MINI-MENTAL STATE EXAMINATION IN HOSPITALIZED POST COVID-19 PATIENT TO IDENTIFY THE RISK OF ALZHEIMER`S DEVELOPMENT

By

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A thesis submitted to the School of Pharmacy in partial fulfillment of the requirements for the degree of Bachelors of Pharmacy (Hons.)

> School of Pharmacy BRAC University February, 2023

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Declaration

It is hereby declared that

- The thesis submitted is my/our own original work while completing degree at Brac University.
- 2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
- 3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
- 4. I/We have acknowledged all main sources of help.

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Approval

The thesis/project titled "Development of Alzheimer's in Post Hospitalized Covid Patient" submitted by Muhammad Muhtashim (19146062) of Spring, 2023 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelors of Pharmacy (Hons.) on

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Ethics Statement

This study does not involve any kind of human and animal trial.

Abstract

SARS Covid-19 has affected 6 million people in 2020 to 2022. The primary difficulty the patient faces respiratory difficulty. But the virus affects several peripheral systems as well. Central nervous system is one of the system affected by covid-19 Virus. This effect may lead to several neurological complexities including Alzheimer's or Dementia as most hospitalized post covid patient has the symptom of memory loss or forgetting information to some extent. A Mini Mental State Examination (MMSE) test was done on 15 hospitalized post covid patients where the test revealed mental state of the patient. Comparing the achieved result with the MMSE test of 6 Alzheimer's patient it was found that 40% of hospitalized post covid patient falls under the spectrum of Alzheimer's spectrum. The rest 20% scored normal in the MMSE test. Thus, most hospitalized covid-19 patients has the risk of developing Alzheimer's disease.

Keywords: Alzheimer's, MMSE, SARS Covid-19, Brain fog, Memory loss, Hospitalized Post Covid Patient & Dementia patient.

Dedication

The Article is dedicated to my supervisor Dr. Afrina Afrose, Ph.D who has supported me

throughout the courses and believed in my potentials.

Acknowledgement

It has been my Honor and Pleasure to have worked with Dr. Afrina Afrose. It was quite difficult to gather information of covid patients as pandemic is no longer continued. And hospitalized post covid patients are harder to find. Dr. Afrina Afrose ma'am has made it easier by guiding me the right way. Besides the gathering information of Alzheimer's patient was also challenging. Ma'am was there in the right time and has arranged us to attend "Alzheimer's Rally" in Ramna Park where we found patient of Alzheimer's to collect data from. And through thick and thin she was there as a blessing in disguise. By the grace of Almighty, the Thesis report was completed in due time. Moreover, Alzheimer society of Bangladesh is one of the major organizations who has helped us in the research. It was a wonderful experience working with them and through their assistance we were able to gather information on Alzheimer patients. Without them, it would have been much difficult to search and gather information On Alzheimer patients. Finally, I want to acknowledge School of Pharmacy and BRAC University who has supported me throughout the research.

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List of Acronyms

MMSE	Mini-Mental State Examination
ACE2	Angiotensin Converting enzyme 2
IL-1	Interleukins - 1
IL-6	Interleukins - 6
CKAP4	Cytoskeleton Associated Protein 4
GAL-9	Galectin - 9
APOE4	Apolipoprotein 4

Glossary

Brain Fog:	Brain fog, also known as forgetfulness or slow thinking, can occur for a number of reasons, including lack of sleep, illness, or pharmaceutical side effects that make a person drowsy. In addition, concussion may cause brain fog to appear. (Anon n.da)
Alzheimer`s:	A state where brain cannot remember instant or short-term information.
Hospitalized Post Covid-19 Patient:	Patient who were infected by Covid and was hospitalized for more than 1 and half month.

Chapter 1: Introduction

1.1 Background

SARS Covid 19 has spread throughout the world in the year of 2020 to 2022. The virus has affected 674,808,969 people worldwide with 6,759,086 deaths. About 646,938,038 patients recovered from the infection. The patients vary from various age range and occupation. After the infection the patient has shown several symptoms from breathlessness, weakness and decrease oxygen count. But some symptoms are common in all of the patient. The most common symptom found in all the patient is "Brain Fog". Brain fog, a phrase for slow or sluggish thought, can happen in a variety of situations, such as when a person is sleep deprived, is ill, or has drowsiness-inducing side effects from taking medication. Additionally, brain fog might develop after chemo or a concussion (Anon n.d.-a). Dementia is a disorder when memory and reasoning abilities are compromised to the extent that they make it difficult to carry out daily duties. The emotional instability and changes in personality that some dementia sufferers experience. According to (Canevelli et al. 2020) there several Covid cases has shown dementia. It has been also stated that the prolonged isolation due to quarantine has behavioral changes in the patient which may lead to dementia. Besides similar outcomes were observed in another article by (Ghaffari et al. 2021). In their statement, most patient has shown several CNS affecting symptoms most common being headache followed by worst case as Dementia. Most recent work was done by Ciaccio et al., 2021. He stated that the neurological damage caused by SARS Covid-19 that could result in the emergence of neurodegenerative illnesses like Alzheimer's (AD). There appears to be a mutualistic link between AD and COVID19. Patients with COVID-19 appear to be more likely to acquire AD. However, AD individuals may be more vulnerable to a severe COVID-19 (Ciaccio et al. 2021). Patient with severe Covid 19 infection has been prone to more episodes of Dementia. The intensity of dementia varies from the subtlest stage, where it is just starting to interfere with a people's function, until the most severe level, when a person must fully rely on others to perform basic daily functions like

feeding themselves (Anon n.d.-d). Hospitalized post covid patient shows various range of memory loss which has a severe possibility in developing Alzheimer's or in layman's term memory loss or Dementia. The thesis entitles the risk of development of Alzheimer's in hospitalized covid patient.

1.2 Research Gap

There is no data on the risk of Development of Alzheimer's in hospitalized post covid patient. Though there has been significant research done on respiratory complexities on Covid-19, few to no data exist on neurological effect of the virus. Some articles provide crucial evidence that the virus has the ability of entering the Central Nervous System. But the effect of the CNS infection and the post infection diagnosis is not analyzed. Based on the symptom of memory loss in post hospitalized Covid patient, the following research was conducted.

1.3 Objectives

The objective of the research is to identify the risk of developing dementia or Alzheimer's disease in hospitalized post Covid patients using a mini-mental state examination result.

1.4 Significance

The research done is to find out the development of Alzheimer's in hospitalized post covid patient. The patient who were discharged after a covid admission is found to have several symptoms correlating to Alzheimer's.

The research will produce data on the probability of developing Alzheimer in hospitalized post covid patient. This may allow healthcare professional to diagnose and treat patients who has developed Alzheimer's. Thus, it would make the patient's life easier after being discharged from hospital after covid-19 infection.

Chapter 2: Methodology

MMSE test was run on hospitalized post covid-19 patient. The participants were asked basic questions about their current situation and was post complications were determined.

MMSE test were also run on Alzheimer's patient to compare the MMSE scores of hospitalized post covid patient.

The number of data collected in MMSE is given in Table 1.

Table 1: Amount of Data Collected

Total Number of Hospitalized Post Covid Patient	15
Alzheimer`s Patient	6

The research method is shown in the flow diagram in Figure 1:

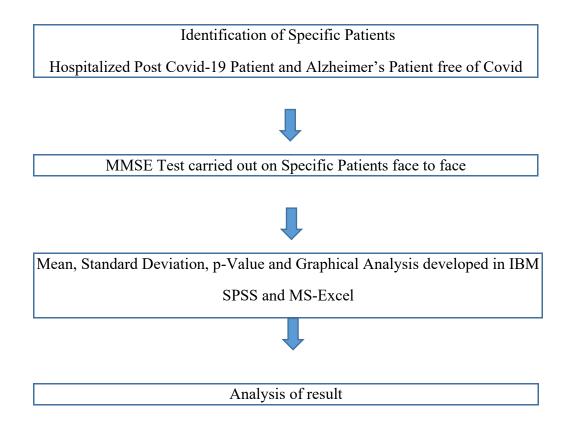


Figure 1: Flow diagram of research methodology

2.1 Identification of Specific Patients Hospitalized Post Covid-19 Patient and

Alzheimer's Patient free of Covid

The Covid-19 Patients selected were Hospitalized and not diagnosed for Alzheimer's. On the other hand, the Alzheimer's patients were not Covid positive.

2.2 MMSE Test carried out on Specific Patients face to face

The MMSE test was conducted face to face. The scores were given based on the answers and tasks done by the participants individually. The participants were asked questions to comply with the patient specifications.

2.3 Mean, Standard Deviation, p-Value and Graphical Analysis developed in IBM SPSS and MS-Excel

The data was entered in IBM SPSS and MS-Excel for calculation. Mean, Standard Deviation, p-Value and Graphical Analysis were done to achieve the research results.

2.4 Analysis of result

The achieved results were analyzed to develop the conclusion. Means of Hospitalized Post Covid-19 Patients and Alzheimer's Patient were compared. The standard deviation of the two sets of data were calculated and also their p-value. The Graph was developed by placing the score of Hospitalized Post Covid-19 Patients on the mean spectrum of the score of Alzheimer's Patients.

Chapter 3: Literature Review

3.1 COVID-19 post complications:

The aftermath of Covid-19, leaves the patient with series of physical and mental complications. The patient after recovering from Covid-19 has reported several symptoms relating to Cardiopulmonary symptoms and Central Nervous Systems. The majority of post-COVID-19 problems appear to be linked to the cardiopulmonary systems, according to the information that is currently available. , Arrhythmia, Myocarditis and ischemia are among the cardiac postCOVID-19 symptoms, whereas , pneumothorax, bacterial pneumonia and pleural effusion are the most often reported pulmonary consequences. In addition, systemic post-COVID-19 symptoms such exhaustion, headaches, body aches, dyspnea, and anxiety or despair are frequently reported (Suvvari et al. 2021). Besides Covid-19 is a Neurotropic virus (Ciaccio et al. 2021). This means the virus effects the Central Nervous System and can cause several symptoms to appear like memory loss, forgetting information and difficulties in day to day activities.

3.2 Alzheimer's Disease: Alzheimer's

disease is the leading cause of Dementia. The molecular pathophysiology of the disease's hallmarks, plaques made of amyloid (A) and tangles made of hyperphosphorylated tau, is now well understood because to developments in science (Blennow, de Leon, and Zetterberg 2006). The patient who suffers from Alzheimer's develops symptoms such as:

- i. Memory loss
- ii. Difficulty in day-to-day task
- iii. Confusion with time and place.

iv. Communication difficulty.



Figure 2: Symptoms of Alzheimer's disease

Alzheimer's is very common in old people. But the disease has no correlation with age. Alzheimer's disease or Dementia is not always a result of aging, according to data on centenarians2, but the likelihood of getting the diagnosis beyond the age of 85 is more than one in three. By the middle of the century, the prevalence inside the US will be close to 13.2 to 16.0 M cases as the population ages (Querfurth and LaFerla 2010).

3.3 MMSE: Definition, application, interpretation, relation AD.

MMSE or Mini Mental State Examination is a diagnosis process to carry out the measurement of memory status to achieve significant data on their neurological and motor capabilities. Doctors and other healthcare providers frequently utilize the Mini Mental State Examination (MMSE), a collection of 11 questions, to assess cognitive impairment (problems with understanding, thinking and memory) (Australia 2022).

The MMSE has the ability to evaluate six different types of mental skills, such as:

- i. Recognizing the time and location of our attention/concentration
- ii. Understanding the time and location of our attention/concentration
- iii. Instantaneous memory (recall)
- iv. Speaking abilities
- v. Visual and spatial links between things and the capacity to comprehend
- vi. Understand and follow commands

The Test has 11 Questions of which first 6 involves instantaneous awareness, memory test and

simple object identification. The 7th question measures the speech ability of the patient. 8th to

11th questions measure the motor ability of the patient as well as following commands. The MMSE allows for a maximum score of 30. A normal score is one of 25 or higher. A score

of less than 24 is typically seen as abnormal and indicative of possible cognitive impairment

(Australia 2022).

3.4 Neuropathology of COVID-19 & Alzheimer's

The research is carried out to signify the probable state of Dementia in Post Covid patient.

Through various survey and research article it has been reported that people are suffering from

brain fog or Alzheimer's symptoms in the Covid patients.

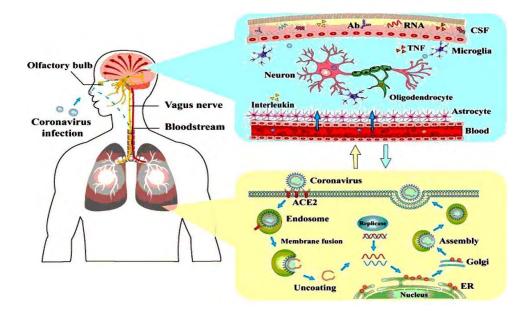


Figure 3: SARS-Cov-2 Pathogenesis

The State of decreased neurological functioning or tendency of forgetting simplest information's are found in the post Covid patients.

According to Ciaccio et al., 2021, SARS CoV-2 attacks the olfactory neurons before spreading to the olfactory bulb in hypothalamus via the central nervous system of the olfactory mucosa. Mast cells, microglial, astrocytes, and other non-neuronal cells are activated by SARS CoV-2 in olfactory bulb, and these cells release pro-inflammatory cytokines into the surrounding tissue. The phospholipids of the cell are used by SARS-CoV-2 to create its own envelope. The result is that the cells, particularly the adaptive immune cells, lack precursors for the production of the Alipamides, which play a crucial role in regulating the excessive reactivity known as autacoid local damage. As a result, the neuroinflammation that results could go out of control, especially in elderly people who have less effective immune system responses. The progression of neurodegenerative illnesses like AD may be favored by neuroinflammation, which is linked to severe oxidative stress and may cause neurodegeneration. Old age and illnesses with such an inflammatory background, like diabetes, atherosclerosis, and sub-clinical dementia, may enhance the chance of developing AD in COVID-19 patients. (Ciaccio et al. 2021)

Again in the statement of Rahman et al., 2021, angiotensin converting enzyme 2 (ACE2) receptors, pro-inflammatory indicators such IL-1, IL-6, cytoskeleton associated CKAP4, GAL9 and the APOE4 common links are shared by COVID-19 and AD.

As there is evidence of CNS effect and olfactory nerve inflammation seen by the Covid 19 virus with neurobiological linkup between Covid-19 and Alzheimer's, the following research was conducted to establish the possibility of development of Alzheimer's in post Covid patient. The Research was narrowed down to Hospitalized patient who possess higher chance of development of Alzheimer's.

Chapter 4: Result and Discussion

4.1 Result

MMSE Test was run on Hospitalized Post Covid-19 Patients and Alzheimer's Patients. The scoring was done out of 30. Based on the individual's performance a score was provided for each 11 tasks.

We took the values of Hospitalized Post Covid Patients as variables and scores of Alzheimer's patient was taken as Standard. The collected data from MMSE tests from both groups are given in Table 2 and Table 3:

Table 2 - Hospitalized Post Covid-19					
SĨ.	Hospitalized Post Covid-19 Score				
1.	25				
2.	26				
3.	20				
4.	19				
5.	25				
6.	24				
7.	23				
8.	17				
9.	25				
10.	20				
11.	18				
12.	24				
13.	26				
14.	26				
15.	18				

Table	2	-	Hospitalized	Post	Covid-19
I able	4	-	позрнание	rost	Covia

Table 3 - Alzheimer`s Score			
SI.	Alzheimer`s S		

SI.	Alzheimer`s Score
1.	19
2.	24
3.	21
4.	22
5.	23
6.	17

Average mean of the test results gathered from the patients are given in Table 4:

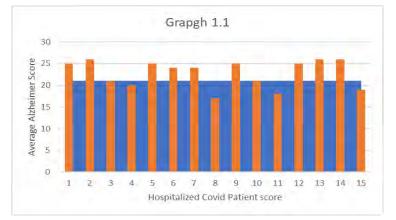
Table 4– Average Mean Result	
Hospitalized Post Covid Patients	22.3636
Alzheimer Patients	21

Table 5 – Standard Deviation Table

Hospitalized Covid Patients comparrission					
Alzheimer P,	Mean	N	Std. Deviation		
.00	22.3333	9	3.60555		
17.00	24.0000	1			
19.00	25.0000	1			
21.00	26.0000	1			
22.00	21.0000	1			
23.00	25.0000	1			
24.00	20.0000	1			
Total	22.8000	15	3.14416		

Report •

[•] We achieve the p-Value at 2.1090



Following Figure 3 represents the graphical analysis of the MMSE test result

Figure 3 – Bar chart of hospitalized post covid patient MMSE score on mean of Alzheimer MMSE score spectrum

In Graph we plotted the bar graph on the area covered by the mean value of Alzheimer score.

We find 9 (60%) of hospitalized post covid patient has a higher score than Alzheimer's spectrum i.e. 21. But only 3 (20%) hospitalized post covid patient has a score higher than 25. Other 6 (40%) lies in the range of 20 to 25.

We find 40% of the patient who lies on the spectrum of Alzheimer has a lower score ranging from 15-20.

4.2: Discussion

From the above analysis we obtain the following conclusion

i. Mean between the Alzheimer score and the hospitalized post covid patient score are very close.

ii. We find the Standard Deviation at 3.1442 and P-Value at 2.1090

iii. 40% hospitalized post covid patient lies on the spectrum of Alzheimer. 40% lies slightly above the Spectrum of Alzheimer. Only 20% is seen above the normal scale.

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Thus, we can say that the hospitalized post covid patient with severe Covid Infection has a higher probability of developing Alzheimer's.

Talking to patient named Mira Dutta who was in hospital for 3 months at Chittagong Medical Hospital and oxygen support. She scored an 18 in MMSE test & has stated her memory has reduced significantly. Difficulty in her day to day activities has started after being discharged from hospital.

Again, after speaking with Tahmina Sultana who was hospitalized for 2 months at Kurmitola Hospital has also stated memory loss in certain aspects though her score was 24.

Chapter 5: Conclusion, Limitation & Future limitation

5.1: Conclusion

The conclusion from the analysis are

- i. Hospitalized Post Covid-19 patients has a chance of developing Alzheimer's.
- ii. Hospitalized Post Covid-19 patients may not develop Alzheimer but may show extent of memory loss.
- iii. Few exceptions of patients may not develop memory loss.
- iv. Covid-19 can affect the central nervous system and cause brain fog which is initial stage of memory loss.

5.2: Limitations

- The Participant size is small to only 15. Hospitalized Post Covid-19 patients are harder to come across. And willing participants are even rare.
- ii. Hospitals and Covid centers are unwilling to share data without Ethical Permission. As due to lack of resources no negotiations were possible.
- iii. Some Participant data was casted out as they left the test mid-way due to stigma & shyness.

7.3: Future Recommendations

The extent of their infection cannot examine to establish severe infection increases the possibility of Alzheimer's. This would require Blood analysis and CSF analysis.

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Appendix A.

MINI-MENTAL STATE EXAMINATION IN HOSPITALIZED POST COVID-19 PATIENT TO IDENTIFY THE RISK OF ALZHEIMER'S DEVELOPMENT

Name: Muhammad Muhtashim

ID: 19146062

University: Brac University

Participants: Post Hospitalized Covid-19 Patient (Random)

Project Supervisor: Dr. Afrina Afrose, PhD

Assistant Professor, Department of Pharmacy, Brac University.

*Required

Disclaimer

All the date for this test will be used for research purpose only. The subject's name and identity will not be disclosed in any research publication.

I acknowledge that I have been asked to participate in a survey regarding social media usage.

This survey is conducted by Muhammad Muhtashim . I understood the disclaimer and agreed to participate willingly. *

Signature:		

Date: _____

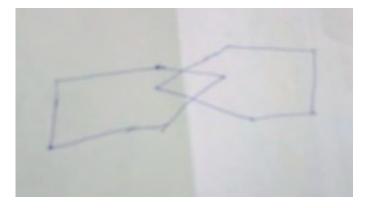
Mini Mental State Examination

Patient's Name: <u>Anonymous</u> Date: <u>12thJanuary</u>,2023

<u>Instructions:</u> Ask the questions in the order listed. Score one point for each correct response within each question or activity.

Maximum	Patient's	Questions	
Score	Score		
5	5	"What is the year? Season? Date? Day of the week? Month?"	
5	5	"Where are we now: State? County? Town/city? Hospital? Floor?"	
3	1	The examiner names three unrelated objects clearly and slowly, then asks the patient to name all three of them. The patient's response is used for scoring. The examiner repeats them until patient learns all of them, if possible. Number of trials:	
5	1	"I would like you to count backward from 100 by sevens." (93, 86, 79, 72, 65, …) Stop after five answers. Alternative: "Spell WORLD backwards." (D-L-R-O-W)	
3	0	"Earlier I told you the names of three things. Can you tell me what those were?"	
2	1	Show the patient two simple objects, such as a wristwatch and a pencil, and ask the patient to name them.	
1	1	"Repeat the phrase: 'No ifs, ands, or buts.'"	
3	2	"Take the paper in your right hand, fold it in half, and put it on the floor." (The examiner gives the patient a piece of blank paper.)	
1	1	"Please read this and do what it says." (Written instruction is "Close your eyes.")	
1	1	"Make up and write a sentence about anything." (This sentence must contain a noun and a verb.)	
1	1	"Please copy this picture." (The examiner gives the patient a blank piece of paper and asks him/her to draw the symbol below. All 10 angles must be present and two must intersect.)	

Patient pic to 11th Question-



Total MMSE Score - 19