

The Prevalence and the Effect of COVID-19 Infection on Older Patients with Dementia: A Single-center Experience in the Light of Comprehensive Geriatric Assessment

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Abstract

Objective: Patients diagnosed with dementia are at increased risk for COVID-19 infection since they are unable to perform hygiene and social distance due to difficulties recalling or their dependency on another person. Also, there is a strong correlation between mortality of COVID-19 and dementia. In this study, we aimed to elucidate the prevalence of COVID-19 in patients with dementia and their cognitive decline during a pandemic.

Materials and Methods: A total of 210 patients diagnosed with dementia and followed up in the outpatient clinics of geriatrics in our university hospital were included in the study. Their records were obtained from the hospital information system. Demographical data, comprehensive geriatric assessments, cognitive changes, COVID-19 infection status, and the dates of deaths were recorded.

Results: Patients were divided into three groups mild, moderate, and severe dementia. COVID-19 prevalence was 11.9% in our study population. When we compared patients according to the history of COVID-19 infection status, there were no differences between the type and the stage of dementia between the COVID-19 infection negative and positive groups ($p>0.05$). Age and sex distribution were similar between these two groups ($p>0.05$). The prevalence of geriatric syndromes was similar in COVID-19 infection positive and negative groups. Furthermore, more than half of the patients in every stage of dementia had cognitive decline during the pandemic course. However cognitive decline rates were not different between COVID-19 positive and negative groups ($p>0.05$).

Conclusion: One in every ten patients with dementia had COVID-19 infection to our results. According to our findings, there is no increase in the frequency of COVID-19 between stages of dementia, the restrictions due to the pandemic cause a decline in cognitive functions. During the pandemic, interventions to protect cognitive functions and periodic health control should not be interrupted for patients with dementia.

Keywords: Dementia, COVID-19, SARS-CoV-2, Alzheimer's, Cognitive decline

Introduction

SARS-COV-2 virus infection has influenced all over the world over the two years, and over 5.6 million deaths occurred globally as of February 1, 2022, even though the vaccination process (1). Chronic comorbidities were determined as risk factors for COVID-19 infection, as well as dementia (2). In older patients hospitalized due to COVID-19, the prevalence of dementia is found elevated in recent observational studies (3). A study that looked at dementia and COVID-19 data from different countries

discovered a relationship between a load of dementia and COVID-19 events (4). Furthermore, the mortality rate because of COVID-19 has been reported to be higher in dementia patients. On the other hand, there is limited data in the literature about the prevalence of COVID-19 in patients with dementia, one study from Spain was reported that the prevalence of COVID-19 in patients with dementia was 15.2% and the mortality rate was 41.9% in patients with COVID-19 (5).

Patients diagnosed with dementia are at increased risk for COVID-19 infection since patients with dementia are unable to

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perform hygiene (hand-washing, usage of face mask) and social distance due to not recalling or dependency on basic activities of daily living. Another reason for catching or spreading COVID-19 in people with dementia is that they have to live in-crowd if they need care (2). It is well-known fact that people with dementia are more frail and frailty in older adults increases the risk of infections while decreasing the immune response, putting the specific population at a higher risk (6,7).

Atypical presentation of the COVID-19 infection in older patients makes it difficult to diagnose leading to increased morbidity and mortality of the infected patients with dementia (8). In a study from Turkey, the presence of dementia increased the risk of mortality in both the 60-79 age and >80 age groups (9).

Moreover, another impact of COVID-19 other than direct physical health is the psychological health of older people with dementia, which was affected due to social isolation policies. Increased frailty, reduced quality of life, high level of stress, increased depressive symptoms were observed during the lockdown period of the pandemic course (10).

In this study, we aimed to elucidate the prevalence of COVID-19 in patients with dementia followed up in our outpatient clinic and to show its relation with other geriatric syndromes. The secondary purpose of the study is to provide information about the cognitive decline in dementia patients during the pandemic course and to show the effect of having COVID-19 on cognitive decline.

Materials and Methods

Study design

Patients who were diagnosed with dementia and followed up in the outpatient clinics of geriatrics in our university hospital were included in the study. We performed a retrospective study using the identified electronic records from the hospital information system who were admitted to the hospital between 11 March 2020 and 31 March 2021. Two hundred forty-four patients with dementia were admitted to the outpatient clinic in this period and 210 patients were included after excluding patients with incomplete data, patients diagnosed with delirium, and patients who did not admit to our clinic regularly during the study period. Other conditions that may impair cognitive test performances including acute illness, infection, electrolyte imbalances, etc. were also excluded from the study. Patients were followed up for three-month periods before and during the pandemic course. Their closest MMSE test or Clock Drawing test to the date of the pandemic beginning was accepted as before pandemic score of cognitive examination. For the standard evaluation, 6 months after the first cognitive examination a second MMSE and/or Clock Drawing test score was recorded a during the pandemic score of cognitive examination. Age, gender, education, marital

status, type and stage of dementia, comorbidities, number of medications were collected from the electronic records of the patient's files. Patients were divided into three groups according to their Clinical Dementia Rating Scale(CDR) (11) as mild, moderate, and severe dementia groups.

Comprehensive geriatric assessments of the patients were also recorded from electronic files. Frailty was defined according to Clinical Frailty Scale(CFS) (12). CFS was defined according to clinical judgment by the physician of the patient between 1 (very fit) to 9 (terminally ill). Patients whose scale was equal to or more than 5 were accepted as patients living with frailty. Incontinence was accepted as either urinary or fecal incontinence or both by expressions of patients or caregivers. Polypharmacy was defined as the usage of 5 or more medications (13). Fall event was recorded if the patient had fallen unintentionally in the previous year. Difficulty in falling asleep, frequent awakening during the night, or awakening early in the morning were categorized as insomnia. Cognitive decline was decided in one of these situations; a) objective decline in cognitive test scores b) getting started on NMDA receptor antagonist treatment according to clinical judgment in patients who were previously diagnosed with mild dementia c) the clinical necessity of antipsychotic treatment in moderate to severe dementia.

The risk of malnutrition was evaluated by Mini-Nutritional Assessment-Short Form (MNA-SF) (14). MNA- SF scores between 8-11 were defined as the risk of malnutrition and, scores lower than 8 were accepted as malnutrition. The presence of depression was assessed by 15-item Yesavage Geriatric Depression Scale (YGDS) (15) and 5 and lower scores were evaluated as depression. Six-item Katz activities of daily living (ADL) score and 8-item Lawton-Brody instrumental activities of daily living (IADL) score were used for assessing the functionality of the patients (16). The cognitive status of patients was evaluated by Mini-Mental State Examination (MMSE) and Clock-Drawing Test (17, 18). In Mini-Mental Status Examination (MMSE) test, six different cognitive domains, orientation, memory registration, attention, delayed recall, language, motor functions, were evaluated. Orientation was assessed through ten questions, year, season, date, day, month, town, county, hospital, floor, and the current president of the Republic of Turkey. Memory registration was tested by memorizing three words, blue, hawk, and tulip. Attention was evaluated by serial 7's backward calculation from 100. 1 point was given for each correct answer and the maximum score was 5. The delayed recall was questioned via memorized three words earlier on the test. The language was rated by naming two objects and repeating a sentence and being given 3 points. Motor functions were scored over 6 points according to the fulfillment of the given tasks. The maximum MMSE score was 30 points. We had scored the "Clock drawing test" according to an article titled "Early Diagnosis of Dementia via a Two-step Screening and Diagnostic Procedure" by Stahelin et al. (19) The patient

was asked to draw a clock as a circle then place the numbers. If the number "12" was at the top, the patient has scored 3 points. If the clock had 12 numbers exactly, the patient was given an additional 1 point. If there were two distinguishable hands, the total score was 5. If the patient showed the time correctly, the maximum score, 6 points, was given.

COVID-19 infection status were obtained from National Health System records through the hospital automation program, and e-Nabız, a free service provided by the Ministry of Health. COVID-19 infection was accepted as positive if the SARS-CoV-2 PCR test was positive. Those who have been exposed to at least two doses of the COVID-19 vaccine were considered to be fully vaccinated. The date of death was obtained from the death notification system till the date of 30 September 2021 to maintain at least a six-month follow-up time. The causes of death were obtained by examining the epicrisis in e-Nabız or hospital automatic program.

Ethical approval

The study protocol was in adherence with the principles in the Declaration of Helsinki. The local ethics committee of our university hospital approved the study protocol.

Statistical Analysis

The data of three groups according to stages of dementia, and two groups according to COVID-19 infection positivity were analyzed. Tests of normality were performed. Categorical variables were stated as number (n) and percentage (%), and continuous variables as median (IQR) or mean \pm Standard deviation (SD) values according to the normal distributions or not. To evaluate relationships between categorical variables, a Chi-square test was used. In the comparison of three variables, Bonferroni correction was wielded. Student- t-test or ANOVA was utilized to compare the normally distributed numerical parameters between two or three independent groups when appropriate, and the Kruskal-Wallis test was used to compare the parameters which were not normally distributed. Wilcoxon analysis was performed for dependent variables, to evaluate the cognitive test results before and during the pandemic course. A value of $p < 0.05$ (two-sided) was accepted as statistically significant. The data obtained in the study were analyzed statistically using IBM SPSS Statistics vn. 24.0 software (IBM Co., Armonk, NY, USA).

Results

Between 11 March 2020 and March 2021, a total of 210 patients with a diagnosis of dementia were included in the final analysis. COVID-19 infection was positive in 25 patients, 11.9% of the study population. When three groups as mild, moderate, and severe dementia were compared; the highest mean age was observed in the severe dementia group whereas

the mild dementia group had the lowest mean age and the difference was statistically significant (p -value:0.006). The female/male ratio was higher in all three groups. The majority of the patients were living at home, whereas only 4 patients were living in long-term care facilities. The most common type of dementia was Alzheimer's Disease (AD) in all three groups. Cognitive decline was revealed in 110 patients, 52.3% of all study population. When the stage of dementia progresses, patients living with frailty become more prevalent according to CFS ($p < 0.001$). There were no differences between dementia groups regarding the prevalence of comorbidities and geriatric syndromes except urinary incontinence. Urinary incontinence was more commonly seen in severe dementia ($p < 0.001$). ADL, IADL, MNA-SF and cognitive tests scores (MMSE, 3 words recall, and clock-drawing test) were all worse in severe dementia and the differences were statistically significant ($p < 0.001$, p -value: 0.006 and p -value:0.001, respectively). On the other hand, no difference was observed in cognitive decline in all three different stages of dementia ($p > 0.05$). More than half of the patients in every stage have become worse during the pandemic course. The median(IQR) MMSE score during the pandemic was 17 (9.0) whereas it was 21(10.0) before the pandemic, and the difference was statistically significant, the p -value was calculated lower than 0.001. No significant difference was seen in the COVID-19 rates according to the stage of dementia, whereas severe dementia patients were more commonly hospitalized due to COVID-19 infection (p -value:0.016). There were similar mortality rates in all three groups during the pandemic course, furthermore, only one patient died from COVID-19 infection in each group. The detailed results were shown in Table 1.

The relationship between COVID-19 disease groups and geriatric syndromes in patients with dementia were summarized in Table 2. No difference was found between COVID-19 PCR positive and negative groups regarding the type and the stage of dementia, age, gender, geriatric syndromes including frailty, falls and polypharmacy. The prevalence of cognitive decline was not different between the two groups ($p > 0.05$).

Discussion

In this study, we aimed to investigate the prevalence of the COVID-19 infection in people with dementia and the effect of the pandemics on that vulnerable population. According to our findings, COVID-19 infection is quite common in people with dementia unrelatedly to the stage of the disease. Furthermore all three groups of dementia patients, mild, moderate, and severe, deteriorated during the pandemic era. The most important outcome of this retrospective analysis is that cognitive decline was observed in over half of the patients with mild, moderate, and, severe dementia regardless of COVID-19 infection status.

Cognitive decline is an expected outcome in patients with dementia, In a study conducted by Ballard et al. during a 1-year

	Mild (n=80)	Moderate (n=105)	Severe (n=25)	p
Age, mean \pm SD	79.44 \pm 6.42	81.70 \pm 6.93	84.16 \pm 7.23	0.006
Age groups, n (%)				
65-74	17 (21.25)	20 (19.1)	3 (12.0)	0.027
75-84	47 (58.75)	47 (44.7)	9 (36.0)	
>85 and older	16 (20.0) ^a	38 (36.2)	13 (52.0)	
Gender, female, n (%)	54 (67.5)	65 (61.9)	20 (80.0)	0.217
Marital status				
Married, n (%)	33 (55.9)	30 (44.1)	7 (50.0)	0.414
Education				
<8 years, n (%)	37 (63.8)	41 (69.5)	10 (76.9)	0.607
Type of dementia, n (%)				
Alzheimer disease	71 (88.8)	91 (86.7)	21 (84.0)	0.862
Others	9 (10.2)	14 (13.3)	4 (16.0)	
Living w/frailty, CFS	21 (15.2) ^a	92 (66.7)	25 (100.0)	<0.001
Comorbidities, n (%)				
Diabetes	23 (28.7)	37 (35.2)	6 (24.0)	0.446
Hypertension	57 (71.3)	69 (65.7)	12 (48.0)	0.102
Coronary artery disease	22 (27.5)	34 (32.7)	4 (16.7)	0.279
Chronic cardiac failure	6 (7.6)	10 (9.6)	1 (4.2)	0.659
Atrial fibrillation	11 (13.9)	19 (18.1)	3 (12.5)	0.664
Hyperlipidemia	15 (19.0)	19 (18.1)	2 (8.4)	0.457
Hypothyroidism	11 (13.9)	9 (8.7)	1 (4.2)	0.296
Asthma	3 (3.8)	4 (3.8)	-	0.622
COPD	6 (7.6)	9 (8.7)	-	0.334
Rheumatological dis.	4 (5.1)	6 (5.8)	1 (4.2)	0.944
Malignancy	10 (12.7)	12 (11.5)	1 (4.2)	0.501
Cerebrovascular disease	5 (6.3)	8 (7.7)	5 (20.0)	0.094
Benign prostate hyperplasia	14 (17.5)	9 (8.7)	3 (12.5)	0.188
Other	17 (21.5)	22 (21.0)	5 (20.8)	0.995
Geriatric syndromes, n (%)				
Incontinence	26 (42.6) ^a	49 (62.8)	21 (100.0)	<0.001
Polypharmacy	54 (74.0)	76 (80.0)	14 (66.7)	0.366
Osteoporosis	34 (54.0)	34 (40.5)	13 (68.4)	0.052
Falls	15 (25.4)	17 (22.1)	9 (47.4)	0.080
Insomnia	18 (30.0)	26 (32.5)	8 (44.4)	0.517
Depression	10 (29.4)	11 (34.4)	2 (66.7)	0.306
Nutritional assessment				
Normal	16 (38.1)	8 (16.7)	-	<0.001
Risk of malnutrition	20 (47.6)	22 (45.8)	3 (21.4)	
Malnourished	6 (14.3)	18 (37.5)	11(78.6)	
CFS, median (IQR)	4.0 (3.0)	5.0 (3.0)	7.0 (0.0)	<0.001
ADL median (IQR)	4.0 (3.0)	4.0 (3.0)	1.5 (-)	<0.001
IADL, median (IQR)	5.5 (5.25)	0.0 (3.5)	0.5 (-)	<0.001
MNA-SF, median (IQR)	10 (4.5)	10 (5.0)	10.5 (-)	<0.001
YGDS median (IQR)	4.5 (6.25)	4.0 (3.5)	8.0 (-)	0.209
Number of medication, median (IQR)	6 (5.25)	6 (5.0)	6.5 (.)	0.157
MMSE median (IQR)	22 (8.25)	15 (16.0)	0.0 (1.0)	<0.001
Three words, median (IQR)	1.0 (2.0)	0.0 (1.5)	0.0 (0.0)	0.006
Clock-drawing test, median (IQR)	2.0 (6.0)	1.0 (4.0)	0.0 (0.0)	0.001
Cognitive decline, n (%)	50 (62.5)	57 (54.3)	3 (52.0)	0.605
COVID-19 PCR positive	8 (10.0)	14 (13.3)	3 (12.0)	0.786
COVID-19 hospitalization	2 (25.0)	1 (7.1)	2 (66.7)	0.016
COVID-19 vaccines (at least two doses)	29 (36.3)	33 (31.4)	7 (28.0)	0.676
Outcomes				
Exitus	8 (10.0)	22 (21.0)	4 (16.7)	0.474
Causes of death				
COVID-19 related	1 (12.5)	1 (4.6)	1 (25.0)	0.380
Other causes	7 (87.5)	21 (95.4)	3 (75.0)	

COPD: Chronic obstructive pulmonary disease, CFS: Clinical frailty scale, ADL: Activities of daily living, IADL: Instrumental activities of daily living, MNA-SF: Mini-nutritional assessment-short form, Yesevage geriatric depression scale, MMSE: Minimal state examination, PCR: Polymerase chain reaction, SD: Standard deviation, COVID-19: Coronavirus disease-2019, ^a After the subgroup analysis, the difference is originated from mild AD

Table 2. Geriatric syndromes according to COVID-19 infection PCR positivity

	COVID positive (n=25)	COVID negative (n=186)	p
Age, mean \pm SD	82.32 \pm 6.34	80.99 \pm 7.06	0.374
Gender, female*	17 (68.0)	122 (65.6)	0.812
Type of dementia, AD*	23 (92.0)	161 (86.6)	0.769
Stage, moderate*	13 (54.2)	88 (48.9)	0.821
Living w/frailty, CFS*	18 (75.0)	116 (63.7)	0.277
Incontinence*	9 (50.0)	87 (61.3)	0.358
Polypharmacy*	18 (81.8)	126 (75.4)	0.510
Osteoporosis*	14 (66.7)	67 (46.2)	0.080
Falls*	2 (10.5)	39 (28.7)	0.093
Insomnia*	8 (42.1)	44 (31.7)	0.363
Cognitive decline*	10 (40.0)	110 (59.5)	0.182

*n (%), AD: Alzheimer's disease, CFS: Clinical frailty scale, SD: Standard deviation, COVID-19: Coronavirus disease-2019, PCR: Polymerase chain reaction

follow-up period, 4–5 points decline was found in MMSE scores in patients with Alzheimer's Dementia, Lewy body dementia, and Vascular Dementia (20). However, this decline becomes more noticeable during the pandemic era. Ismail et al. showed 0.53 \pm 0.3 points decline monthly in MMSE scores during the lockdown period in patients with dementia and mild cognitive impairment (21). Similar to these studies, we also found 4 points of decline in MMSE scores in a 6-month of the period according to our results. Consistent with our findings, in a study from China, it was shown that social isolation correlated with the accelerated decline of cognitive function and neuropsychiatric symptoms both in patients with Alzheimer's Dementia and Dementia with Lewy Body (22). Another study conducted in Greece revealed that a significant overall decline in people with mild cognitive impairment and dementia was observed, and the domains most affected were communication, mood, movement, and compliance with the new measures (23).

It is known that clinical conditions of patients with dementia and living with frailty worsen due to the enhancing effect of the pandemics directly increasing the risk of morbidity and mortality from COVID-19 infection, or indirectly diminishing social support and decreasing interaction with the health care system. People with dementia are more vulnerable, neglected, and negatively discriminated and they are not capable of caring for themselves. Plenty of studies shows that people with dementia are affected negatively by health decisions in relation to COVID-19 and its long-term effects including neurological damage (24).

There are several factors contributing to the clinical decline in patients with dementia. During social isolation, cognitively intact people could use technology to stay socially connected,

on the other hand, people with cognitive impairment who live alone had trouble with using technology. Furthermore, patients with dementia had difficulty in admission to healthcare facilities. A special article by Brown et al. mentioned that follow-ups by telephone or video-conferencing may not be adequate to monitor disease progression (25).

Dementia is a known risk factor for COVID-19 infection. In a retrospective study from the UK Biobank cohort (23), all-cause dementia was associated with a higher risk of COVID-19 infection. However, age was a confounding factor, since patients with dementia were significantly older than non-dementia patients (23). On the other hand, in our study mean age was not different between COVID-19 PCR positive and negative groups.

Another study executed from electronic health records of the United States revealed that the highest risk of COVID-19 infection belonged to vascular dementia, and they speculated that impaired cerebral blood flow, or damaged endothelium, could be a risk for SARS-CoV 2 entry (26). However, in the current study, we could not find any relationship between the types of dementia and COVID-19 infection since the most common type of dementia in our study was Alzheimer's Disease.

In a case-control study from Spain, the mortality rate of COVID-19 infection in patients with primary neurodegenerative dementia was 43.4 % whereas 21.5% in the control group (27). In another study from Spain, the frequency of COVID-19 in dementia patients was 15.2% and the mortality rate was 41.9 % in COVID-19 positive patients (5). In our study, the prevalence of COVID-19 was 11.9%, however, it would not be appropriate to comment on the mortality rate since only 3 patients died from COVID-related causes. The mortality rate was significantly higher in patients living in care homes in a previous study (5), however in our study, the number of patients who were living in care homes were too low, therefore this may be the situation explaining the relatively lower mortality rate due to COVID-19 in patients with dementia.

In a review by Azarpazhooh et al., there was a strong correlation between mortality from COVID-19 and dementia (4). In another review, the presence of dementia increased by 4.2% in the mortality (28). A nationwide study by Esme et al. also found that the presence of dementia increased the risk of mortality by 1.63 times in the 60–79 age group, and 1.47 times in patients older than 80 years of age (9).

According to our findings, there were no differences in other geriatric syndromes including frailty and malnutrition between COVID-19 PCR positive and negative patients. In an international multi-center study, frailty was increased mortality risk three times independently of other conditions. Frailty was also associated with increased risk of care requirements (29). Malnutrition is also important for COVID-19 infection. A systematic review

stated that the prevalence of malnutrition among older patients with COVID-19 was high and it was associated with negative outcomes including hospital deaths and transfer to intensive care units (30). Analysis of the data from UK Biobank unlike our findings demonstrated that polypharmacy was associated with COVID-19 (31). Although there are some studies on the relationship between geriatric syndromes and COVID-19 infection, our study was conducted on patients with dementia and included a relatively small sample. When considering the close relationship of dementia with all geriatric syndromes, this could be the reason why there was no difference between COVID-19 positivity and geriatric syndromes. Despite all these limitations, our study is a rare study that combined COVID-19 infection and CGA in patients with dementia.

Study Limitations

This study is an observational study from a university hospital and it has some limitations, first of all, it has a retrospective design with a relatively small population, and there is not a control group of cognitively intact patients to evaluate cognitive decline. Our findings could not be generalized to the whole population, because the number of hospitalized patients with dementia was too low. On the other hand, there are few studies about COVID-19 and dementia. Therefore, although its retrospective design, the study presented the comprehensive geriatric assessment results and their relationship with COVID-19 infection, revealing the study's strength. This study provides "real-world" data giving the frequency of COVID-19 infection in a specialized patient group is another strength of the study.

Conclusion

It is a known fact that patients with dementia are at higher risk for infection, and they have increased morbidity and mortality rates. Since they have trouble with accessing health care facilities and need help in daily living activities, they are vulnerable and need protection. Patients with cognitive impairment need additional support to adequately practice infection control procedures during the pandemic era. These procedures are also crucial for caregivers of patients with dementia who may be at risk of COVID-19. Comprehensive geriatric assessments and cognitive evaluations are essential for every dementia patient. To the best of our knowledge, it is the first study to investigate the prevalence of COVID-19 in patients with dementia from Turkey. Although there is no increase in the frequency of COVID-19 between stages of dementia, the restrictions due to the pandemic cause a decline in cognitive functions. During the pandemic, interventions to protect cognitive functions and periodic health control should not be interrupted for patients with dementia.

Ethics

Ethics Committee Approval: The study protocol was in adherence with the principles in the Declaration of Helsinki. The local ethics committee of our university hospital approved the study protocol.

Informed Consent: Retrospective study.

Authorship Contributions

Concept: M.G.O., Y.Ö., A.O.B., S.C., B.B.D., M.C., M.G.H., Design: M.G.O., Y.Ö., M.G.H., Data Collection or Processing: M.G.O., Y.Ö., A.O.B., S.C., M.G.H., Analysis or Interpretation: M.G.O., Y.Ö., A.O.B., S.C., B.B.D., M.C., M.G.H., Literature Search: M.G.O., A.O.B., S.C., M.G.H., Writing: M.G.O., Y.Ö., S.C., B.B.D., M.C., M.G.H.,

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