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Cognition, Behavior, and Caregiver Stress in Dementia during the COVID-19 Pandemic: An Indian Perspective

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Keywords
Dementia · Cognition · Caregiving · COVID-19 · Pandemic · India · Lower middle-income countries

Abstract

Objectives: Little is known regarding the cognitive and behavioral status of patients with dementia and their caregivers in lower middle-income countries during the COVID-19 pandemic. This study aimed to understand the impact of the pandemic on persons with dementia and their caregivers in India. ***Methods:*** This was an observational study. A cohort of 66 persons with dementia and their caregivers were evaluated during the COVID-19 pandemic in 2 specialist hospitals in South India. Caregivers were interviewed at 2 distinct time points of the pandemic: during the national lockdown and 5 months after during later periods of the "cluster of cases" transmission phase. Participants were assessed via telephone utilizing validated instruments (Neuropsychiatric Inventory [NPI], Clinical Dementia Rating [CDR] Scale, and Depression, Anxiety and Stress Scale [DASS-21]) and a semi-structured questionnaire. The questionnaire documented sociodemographic information, clinical history, infection measures adopted, changes in caregiving routines, involvement in functional rehabilitation activities, and access to medical and long-term care support services. ***Results:*** The 2-phase follow-up study found a significant worsening of behavior in dementia patients, demonstrated by a difference in the NPI sub-domain scores for anxiety (mean difference [standard deviation, SD] = −0.552 [1.993], $t_{58} = -2.109$, $p = 0.039$) and eating disturbances (mean difference [SD] = −1.121 [2.493], $t_{59} = -3.424$, $p = 0.001$). A relatively high proportion of patients developed anxiety (cumulative incidence = 24.53%) and eating disturbances (cumulative inci-

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dence = 26.92%), without having these symptoms at baseline. There was a trend toward an increase in proportion of persons with severe dementia (19.7% vs. 39.4%) on follow-up. Caregiver distress reported was significantly associated with neuropsychiatric symptoms ($r = 0.712$, $p < 0.001$) and dementia severity ($\rho = 0.365$, $p = 0.004$). In addition, difficulties in accessing medical care persisted between the 2 assessments, and there were statistically significant differences between functional rehabilitation activities such as indoor activities ($p < 0.001$), outdoor activities ($p = 0.013$), and physical exercises ($p = 0.003$) between baseline and follow-up. ***Conclusion:*** Findings suggest interruption of functional rehabilitation activities and disruption in medical care services are likely to have had an adverse impact on patients with dementia and contributed toward caregiver distress.

Introduction

There has been an unprecedented rise in the spread of the COVID-19, with over 171 million cases reported worldwide and over 28.5 million cases in India as of June 4, 2021 [1]. Elderly and those who report comorbidities are disproportionately affected, with elderly accounting for 53% of all confirmed deaths [2] and people with comorbidities reporting a higher case fatality (17.9% vs. 1.2%) [3].

There are currently 5.29 million people estimated to be living with dementia in India [4]. People with dementia have a greater susceptibility to developing infection [5, 6], are at risk of contracting severe infection [7], and have higher associated mortality [8]. In addition, efforts to prevent virus spread (e.g., nationwide lockdown) have unintentionally affected access to medical and social supports that families rely on [9, 10]. Studies from mainly high-income countries have demonstrated that isolation measures associated with the pandemic have contributed to worsening of neuropsychiatric symptoms [11–15], cognitive decline [11, 12, 14], and increased caregiver distress [11–13]. However, there is limited evidence on impact of the COVID-19 pandemic on persons with dementia and their caregivers in lower middle-income countries (LMICs). In light of this dynamically evolving health crisis, the current study aimed to evaluate cognition and behaviors in dementia and assess associated caregiver distress as the COVID-19 pandemic evolved: during phased relaxations of the national lockdown and subsequently later periods of the "cluster of cases" transmission phase (large concentration of cases in a given area) in India.

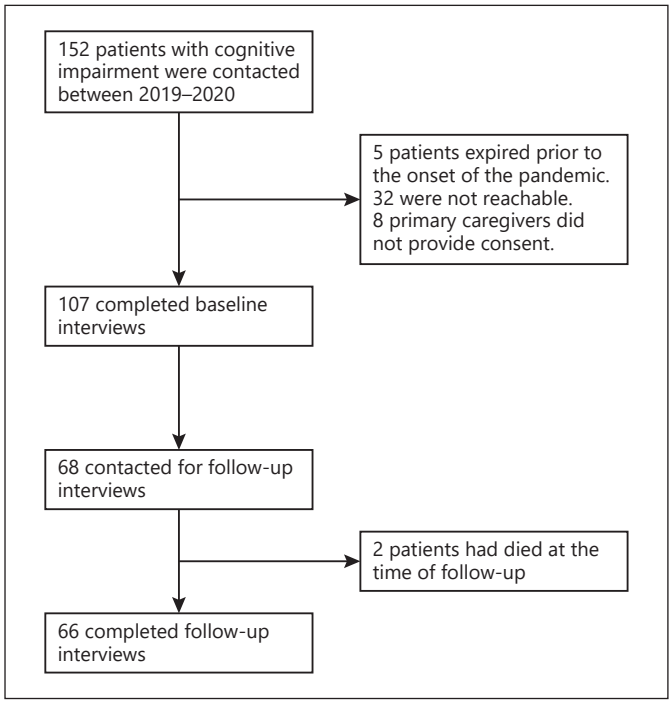

Fig. 1. Flow diagram of the recruitment process.

Materials and Methods

This was an observational study. Patients with dementia and their caregivers were evaluated at 2 distinct phases of the COVID-19 pandemic in South India: (1) phased relaxations of the nationwide lockdown (May 15–June 25, 2020) and (2) later periods of the "cluster of cases" transmission phase (October 21–November 7, 2020). All patients with dementia who attended the Cognitive Disorders Clinic of the National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, and the Neuropsychiatric Department of ASHA Hospital in partnership with Alzheimer's and Related Disorders Society of India (ARDSI), Hyderabad Deccan Chapter, between April 1, 2019 and March 15, 2020 were eligible and recruited. From the 152 patients with cognitive impairment evaluated over 1 year, 107 were reachable for baseline interviews: 5 had expired prior to the onset of the pandemic, 32 were not reachable, and 8 primary caregivers did not provide consent. Of these 107, 66 patients with dementia participated in follow-up interviews. A flow diagram of the recruitment process is depicted in Figure 1.

All patients underwent comprehensive clinical and cognitive evaluation with tests adapted for Indian languages [16]. The diagnosis of dementia and its subtypes was made on the basis of standard criteria prior to the pandemic [17–20]. All semi-structured interviews were carried out by trained personnel via telephone at two points in time. The interviews documented sociodemographic details of participants, clinical history, COVID-19 status, and possible exposures to infection, infection measures adopted, changes in caregiving routines, involvement in functional rehabilitation activities (we asked caregivers if the patient with dementia had been engaging in any physical exercise such as walking,

Table 1. Sociodemographic and clinical characteristics of participants with follow-up

	Persons with dementia (*N* = 66) mean (SD) or *N* (%)
Age, years	67.48 (9.46)
Gender	
Male	33 (50.0%)
Female	33 (50.0%)
Education*	
Professional degree	14 (21.5%)
Graduate or postgraduate	22 (33.8%)
Upto high school	29 (39.9%)
Illiterate	3 (4.6%)
Duration of illness*, months	38.77 (35.31)
Subtypes of dementia	
AD	20 (30.3%)
FTD	14 (21.2%)
VaD	9 (13.6%)
Others	23 (34.8%)
Occupation*	
Professional (white collar)	1 (1.6%)
Semiprofessional	31 (46.3%)
Clerical, shop-owner/farm	6 (9.0%)
Skilled/semiskilled worker	6 (9.0%)
Unskilled worker	3 (4.5%)
Unemployed	17 (25.4%)
Socioeconomic (SES) class*	
Upper class	1 (1.8%)
Middle class	51 (89.47%)
Lower class	5 (8.8%)

SD, standard deviation * Missing values: education – 1; occupation: – 2; duration of illness – 2; SES – 9

Table 2. Sociodemographic profile of the caregivers

Variable	Categories	
Mean age, years (SD)		46.18 (16.11)
Gender, *n* (%)	Male	45 (68.18)
	Female	18 (27.24)
Relationship with patient, *n* (%)	Husband	11 (16.67)
	Wife	7 (10.60)
	Daughter	6 (9.09)
	Son	32 (48.48)
	Daughter-in-law	4 (6.06)
	Son-in-law	2 (3.03)
Type of caregiver, *n* (%)	Primary caregiver	51 (77.27)
	Secondary caregiver	11 (16.67)

Missing values: age – 5; gender – 3; number of caregiving hours – 4; type of caregiver – 4; relationship with the patient – 4. Relationship between caregiver demographics on NPI and caregiver distress. There is a no correlation between caregiver demographics and NPI and caregiver distress.

purposeful indoor activities such as folding clothes, preparing food, etc., and purposeful outdoor activities such as visiting a park/temple) and access to medical and long-term care support services. Socioeconomic status was measured using the Kuppuswamy socioeconomic scale [21]. Severity of dementia, behavioral symptoms, and caregiver stress were assessed via telephonic interviews using the Clinical Dementia Rating Scale (CDR) (only the caregiver interview was conducted) [22], the Neuropsychiatric Inventory (NPI) (which includes the Neuropsychiatric Inventory-Caregiver Distress [NPI-CD]) [23], and Depression, Anxiety and Stress Scale-21 (DASS-21) [24], respectively. All assessments were conducted with caregivers. Informed verbal consent was obtained from all caregivers prior to conducting interviews. Ethics approval was provided by the (NIMHANS Institutional Ethics Committee and the ASHA Hospital Ethics Committee, Hyderabad.

Data Analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS) software version 16.0 (SPSS, Chicago, IL, USA). Variables were expressed in terms of mean (standard deviation, SD) for continuous variables and frequency (percentage) for categorical variables. The paired *t* test/Wilcoxon signed-rank test was used to compare pre- and post-scores of Clinical Dementia Rating, NPI, and DASS-21 scores. Spearman's correlation coefficient was used to assess the correlation between NPI, CDR, and DASS-21 scores. In addition, estimates (percentage) of prevalence and cumulative incidence of NPI symptoms and sub-syndromes (based on NPI ≥4) were reported. Cumulative incidence was calculated by dividing the number of new cases of NPI symptoms (based on NPI ≥4) in the follow-up by the total number of patients in the population at risk at baseline. The difference in functional rehabilitation activities at baseline and follow-up period was analyzed using the McNemar test.

Results

Participant Characteristics

Of the 68 participants contacted, 2 patients had died at the time of follow-up, and hence, 66 were re-assessed: deaths were unrelated to COVID-19 infection. The mean duration between the 2 interviews was 150.83 (11.31) days. The mean age of patients with dementia was 67.48 (SD 9.46) years, 33/66 (50%) were male, and the duration of illness was 38.77 (35.31) months. Sociodemographic and clinical characteristics of patients are provided in Table 1. Forty-five of 66 (68.2%) caregivers were male, and 51/62 (82.2%) were primary caregivers (refers to those family members that are predominantly responsible for care provision). Sociodemographic characteristics of caregivers are provided in Table 2.

Table 3. Comparison of dementia severity, neuropsychiatric symptoms in persons with dementia, and caregiver distress between baseline and follow-up assessment

Instrument	Baseline *N* (%) or mean (SD)	Follow-up *N* (%) or mean (SD)	Mean difference	*p* value (<0.05)
Patient scales				
CDR				
Questionable*	14 (21.2%)	17 (25.8%)		0.057
Mild	16 (24.2%)	14 (21.2%)		
Moderate	23 (34.8%)	9 (13.6%)		
Severe	13 (19.7%)	26 (39.4%)		
NPI	12.00 (15.16)	12.39 (15.32)	0.07 (12.81)	0.967
Caregiver scales				
NPI-CD	4.17 (5.29)	5.98 (6.83)	−0.77 (5.52)	0.359
DASS-21				
Depression	3.92 (6.50)	5.06(7.24)	−1.08 (8.02)	0.303
Anxiety	2.73 (5.51)	4.05 (5.69)	−1.08 (6.32)	0.193
Stress	5.39 (8.18)	6.46 (9.48)	−0.69 (7.16)	0.459
Total score	11.84 (18.82)	15.57 (20.24)	−3.68 (20.53)	0.170

Baseline missing values: NPI – 4, DASS-21 – 4; follow-up missing values: NPI – 4, DASS-21 – 3. CDR, Clinical Dementia Rating Scale; NPI, Neuropsychiatric Inventory; NPI-CD, Neuropsychiatric Inventory Caregiver Distress; DASS-21, Depression, Anxiety and Stress Scales; SD, standard deviation. * CDR category "Questionable" refers to a possibly very mild case of dementia [37].

Table 4. Prevalence and cumulative incidence (CI) of neuropsychiatric symptoms and comparison of NPI-associated caregiver distress (CD) in baseline and follow-up

Domain	Prevalence				CI	Comparison of NPI-CD at baseline and follow-up		
	baseline		follow-up			baseline	follow-up	difference
	NPI ≥4, %	CD, mean (SD)	NPI ≥4, %	CD, mean (SD)	NPI ≥4, %	mean (SD)	mean (SD)	mean (SD)
Delusions	9	0.31 (0.86)	11.9	0.45 (1.00)	5.45	0.33 (0.98)	0.45 (1.02)	−0.12 (0.83)
Hallucinations	11.9	0.46 (0.86)	11.9	0.50 (1.14)	1.89	0.48 (1.13)	0.41 (1.06)	0.07 (0.65)
Agitation	23.9	0.80 (0.86)	23.9	0.92 (1.34)	15.56	0.79 (1.21)	0.95 (1.37)	−0.16 (1.28)
Depression	13.4	0.54 (0.86)	17.9	0.73 (1.28)	11.54	0.78 (1.31)	0.57 (1.27)	0.21 (1.29)
Anxiety	11.9	0.39 (0.86)	20.9	0.77 (1.24)	24.53	0.41 (0.88)	0.76 (1.20)	−0.35 (1.16)*
Elation	7.5	0.26 (0.86)	9.0	0.35 (0.90)	5.36	0.34 (0.91)	0.28 (0.74)	0.07 (0.88)
Apathy	14.9	0.54 (0.86)	11.9	0.42 (0.96)	11.76	0.53 (1.14)	0.41 (0.97)	0.12 (1.51)
Disinhibition	4.5	0.21 (0.86)	1.5	0.13 (0.46)	1.72	0.12 (0.46)	0.22 (0.77)	−0.10 (0.67)
Irritability	22.4	0.72 (0.86)	29.9	1.05 (1.34)	15.91	0.71 (1.20)	1.03 (1.27)	−0.33 (1.13)*
Aberrant motor	10.4	0.36 (0.86)	13.4	0.37 (0.92)	7.41	0.36 (0.93)	0.38 (0.95)	−0.02 (1.15)
Sleep disturbances	29.5	0.80 (0.86)	20.9	0.79 (1.26)	18.18	0.76 (1.28)	0.81 (1.29)	−0.05 (1.52)
Eating disturbances	13.4	0.44 (0.86)	32.8	1.00 (1.37)	26.92	0.41 (0.86)	1.00 (1.35)	−0.59 (1.27)**

Baseline missing values: NPI-CD, 4; follow-up missing values: NPI-CD, 4. NPI, Neuropsychiatric Inventory; SD, standard deviation. ** *p* value <0.01. * *p* value <0.05.

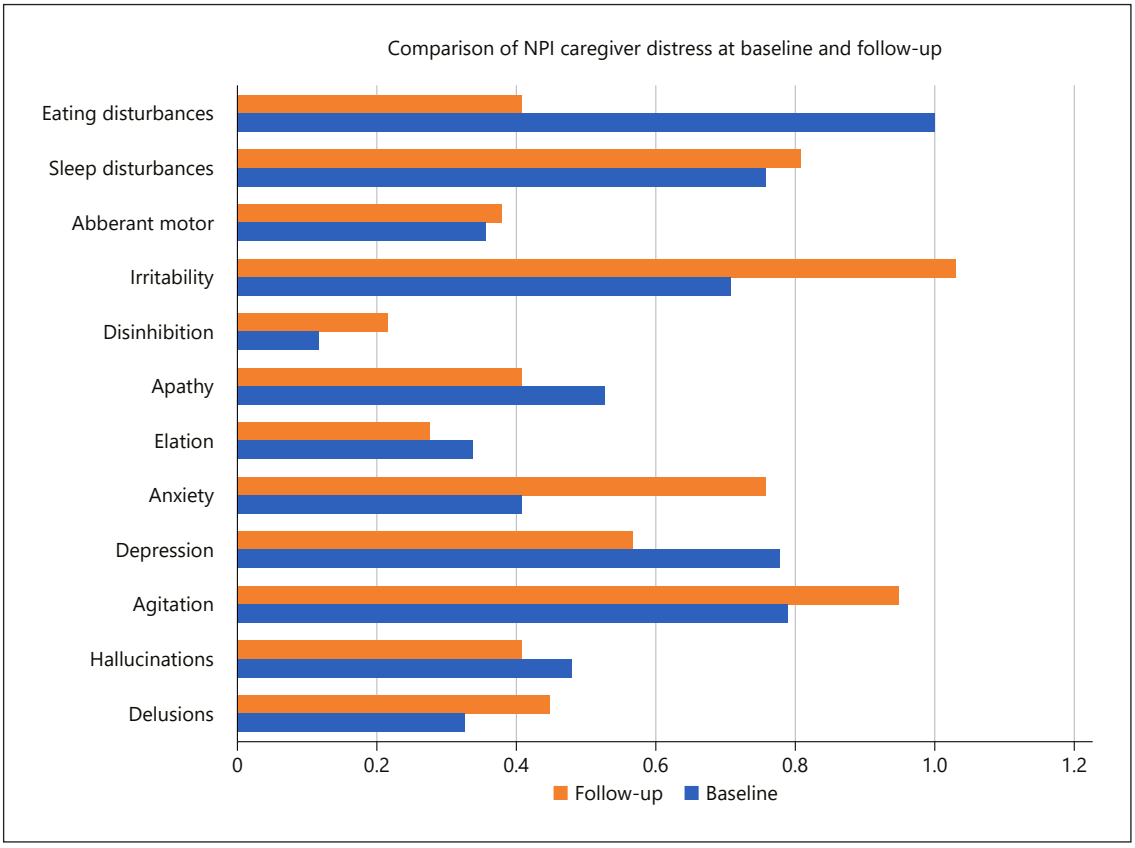

Fig. 2. Comparison of NPI-CD at baseline and follow-up. NPI, Neuropsychiatric Inventory.

Cognitive Status

At baseline, 52/66 patients with dementia met the criteria for mild (CDR 1: 24.2%), moderate (CDR 2: 34.8%), or severe dementia (CDR 3: 19.7%). The proportion of patients with severe dementia (CDR 3) increased to 39.4% at follow-up (Table 3) ($z = -1.902$, $p = 0.057$).

Behavioral Symptoms

The mean (SD) total NPI increased from 12 (15.16) at baseline to 12.39 (15.32) at follow-up (Table 3). While there was no statistically significant difference between total NPI scores at baseline and follow-up (mean difference = 0.07, $t_{57} = 0.041$, $p = 0.967$), a significant difference was found between scores for anxiety (mean difference [SD] = −0.552 [1.993], $t_{58} = -2.109$, $p = 0.039$) and eating disturbances (mean difference [SD] = −1.121 [2.493], $t_{59} = -3.424$, $p = 0.001$). The prevalence of clinically significant neuropsychiatric symptoms (NPI ≥4) at baseline and follow-up are provided in Table 4. The most prevalent symptoms were sleep disturbances (29.5%), agitation (23.9%), and irritability (22.4%) at baseline. During follow-up, the most common symptoms reported were eating disturbances (32.8%), irritability (29.9%), agitation (23.9%), anxiety (20.9%), and sleep disturbances (20.9%). The cumulative incidence was the highest for anxiety (24.53%) and eating disturbances (26.92%) (Table 4), indicating that a relatively high proportion of patients without these symptoms at baseline manifested them by subsequent assessment.

Caregiver Stress

The mean total NPI-CD score increased from 4.17 (5.29) at baseline to 5.98 (6.83) at follow-up (Table 3) (mean difference [SD] = −0.77 [5.52], $t_{43} = -0.928$, $p = 0.359$). There was a statistically significant difference between the mean NPI-CD score for anxiety (mean difference [SD] = −0.345 [1.16], $t = -2.258$, $p = 0.028$), irritability (mean difference [SD] = −0.328 [1.130], $t = -2.208$, $p = 0.031$), and eating disturbances (mean difference [SD] = −0.586 [1.271], $t = 3.513$, $p = 0.001$) (Table 4). Figure 2 provides a comparison of NPS associated with caregiver distress at baseline and follow-up. As per DASS-21, the mean scores for the depres-

Table 5. Frequency of depression, anxiety, and stress among caregivers during baseline and follow-up assessment

DASS-21	Depression		Anxiety		Stress	
	baseline* *N* (%)	follow-up* *N* (%)	baseline* *N* (%)	follow-up* *N* (%)	baseline* *N* (%)	follow-up* *N* (%)
Normal	54 (81.8)	47 (12.2)	56 (84.8)	47 (71.2)	53 (80.3)	47 (71.2)
Mild	2 (3.0)	8 (12.1)		2 (3.0)	3 (4.5)	9 (13.6)
Moderate	5 (7.6)	6 (9.1)	4 (6.1)	9 (13.6)	3 (4.5)	3 (4.5)
Severe			1 (1.5)	3 (4.5)	2 (3.0)	2 (1.5)
Extremely severe	1 (1.5)	2 (3.0)	1 (1.5)	2 (3.0)	1 (1.5)	2 (3.0)

DASS-21, Depression, Anxiety and Stress Scales. * Baseline missing values: depression – 4, anxiety – 4, and stress – 4; follow-up missing values: depression – 3, anxiety – 3, stress – 3.

sion, anxiety, and stress subscale were 3.92 (6.50), 2.73 (5.51), and 5.39 (8.18), respectively, at baseline and increased to 5.06 (7.24) for depression, 4.05 (5.69) for anxiety, and 6.46 (9.48) for stress at follow-up (depression: mean difference [SD] = −1.08 [8.02], $t_{58} = -1.039$, $p = 0.303$; anxiety: mean difference [SD] = −1.08 [6.32], $t_{58} = 1.318$, $p = 0.193$; stress: mean difference [SD] = −0.69 [7.16], $t_{58} = -0.745$, $p = 0.459$). At baseline, the proportion of caregivers that experienced mild to severe depression, anxiety, and stress were 12.1%, 9.1%, and 13.5%, which increased to 24.2%, 24.1%, and 22.6%, respectively, at follow-up (Table 5). We found a significant positive correlation between NPI-total and DASS-21 depression ($r = 0.572$; $p < 0.001$), anxiety ($r = 0.662$, $p < 0.001$), and stress ($r = 0.695$, $p < 0.001$) scores and DASS-21 total scores ($r = 0.712$, $p < 0.001$) after controlling for duration of illness. A significant positive association was also found between CDR and DASS-21 depression ($\rho = 0.374$, $p = 0.003$), anxiety ($\rho = 0.302$, $p = 0.017$), and stress ($\rho = 0.327$, $p = 0.010$) scores and DASS-21 total scores ($\rho = 0.365$, $p = 0.004$).

Dementia Care

Functional Rehabilitation

Forty-one of 66 (62.1%) patients with dementia at baseline frequently participated in some form of physical exercise, 46/66 (69.7%) were involved in indoor activities, 34/66 (53.1%) were socially interacting with friends/family members, and 31/66 (46.7%) engaged in outdoor activities prior to the lockdown. At follow-up (after a period of 8 months since activities at baseline were from pre-lockdown), 25/46 (54.3%) patients with dementia stopped engaging in indoor activities ($p < 0.001$), and 21/31 (67.74%) patients stopped from partaking in outdoor activities ($p = 0.013$). Twenty-four of 41 (58.5%) had stopped any form of physical exercise during the pandemic at follow-up ($p = 0.003$). Out of 66 patients, 34 (53.1%) were socially interacting with friends/family members at baseline, compared to 30 (47.6%) at follow-up ($p = 0.556$).

Medical Care

Seven of 66 (10.6%) patients with dementia experienced medical problems at baseline and 7 (10.6%) at follow-up. Difficulties in accessing medical care persisted between the two assessments. Out of 66 patients, 19 (8.4%) faced difficulty in getting follow-up appointments, 11 (16.7%) had difficulties in getting health checkups, and 9 (13.6%) were unable to procure medications at baseline. Out of 62 patients, 16 (25.8%) were unable to access appointments, and 19 (30.6%) were unable to get health checkups at follow-up.

Long-Term Care Support and Services

At baseline, 5/5 of patients (only 5/107 had attended daycare centers) with dementia had stopped visiting daycare centers due to suspension of services. During follow-up, 2/5 revealed continued difficulty to access these services. Changes in supports were observed by caregivers at follow-up: 8/63 (12.7%) received additional family support, whereas 2/63 (3.17%) experienced reduced support, as certain family members returned to their taxing schedules post-lockdown. Figure 3 provides an overview of access to care services and involvement in functional activities.

COVID-19 Awareness, Exposures, and Prevention

The majority of caregivers at baseline (52/66 [78.7%]) and follow-up (59/63 [93.6%]) were following infection prevention measures. Fifty of 63 (79.4%) patients reported washing hands regularly, 45/63 (71.4%) reported maintaining social distancing, and 42/63 (66.6%) reported wearing masks outdoors. While no patients or their caregivers re-

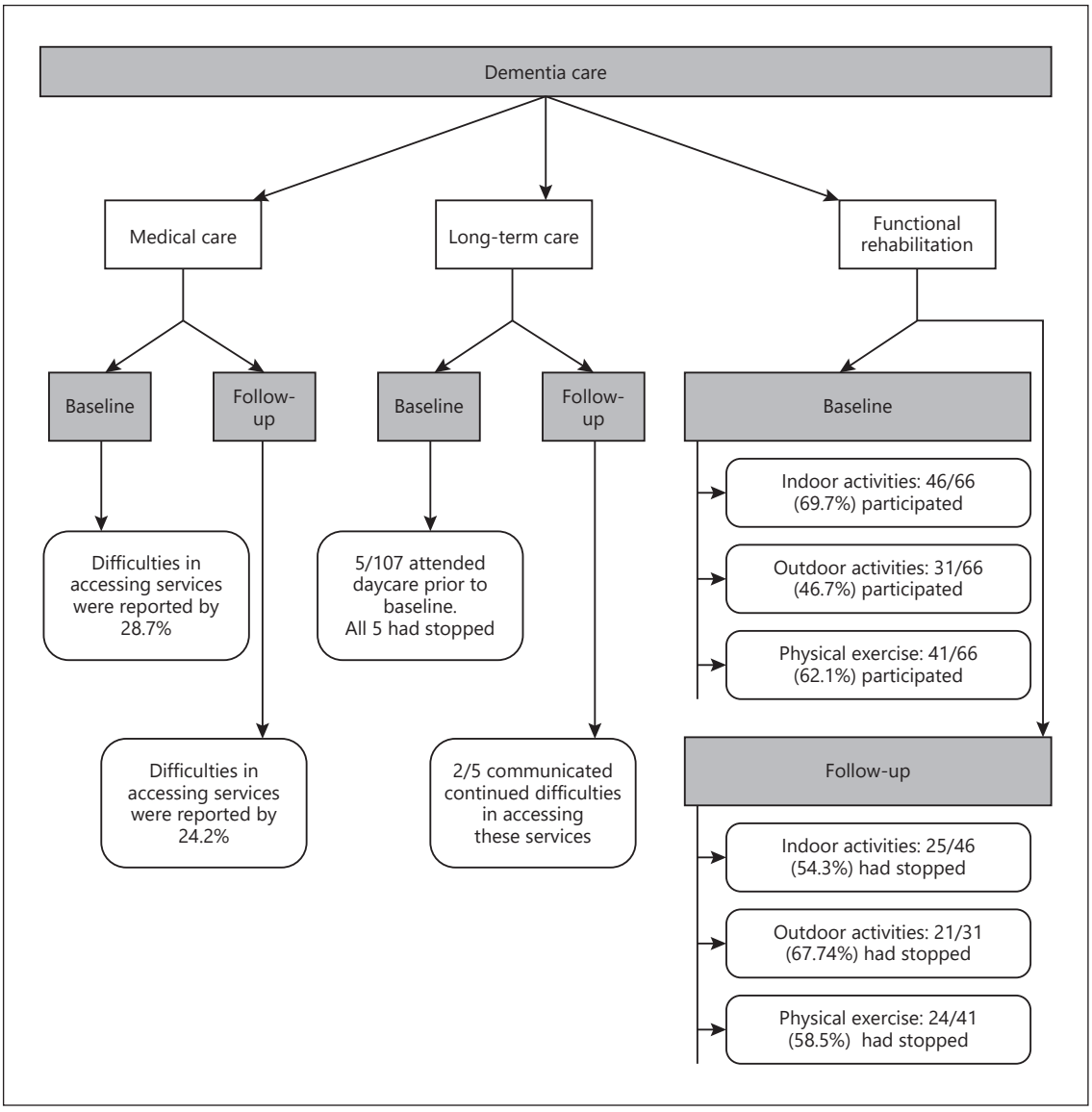

Fig. 3. Functional rehabilitation involvement and access to dementia care-related services.

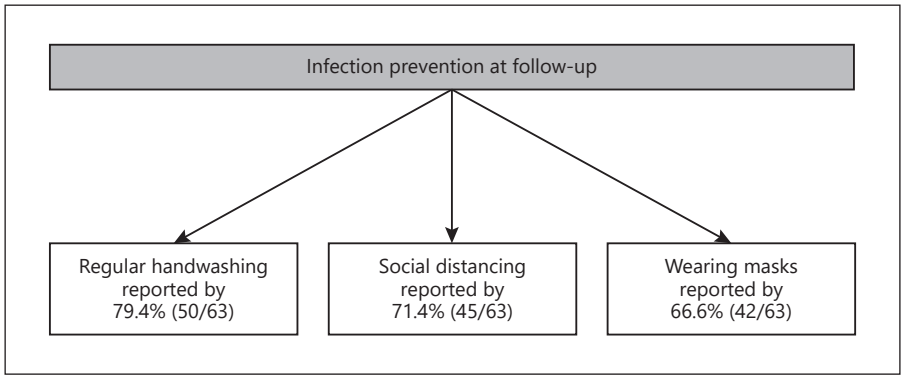

Fig. 4. COVID-19 infection prevention measures adopted at follow-up.

ported COVID-19 infection at baseline, 1 patient and their caregiver developed infection at follow-up. While no patient with dementia or caregiver reported exposure to COVID-19 infection at baseline, possible exposures through family, neighborhood, or work contacts were reported at follow-up in 14/63 (22.2%). Figure 4 provides an overview of COVID-19 measures adopted by the study cohort.

Discussion

This is the first study to evaluate cognition, behavior in dementia, and assess caregiver stress during two distinct periods of the COVID-19 pandemic in an LMIC setting. Findings highlight that there was a rise in the proportion of patients progressing to severe dementia and also worsening of behavioral symptoms, in particular, anxiety and eating disturbances, in the period between phased relaxations of the lockdown and later periods of the pandemic. This was associated with increase in numbers of caregivers experiencing mild to severe depression, anxiety, and stress at follow-up. Difficulties in accessing medical services persisted and functional rehabilitation activities stopped due to restrictions. Results indicate that the COVID-19 pandemic resulted in adverse neuropsychiatric outcomes for patients with dementia that could be attributed to interruption of medical and nonpharmacological therapies.

Compared to baseline evaluation, there was an increase in the proportion of patients with severe dementia (CDR = 3:19.7% vs. 39.4%) at follow-up. Few studies have examined the natural history of cognitive decline of dementia using the CDR. One study modeling the disease progression for CDR-sum of boxes (which has a maximum score of 18 points) found that the progression rate for mild Alzheimer's disease was approximately 1.4 points/year [25]. Similarly, another study found an annual rate of change (slope) in CDR-sum of boxes score of 1.91 (SE = 0.07) in the CDR 1 sample [26]. The cognitive decline observed in our study is higher than what has been established by these studies. While this is not a statistically significant finding, the trend is consistent with reports that indicate worsening of cognition in dementia during the pandemic [11, 12, 14]. A recent review [27] found that cognitive decline in persons with dementia or mild cognitive impairment during the COVID-19 pandemic occurred also in a very short window of time (3–4 months), which does not seem to be attributable to the natural course of cognitive decline in dementia. Considering, only a small proportion of patients were involved in outdoor activities and physical exercise, respectively, at follow-up. The limited involvement in functional activities may have contributed to this decline in cognition as evidenced by prior studies [28, 29]. These results indicate the need to study the effects of nonpharmacological treatment on dementia progression more systematically in the future.

The most common neuropsychiatric symptoms that presented at follow-up were irritability (29.9%), agitation (23.9%), and eating disturbances (32.8%). There were statistically significant differences in anxiety ($p = 0.039$) and eating disturbances ($p = 0.001$) between the two consecutive assessments. A significant proportion were found to have developed anxiety (cumulative incidence = 24.53%) and eating disturbances (cumulative incidence = 26.92%) at follow-up, while not having these symptoms at baseline. This finding is similar to European studies, which reported increased anxiety in dementia during quarantine [12, 15, 30], and one study [30] attributed this to a post-traumatic stress disorder-like condition that develops as a result of a "stressor event." The increase in the proportion of persons with dementia experiencing eating disturbances was an interesting finding. An Italian study [30] conducted during the COVID-19 pandemic found changes in appetite to be frequent in frontotemporal dementia, increased appetite being one of the key symptoms of this subtype. Considering that frontotemporal dementia was the second most common diagnosis in our cohort, this may partly explain our results. It is also plausible that the increased severity of dementia in the cohort contributed to a rise in eating disturbances, as has been frequently reported with disease advancement [31, 32]. Moreover, our study further reported statistically significant changes in functional, rehabilitation activities between the two assessments, with a very small proportion of patients with dementia engaging in these activities at follow-up. This is likely to have also contributed to the increase in neuropsychiatric symptoms reported as regular engagement in functional activities have been found to aid in attenuating symptoms [28, 33].

The worsening of neuropsychiatric symptoms and an increase in dementia severity significantly influenced caregiver distress as well; a significant difference was found between anxiety, irritability, and eating disturbances between the two assessments and the strong positive correlations found for both NPI and CDR with DASS scores at follow-up. These findings possibly explain the increase in numbers of caregivers experiencing mild to severe depression, anxiety, and stress at follow-up. This caregiver distress may also be attributed to the difficulties in accessing medical and long-term care support services.

More than one-tenth of the cohort experienced medical problems during both baseline and follow-up, and difficul-

ties in accessing medical services persisted. This is possibly due to continued fears of infection as the elderly are encouraged to delay any nonemergency consultations [34]. While teleconsulting services have been provided, these are inadequate as cognitive screening and major treatment changes are difficult to conduct on virtual platforms [9]. These difficulties in accessing medications may have also contributed to the increase in severity of dementia observed. Furthermore, the continued suspension of long-term care services such as daycare is also likely to have negatively impacted both patients with dementia and their caregivers.

There were some limitations to this study. The urban clinic-based nature of the study is not representative of the general population affected with dementia in the country; a high proportion resides in rural areas, and there is low awareness [35]. Another shortcoming was the inability to reach out to all baseline participants for follow-up, which we believe may have reduced the statistical significance and representativeness of our findings as well as contributed to certain biases. We were also unable to determine the type of eating disturbances patients experienced. Continued follow-up and reaching out to patients with dementia are ongoing as the pandemic continues to evolve.

The implications of our study are wide-ranging. Given the rising burden of dementia in the country [4], it is necessary to recognize and address challenges experienced by persons with dementia and their caregivers during the pandemic, to improve our response to current and future health emergencies [5]. Strong infection prevention regulations must be put into place at hospital settings and long-term care centers in combination with telemedicine services in order to reduce delays in diagnosis, treatment, and allow for continuity of care [34]. It is further essential for a greater number of psychosocial services and social security to be developed to support informal caregivers, who constitute the bulk of caregivers in India [36]. In order to achieve these objectives, the sustained collaboration of stakeholders from multiple domains as seen in response to the pandemic [6] must be applied to reframe existing models of dementia care services in India.

In conclusion, the present study has demonstrated an increase in severity and worsening of behavioral disturbances in dementia and a rise in caregiver distress. This may be attributed to the interruption of rehabilitation and disruption in medical care. The risk of infection remains as the COVID-19 pandemic continues to disproportionately affect vulnerable populations such as persons with dementia, while simultaneously exposing the underlying vulnerabilities of health and social care systems in LMICs.

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Statement of Ethics

This study protocol was reviewed and approved by the NIMHANS Institutional Ethics Committee (No.NIMH/DO/IEC (BS & NS DIV1/2020) and the ASHA Hospital Ethics Committee Hyderabad (AH/2020/1_NIMHANS/25720). Due to the circumstances of the pandemic and lockdown, informed verbal consent was obtained by telephone from all caregivers prior to conducting interviews.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

S.A., P.T.T., and F.A. conceptualized the study and developed with J.R. F.A., R.M.H., V.S.N, D.B.P.R., R.B.R., G.R., S.H., S.R.D., P.V.G., T.S.M., and G.N.R. managed data collection. C.K. and S.K. were involved in administrative data management. F.V., J.R., A.P., and S.M. were involved in data analysis. J.R., S.A., F.V., F.A., G.N.R., and P.T.T. drafted the manuscript. All co-authors read through the drafts and approved the revised version.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy and ethical restrictions.

References

1 World Health Organization. WHO coronavirus (COVID-19) dashboard. 2021 Jun 4. Available from: https://covid19.who.int/.
2 Ministry of Health and Family Welfare. It is more important now to follow COVID appropriate behaviours because of the upcoming festival season, arrival of winter, opening up of economy: Dr. V.K. Paul. 2020 Oct 13. Available from: https://pib.gov.in/PressReleasePage.aspx?PRID=1664105.
3 Press Information Bureau. India's case fatality rate is 1.53% compared to 17.9% with comorbid people and 1.2% for people without comorbidities: secretary. 2020 Oct 13. Available from: https: //twitter.com/pib_india/status/1315978147792211970.
4 Alzheimer's and Related Disorder's Society of India. Dementia India Report. 2010. Available from: http://ardsi.org/downloads/mainreport.pdf.
5 Rajagopalan J, Huzruk S, Arshad F, Raja P, Alladi S. The COVID-19 long-term care situation in India. LTCcovid, international long-term care policy network, CPEC-LSE. 2020 May 30.
6 Suzuki M, Hotta M, Nagase A, Yamamoto Y, Hirakawa N, Satake Y, et al. The behavioral pattern of patients with frontotemporal dementia during the COVID-19 pandemic. Int Psychogeriatr. 2020;32:1231–4.
7 Atkins JL, Masoli JA, Delgado J, Pilling LC, Kuo CL, Kuchel G, et al. Preexisting comorbidities predicting severe COVID-19 in older adults in the UK Biobank community cohort. J Gerontol A Biol Sci Med Sci. 2020 Oct 15;75(11):2224–30.
8 Bianchetti A, Rozzini R, Guerini F, Boffelli S, Ranieri P, Minelli G, et al. Clinical presentation of COVID19 in dementia patients. J Nutr Health Aging. 2020;24(6):560–2.
9 Brown EE, Kumar S, Rajji TK, Pollock BG, Mulsant BH. Anticipating and mitigating the impact of the COVID-19 pandemic on Alzheimer's disease and related dementias. Am J Geriatr Psychiatry. 2020;28(7):712–21.
10 Vaitheswaran S, Lakshminarayanan M, Ramanujam V, Sargunan S, Venkatesan S. Experiences and needs of caregivers of persons with dementia in India during the COVID-19 pandemic-A Qualitative Study. Am J Geriatr Psychiatry. 2020;28(11):1185–94.
11 Borges-Machado F, Barros D, Ribeiro Ó, Carvalho J. The effects of COVID-19 home confinement in dementia care: physical and cognitive decline, severe neuropsychiatric symptoms and increased caregiving burden. Am J Alzheimers Dis Other Demen. 2020;35:1533317520976720.
12 Barguilla A, Fernández-Lebrero A, Estragués-Gázquez I, García-Escobar G, Navalpotro-Gómez I, Manero RM, et al. Effects of COVID-19 pandemic confinement in patients with cognitive impairment. Front Neurol. 2020;11:589901.
13 Boutoleau-Bretonnière C, Pouclet-Courtemanche H, Gillet A, Bernard A, Deruet AL, Gouraud I, et al. Impact of confinement on the burden of caregivers of patients with the behavioral variant of frontotemporal dementia and alzheimer disease during the covid-19 crisis in france. Dement Geriatr Cogn Dis Extra. 2020 Sep-Dec;10(3):127–34.
14 Rainero I, Bruni AC, Marra C, Cagnin A, Bonanni L, Cupidi C, et al. The impact of COVID-19 quarantine on patients with dementia and family caregivers: a nation-wide survey. Front Aging Neurosci. 2021 Jan 18;12:507.
15 Cohen G, Russo MJ, Campos JA, Allegri RF. COVID-19 epidemic in Argentina: worsening of behavioral symptoms in elderly subjects with dementia living in the community. Front Psychiatry. 2020;11:866.
16 Mekala S, Paplikar A, Mioshi E, Kaul S, Divyaraj G, Coughlan G, et al. Dementia diagnosis in seven languages: the addenbrooke's cognitive examination-III in India. Arch Clin Neuropsychol. 2020;35(5):528–38.
17 McKeith IG, Boeve BF, Dickson DW, Halliday G, Taylor JP, Weintraub D, et al. Diagnosis and management of dementia with lewy bodies: fourth consensus report of the DLB consortium. Neurology. 2017;89(1):88–100.
18 McKhann GM, Knopman DS, Chertkow H, Hyman BT, Jack CR Jr, Kawas CH, et al. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on aging Alzheimer's association workgroups on diagnostic guidelines for Alzheimer's disease. Alzheimers dement. 2011;7(3):263–9.
19 Rascovsky K, Hodges JR, Knopman D, Mendez MF, Kramer JH, Neuhaus J, et al. Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. Brain. 2011;134(9):2456–77.
20 Sachdev P, Kalaria R, O'Brien J, Skoog I, Alladi S, Black SE, et al. Diagnostic criteria for vascular cognitive disorders: a VASCOG statement. Alzheimer Dis Assoc Disord. 2014;28(3):206–18.
21 Wani RT. Socioeconomic status scales-modified Kuppuswamy and Udai Pareekh's scale updated for 2019. J Family Med Prim Care. 2019 Jun;8(6):1846.
22 Juva K, Sulkava R, Erkinjuntti T, Ylikoski R, Valvanne J, Tilvis R. Usefulness of the clinical dementia rating scale in screening for dementia. Int Psychogeriatr. 1995;7(1):17–24.
23 Cummings JL. The Neuropsychiatric Inventory: assessing psychopathology in dementia patients. Neurology. 1997;48(5 Suppl 6):10S–16S.
24 Henry JD, Crawford JR. The short-form version of the depression anxiety stress scales (DASS-21): construct validity and normative data in a large non-clinical sample. Br J Clin Psychol. 2005;44(2):227–39.
25 Samtani MN, Raghavan N, Novak G, Nandy P, Narayan VA. Disease progression model for clinical dementia rating-sum of boxes in mild cognitive impairment and Alzheimer's subjects from the Alzheimer's disease neuroimaging initiative. Neuropsychiatr Dis Treat. 2014;10:929.
26 Williams MM, Storandt M, Roe CM, Morris JC. Progression of Alzheimer's disease as measured by clinical dementia rating sum of boxes scores. Alzheimers Dement. 2013 Feb 1;9(1):S39–44.
27 Suárez-González A, Rajagopalan J, Livingston G, Alladi S. The effect of COVID-19 isolation measures on the cognition and mental health of people living with dementia: a rapid systematic review of one year of quantitative evidence. EClinicalMedicine. 2021; 39:101047.
28 Ruthirakuhan M, Luedke AC, Tam A, Goel A, Kurji A, Garcia A. Use of physical and intellectual activities and socialization in the management of cognitive decline of aging and in dementia: a review. J Aging Res. 2012;2012:384875.
29 Christofoletti G, Oliani MM, Bucken-Gobbi LT, Gobbi S, Beinotti F, Stella F. Physical activity attenuates neuropsychiatric disturbances and caregiver burden in patients with dementia. Clinics. 2011;66(4):613–8.
30 Cagnin A, Di Lorenzo R, Marra C, Bonanni L, Cupidi C, Laganà V, et al. Behavioral and psychological effects of coronavirus disease-19 quarantine in patients with dementia. Front Psychiatry. 2020;11:578015.
31 Cipriani G, Carlesi C, Lucetti C, Danti S, Nuti A. Eating behaviors and dietary changes in patients with dementia. Am J Alzheimers Dis Other Demen. 2016 Dec;31(8):706–16.
32 Diehl-Schmid J, Pohl C, Perneczky R, Förstl H, Kurz A. Behavioral disturbances in the course of frontotemporal dementia. Dement Geriatr Cogn Disord. 2006;22(4):352–7.
33 Fukushima RLM, do Carmo EG, Pedroso RDV, Micali PN, Donadelli PS, Fuzaro G, et al. Effects of cognitive stimulation on neuropsychiatric symptoms in elderly with Alzheimer's disease: a systematic review. Dement Neuropsychol. 2016 Sep;10(3):178–84.
34 D'Cruz M, Banerjee D. Caring for persons living with dementia during the COVID-19 pandemic: advocacy perspectives from India. Front Psychiatry. 2020;11:1125.
35 Nulkar A, Paralikar V, Juvekar S. Dementia in India – a call for action. J Glob Health Rep. 2019; 3: e2019078. https: //www.joghr.org/article/12221-dementia-in-india- a-call-for-action.
36 Brinda EM, Rajkumar AP, Enemark U, Attermann J, Jacob KS. Cost and burden of informal caregiving of dependent older people in a rural Indian community. BMC Health Serv Res. 2014 Dec;14(1):207–9.
37 Morris JC, Storandt M, Miller JP, McKeel DW, Price JL, Rubin EH, et al. Mild cognitive impairment represents early-stage Alzheimer disease. Arch Neurol. 2001 Mar 1;58(3):397–405.