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Association Between Immunity and Cognitive Status in COVID-19 Survivors: An Exploratory Study

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Abstract

COVID-19 pandemic is being intolerable and unbearable for every individual across the world. The risk factors are well presented which could increase the chances of being infected. Individuals with co-morbid health conditions and low immunity are found to be vulnerable factors to the disease severity and suffering. Cognitive decline is highly associated with the pathogenesis of the virus and it increases the chance for individuals who have a co-morbid illness. In the present study, a total of 35 COVID-19 survivors of both sexes were selected, where all were assessed for immunity and cognitive status. The purpose was to explore the cognitive functioning of COVID-19 survivors in relation to immune response and co-morbid physical illness conditions. Results suggest a significant difference in cognitive functioning among subjects with and without co-morbid conditions. Further, it was found that immune status among COVID -19 survivors determines the cognitive impairment.

Keywords: COVID-19, immunity, cognition, comorbidity

Abbreviations: MMSE: Mini-Mental State Examination; BCRS: Brief Cognitive Rating Scale; ISQ: Immune Status Questionnaire

Introduction

The human immune system protects organs from viruses and diseases, helps to produce antibodies and antigens, and reduces the risk of pathogenesis. In the immune system, the main component is white blood cells which travel all over the body through blood vessels. To enable the lymphatic system, immune system exchanges of blood and lymphatic vessels take place, and invaded microbes are monitored. The lymph node in lymphatic system contains compartments to carry the antigens and immune cells concentrate, operate, and confront the antigens [1]. The COVID-19 virus starts

to generate with limited innate immune responses and could be detected through nasal swabs. It propagates to respiratory tracts where it is exposed to a more vigorous immune response which is predictive of the clinical course of COVID-19 disease condition [2]. Immune molecules, cytokines are involved in the functioning of the central nervous system and cytokines work as triggers, messengers, effectors of immune systems which are associated with inflammation and illness behaviour [3]. Inflammation slows down brain functioning and leads to neurodegenerative and affective disorders [4].

A decreased immune response is associated with the presence of co-morbid conditions [5]. Researchers suggested that individuals with chronic diseases, immune-deficiency diseases, metabolic diseases are more vulnerable to be infected and the impact could be more fatal than individuals without co-morbid diseases. The COVID-19 pandemic is in its second year and the treatment focus is mostly on the severity of the impact caused by the illness along with long-term deficiency or incapacity in terms of physical functioning, cognitive functioning, and activities of daily living. It has been seen that patients with chronic diseases *i.e.*, diabetes, hypothyroidism, asthma have a specific neurocognitive sequel which could directly lead to adverse cognitive functioning [6]. Cognitive deficits including the domains of working memory, memory, learning, cognitive flexibility, and executive functioning are the most affected areas due to chronic diseases. Infirmity in adults increases the risk of infections along with decreased immune response lead to altered brain functioning. Risk factors of cognitive decline are related to the inflammation caused by COVID-19 infection and it reflects on the daily functioning of the individuals infected by the virus [7].

The present study is aimed to explore the cognitive functioning of COVID-19 survivors in relation to immune response and co-morbid physical illness conditions.

Materials and Methods

Participants

In the present study, a total of 35 COVID-19 survivors of both sexes, age range between 18–60 years were selected from the first wave of outbreak following purposive sampling technique. Individuals with three months post-infection and those who showed mild to severe levels of symptoms were only included. Individuals with neurological disorders were excluded from the study. Consent was taken from each participant.

Tools used

- Socio-demographic datasheet: A tailor-made socio-demographic datasheet was prepared for data collection which includes information about age, sex, education, COVID-19 infection and severity, and presence of any other medical conditions.

- Immune Status Questionnaire: The Immune Status Questionnaire (ISQ) is a short questionnaire to assess the immune status. It is a 7-item perceived immune status assessment [8]. It is a subjective marker of the immune functioning where 0 = very poor, 10 = excellent perceived immune status with a cut-off for reduced immune functioning ISQ < 6.

- Mini-Mental State Examination: The Mini-Mental State Examination (MMSE) was used to screen the presence of cognitive impairment among participants [9].

- Brief Cognitive Rating Scale: The Brief Cognitive Rating Scale (BCRS) was used to assess functional and cognitive abilities. The BCRS indicates objective ratings of multiple domains of cognitive functioning. On this scale, higher scores indicate higher cognitive impairment [10].

Statistical analysis

Scales were scored and analyzed by descriptive statistics, students' t-test, and Pearson's product-moment correlation.

Results

Variables		Mean ± SD
Age		41.03 ± 16.20
Education (in years)		16.25 ± 1.88
		Number (Percentage)
Severity of COVID infection	Moderate	10 (28.57%)
	Moderately severe	15 (42.85%)
	Severe	10 (28.57%)
Presence of co-morbid conditions	Yes	17 (48.57%)
	No	18 (51.42%)
Immune status	Reduced (0–5)	15 (42.85%)
	Good (6–10)	20 (57.14%)

Table 1: Socio-demographic and clinical details of the sample.

Domains	Sub-domains	Group A (n = 17) (Mean ± SD)	Group B (n = 18) (Mean ± SD)	t-value	p-value
Mini-Mental State Examination (MMSE)	Orientation	4.77 ± 0.54	4.56 ± 0.81	-0.914	0.368
	Registration	4.72 ± 0.79	4.31 ± 0.79	-1.73*	0.04
	Recall	2.94 ± 0.23	2.68 ± 0.47	-2.02*	0.05
	Attention and concentration	4.38 ± 0.91	4.31 ± 0.87	-0.24	0.80
	Language	7.77 ± 0.54	7.50 ± 0.73	-1.26	0.21
	Copying	0.94 ± 0.23	0.81± 0.40	-1.18	0.24
Brief Cognitive Rating Scale (BCRS)	Concentration	1.22 ± 0.64	2.18 ± 0.83	3.79**	0.001
	Recent memory	1.27 ± 0.57	1.93 ± 0.85	2.67**	0.01
	Past memory	1.27± 0.57	1.56 ± 0.81	1.18	0.24
	Orientation	1 ± 0.00	1.12 ± 0.34	1.55	0.13
	Functioning and self-care	1.16 ± 0.38	1.87 ± 1.08	2.59**	0.01

Table 2: Comparison of cognitive functioning between COVID-19 survivors with co-morbidities (Group A) and without co-morbidities (Group B). #Higher scores in MMSE indicate better cognitive functioning and higher scores in BCRS indicate lower cognitive functioning. *p-value < 0.05; **p-value < 0.01 using t-test for group comparison. SD: standard deviation.

Cognitive tools	Domains	Immune Status Questionnaire (ISQ)	
		r-value	p-value
Mini-Mental State Examination (MMSE)	Total score	0.42**	0.01
Brief Cognitive Rating Scale (BCRS)	Concentration	-0.61**	0.00
	Recent memory	-0.63**	0.00
	Past memory	-0.39*	0.02
	Orientation	-0.39*	0.02
	Functioning and self-care	-0.54**	0.00

Table 3: Relationship between immune status and cognitive functioning of COVID-19 survivors. #Higher scores in ISQ indicate better immune status. *p-value < 0.05; **p-value < 0.01 using Pearson's correlation.

Discussion

The present study was aimed to explore the impact of immune status and presence of co-morbid conditions on the cognitive functioning of COVID-19 survivors. Immune status was measured by subjective reporting on ISQ and by the presence of co-morbid physical conditions, and cognitive functioning was assessed by cognitive tools *i.e.*, MMSE and BCRS. The study was planned as it has been seen in research that the vulnerability to COVID-19 infection and

severity is higher among the individuals who are having low immunity and co-morbid physical illness which could be chronic or critical illness [11]. Multifactorial facets are present in the development of COVID-19 infection, presentation, and recovery rates. Some specific risk factors like severity of infection, co-morbid physical illness, the status of immunity are determining the impact in COVID-19 condition (Table 1) [12].

In the present study, almost 50% of individuals were presented with co-morbidities *i.e.*, cardiovascular disorders (4), hypertension (6), diabetes (5), hypothyroidism (1), and allergic rhinitis (1) with the duration of at least 5 years or above. In the table, where two groups, with and without co-morbid conditions were compared on cognitive functioning, on MMSE in the domains of registration (t-value: -1.73; p-value: 0.04) and recall (t-value: 2.02; p-value: 0.05) significant differences were evident between the two groups (Table 2). In BCRS, there is a significant difference between the survivors with and without co-morbid conditions in the domains of concentration (t-value: 3.79; p-value: 0.001), recent memory (t-value: 2.67; p-value: 0.01), functioning and self-care (t-value: 2.56; p-value: 0.01). The findings suggest that primarily memory functioning is getting impacted, which is a major cognitive domain required in everyday functioning. It has been found that the co-morbidity indicates the higher chances of getting infected by the virus and the presence of physical illnesses or chronic health diseases is indicative of the decline in cognitive and functional abilities. In chronic health diseases, functionality is reduced and pathogenesis could be critical in nature which suggest altered psychological and cognitive functioning [13–15].

The table is showing a significant relationship between immune status and cognitive functioning which is indicated by total MMSE score as well as all domains in BCRS (Table 3). On MMSE, positive relations suggest better cognitive functioning with high immunity, whereas on BCRS negative relations also indicate similar findings where the scoring is reverse. It is already well studied that the development of antigens and reduction of pathogenesis is controlled through the immune system, and low immune system has a strong connection with poor cognitive functioning [16]. In the COVID-19 condition, deterioration of cognitive function may result from immune deficiency which influences neural function and is even more prevalent with co-morbid illness [17, 18]. The findings suggest that primarily memory functioning is impaired which may be due to the impact of COVID-19 infection, increased inflammation over the hypothalamus and hippocampus circuit which reduces the information processing speed and capacity to memorize [19, 20].

The present study findings, along with previous studies suggest that the global capacity of cognitive functioning could be affected by the novel coronavirus and the immune deficiency or poor immune status decides the severity of COVID infection. Reduction of immune activation, endothelial dysfunction, and lack of pericytes in COVID-19 patients indicated higher cognitive impairment [21].

Conclusion

Since the time of the outbreak, the COVID-19 virus has become intimidating for every aspect of human life, whether in physical or psychological health, financial conditions, or social functioning. Individuals who were suffering from critical or chronic illness conditions previously have become more vulnerable to the virus, and poor immune status is indulging their health deterioration due to the COVID-19 virus. It has been seen that the pathogenesis of the virus is not only impacting their physical functioning but also cognitive functioning is being impaired. Identification of domains and focusing on the cognitive training or remediation to the degenerative cognitive symptoms would prevent and help the survivors of COVID-19.

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