, loss of smell, and impaired sense of taste during the infection was a strong hazard factor for impairment linked to focus, recall, and regulatory functioning. Recollection, focus, and regulatory functioning deficits were also linked to the requirement for oxygen treatment and diarrhoea. Despite the fact that neuropsychological testing revealed no impairment in these individuals, anxiety and sadness were linked to cognitive difficulties. Our findings provide critical new diagnostic data which may assist doctors in becoming more aware of the emergence of cognitive dysfunction in COVID infected individuals. Doctors must consider discovering and assessing these individuals, and also providing lengthy follow up to prevent future deterioration. The link between COVID and cognitive functionality presents serious queries about sufferers' lengthy therapy. Additional research is needed to uncover the health risks and processes that contribute to cognitive impairment, as well as treatment options. With additional reports of Brain connection in COVID patients, it is projected that the present pandemic will be followed by a considerable rise in the incidence of long-term mental dysfunction affecting the capacity to recover to everyday activities. It is most probably related to the behavioural consequences of virus-caused neurological problems, along with subsequent harm to other internal functions, mental illnesses, and worsening of cognitive deficiencies which were present before. The number of people exposed to the virus and are likely to be impacted, as well as the preventive variables at work when no cognitive abnormalities arise, are yet unclear. Few studies of cognitive impairment linked to earlier epidemics have been conducted, and the sample size is insufficient to offer population-level estimates.

CONCLUSION

This is the third coronavirus outbreak in ten years, following SARS and MERS. As a result, medical and scientific communities must explore well beyond immediate crisis to the links between coronavirus exposure and lengthy neurologic consequences. While fundamental scientific investigation would provide insight into the possible mechanistic connections among virus infection and neurological condition, an improved comprehension of such connections will aid in the development of treatment regimens that strive to cure the illness while trying to limit downstream mental impairment. Unless future research demonstrates that load of virus and/or following inflammatory state are related to lengthy cognitive end result, treatment methods in epidemics may decrease the latter by altering the value and length of time of antiviral drugs or adding two stages anti-inflammatory therapies. The choices for breathing aid had no effect on the sensorimotor complaints. The age of the patients was revealed to be a risk factor for COVID-19 induced cognitive impairments. Our findings highlight the importance of lengthy psychosocial help and counselling for COVID-19 patients, as the vast majority of patients still experienced cognitive deficits one month following treatment.

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