ORIGINAL RESEARCH ARTICLE

Study Effect of the COVID-19 Lockdown on the Transition from Mild Cognitive Impairment to Dementia

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ABSTRACT

Background: Dementia represents a significant global health challenge, contributing to high fatality and frailty rates. The worldwide prevalence of dementia is projected to increase by 150% from 2018 to 2051. Countries with low to moderate incomes are expected to experience demographic shifts starting in 2017. The impact of the COVID-19 pandemic on cognitive decline is unclear, but increased social engagement is associated with a lower risk of dementia. We hypothesized that the first nationwide lockdown would lead to a rise in dementia diagnoses, accelerate cognitive decline in at-risk populations, and alter diagnostic patterns due to limited healthcare access.

Methodology: Data collection continued via telephone or audio-video calls during lockdowns, excluding participants with pre-existing dementia. Mild cognitive impairment (MCI) was defined using established criteria, with Clinical Dementia Rating (CDR) scores of 0.5 and Mini-Mental State Examination (MMSE) scores between 24 and 27. Poisson regression with cubic splines adjusted for age was used to estimate dementia incidence before and after 01-Mar-2020.

Results: Among 2140 participants, 200 were diagnosed with dementia before 20-Mar-2020, and 40 after. The incidence rate post-lockdown was not significantly different ($p = 0.470$). Secondary analysis revealed a decreased association between MCI and dementia after February 2020 ($p = 0.021$).

Conclusion: Dementia prevalence did not significantly change after the first lockdown. However, the relationship between MCI and dementia incidence weakened, possibly indicating faster progression to dementia or diagnostic challenges due to remote assessments.

Keywords: Alzheimer's disease, Cognitive disorder, Dementia, COVID-19, mild cognitive

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INTRODUCTION

Dementia is a significant contributor to mortality and frailty globally. Starting in 2017, middle- and low-income nations have begun to undergo significant alteration in their population age structure.[1]

Mild cognitive impairment (MCI) is considered a transitional period between normal cognitive function and dementia.[2,3] Researchers are increasingly focusing on developing preventive therapies during the early stages of dementia.[3] In 2020, research identified 12 modifiable risk factors contributing to 39% of dementia cases, including social isolation (risk factor: 1.5, 95%CI 1.2 – 1.8) in individuals over 65 years. This study clearly establishes the study's primary focus on the impact of COVID-19 lockdown on dementia onset.[4] Due to the limited financial resources in these nations, establishing priorities is essential. Given the scarcity of financial resources in many nations, priority is imperative.[5] Short-term studies (less than 2 years) report of 11 - 15% with a one-year rate of 17.9%.[6-8]

Individuals are advised to exercise regularly (minimum of twice weekly), and participate in cognitive therapies[9-11], including group-based activities, with or without technology support, and maintaining daily social connections[12]. The COVID-19 pandemic introduced factors potentially accelerating dementia onset, such as reduced social engagement, increased alcohol use.[13-16]

During the pandemic, the stringency of protective measures, such as lockdowns, social distancing, and infection control protocols, varied across regions.[17] However, limited research has examined their specific impact on dementia progression and cognitive decline.[4] Individuals with dementia showed a greater tendency for cautious behaviors, such as isolation, during the pandemic. Loneliness levels varied among them based on caregiver roles.[18,19]

During the pandemic, 'social distancing' measures, including isolation and physical separation[20], aimed to reduce viral transmission but may have influenced cognitive decline[21-23].

Further research is needed to understand how the COVID-19 pandemic affects dementia development and cognitive decline. This study, using a large dataset, examines the pandemic's impact on the progression from normal cognition to dementia, hypothesizing that pandemic-related measures in British society accelerated this transition compared to pre-pandemic years. Research on the cognitive effects of COVID-19 has highlighted significant impairments among survivors. Post-COVID patients often experience cognitive deficits, including memory loss, concentration difficulties, and executive dysfunction, though long-term follow-up studies are needed to determine the persistence of these symptoms.[24] Substantial gray matter loss in brain regions linked to memory and cognition, but their findings were limited by a small sample size and lack of diversity.[25] Similarly it was discovered that cognitive deficits in COVID-19 survivors resembled the cognitive aging process by approximately ten years; however, the study did not fully account for pre-existing conditions or mental health disorders.[26] It was linked COVID-19 to persistent neuroinflammation, which may contribute to cognitive decline, yet further mechanistic studies are required to understand the biological basis of these effects.[27] It was found that hospitalized COVID-19 patients had cognitive scores comparable to individuals with mild dementia, but it remains unclear whether these cognitive impairments are reversible.[28] It was reported an increased risk of neurological disorders, including dementia, in COVID-19 patients, highlighting the need for research on interventions to mitigate cognitive decline.[29] These studies collectively underline the substantial cognitive impact of COVID-19 while also revealing critical research gaps that warrant further investigation.

The study was conducted to assess the transition rate from normal cognition or moderate cognitive impairment (MCI) to dementia, comparing the periods before and during the COVID-19 lockdown, with the pandemic considered as the exposure factor.

METHODOLOGY

A prospective cohort study was conducted, and the information was gathered which included persons with and without dementia.[30] Total 2140 individuals participated in the study. Patient data was retrieved from Unique Hospital, Surat, India. along with stated inclusion and exclusion criteria. A qualified Principal Investigator and Site team conducted visits using standardized Case Report Forms (CRFs). Some appointments for identification of patients as per Inclusion and Exclusion criteria were conducted over the phone and they were requested to visit the hospital for further participation in the study. Despite higher education levels, the BDR cohort represents the older adult population in terms of race and gender. For quantitative data, research assistants distributed the ICF, CRF, and questionnaires, which patients completed. For qualitative data, the Principal Investigator (PI) explained the ICF to patients, and questionnaires were completed in their presence. The collected data was then analyzed and translated for further processing.

This study is best characterized as a prospective cohort study rather than a case-control study, as it tracks individuals over time to assess the impact of nationwide lockdowns on dementia progression. Unlike case-control studies, which retrospectively compare individuals with and without a condition, our study follows participants longitudinally to examine changes in dementia incidence and cognitive decline so prospective cohort study was conducted.

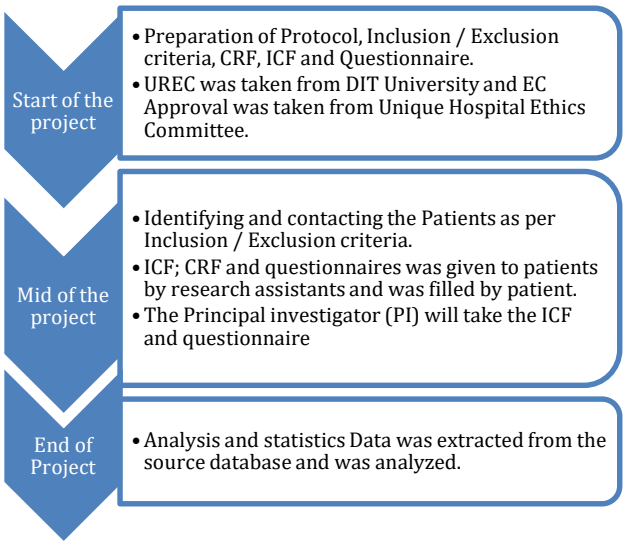

Figure 1: Workflow of the study

Assessment Tools: The assessment of cognitive status during visits using the CDR scale to determine dementia.[31] In our study, mild cognitive impairment was 0.49, and dementia was 0-4 based on the CDR sum of boxes (ranges: 0-17). Dementia was categorized as normal cognition (0), moderate cognitive impairment (1.49-3.49), and dementia (2-17). The Mini-Mental State Examination (MMSE) could not be used to diagnose dementia due to a lack of available data. Data collection also included comorbidities, substance use, living conditions, and medications. Participants with a prior dementia diagnosis or only one visit lacking CDR data were excluded.[32] Summary variables were based on the most severe events (e.g., maximum smoking). Descriptive statistics detailed participants' characteristics like age and smoking status. The study examined the progression from normal or mild cognitive impairment to dementia, assessed at the first visit using tests and the CDR. The variable of interest was the condition of the shutdown during the timeframe. Periods were classified as pre-lockdown (score 0) if ending before 01-Mar-20, and post-lockdown (score 1) if starting after. Intervals starting on 01-Mar-20 were proportionally assigned based on post-lockdown exposure. Peri-lockdown periods were labelled with 2 for risk assessments.[33]

Statistical Analysis: Data was collected in Excel, organized in a wide format for summarization, and transformed for analysis in Stata 17. The main outcome assessed was the transition rate from normal or moderate cognitive impairment (MCI) to dementia, both before to and during the lockdown, with the COVID-19 pandemic regarded as an "exposure."

Secondary outcomes included dementia incidence and progression probabilities from MCI or normal cognition, measured by the CDR. A Poisson model using interval-separated data was used to evaluate the correlation between lockdown status and dementia incidence. Poisson regression was selected for this study to model the incidence rate of dementia post-lockdown while adjusting for key confounders. Despite the relatively small sample size (40 cases), Poisson regression allows for direct estimation of incidence rate ratios (IRRs) and is well-suited for count data with an exposure period. While a Cox proportional hazards model is typically used for time-to-event analysis, the limited number of events and potential violations of the proportional hazard's assumption led to the preference for Poisson regression. Additionally, model fit was assessed using goodness-of-fit tests, and sensitivity analyses were conducted to compare results with alternative modelling approaches, including Cox regression, to ensure robustness. Period lengths were halved, assuming events occurred mid-interval The study adjusts for potential confounders using multivariate regression models. Variable selection was guided by prior literature and clinical relevance, incorporating age (modelled using cubic splines), education level, socioeconomic status, and pre-pandemic health status. Model specification followed a stepwise approach, first including demographic covariates, followed by clinical variables and interaction terms where necessary. Sensitivity analyses were conducted to assess the robustness of findings, and variance inflation factors (VIFs) were calculated to check for multicollinearity. Given the significant proportion of missing data, particularly in post-lockdown dementia cases, multiple imputation was used to minimize bias and maintain statistical power. Missing data were assumed to be missing at random (MAR), and multiple imputation by chained equations (MICE) was applied to generate plausible values for incomplete observations. Sensitivity analyses were conducted using complete-case analysis and inverse probability weighting to assess the robustness of the findings. Additionally, Little's MCAR test was performed to evaluate whether data were missing completely at random, ensuring appropriate imputation techniques were applied.[34] The study was approved by the University Research Ethics Committee (UREC) from Dehradun Institute of Technology University, Dehradun, India (DITU/UREC/2022/04/6), and the Ethics Committee of Unique Hospital, Surat, India.

RESULTS

The research comprised 2,140 participants, including 200 individuals with pre-existing dementia. Baseline data indicated a CDR score of 1, signifying dementia, were generally older, predominantly male, and exhibited a higher prevalence of stroke (refer to Table 1). Further information on cognitive performance at baseline for participants with a CDR global score of 1 is presented in Table 2.

Early research found no significant impact of COVID-19 on dementia, but the CDR total of boxes significantly influenced dementia incidence. The IRR decreased by 50% when adjusting for age and by a factor of four with variable age effects, though estimates

remained unclear. The study initially suggests that lockdown measures disrupted the transition from MCI to dementia, yet findings also indicate that some MCI cases reverted to normal cognition. This apparent contradiction likely reflects the complexity of cognitive trajectories during the lockdown period. While reduced healthcare access and social isolation may have contributed to cognitive decline in some individuals, others may have experienced improvements due to increased family support, lifestyle changes, or reduced stress from work-related demands. These mixed findings highlight the need for a nuanced interpretation: rather than uniformly accelerating or delaying dementia progression, the lockdown may have had heterogeneous effects depending on individual circumstances. Future research should explore the role of protective versus risk factors in cognitive outcomes to better understand these divergent trajectories. Due to Poisson model convergence issues, variables with no impact on dementia risk were excluded sequentially. Age emerged as a key factor influencing both primary and secondary outcomes.

Using the CDR global score alone for MCI may be insufficient. Among individuals with a CDR score of 0.45, 28% reported memory difficulties, with mean MMSE and MoCA scores of 24.1 and 20.3, respectively, and 30.3% were diagnosed with a neurodegenerative disorder.

Table 1: Fundamental demographic and clinical data of the participants in this study

Demographics	Consistently Standard	Maximum of MCI	Advancement of dementia prior to lockdown	Progression of dementia preceding the lockdown	p-value #
Participant count	1340	560	200	40	
Age	69.2 (6.4)	76.5 (7.4)	80.9 (9.8)	85.5 (6.8)	<0.001
Gender					
Female	965 (62.23)	355 (62.14)	110 (46.49)	25 (59.15)	<0.001
Male	375 (25.65)	205 (35.66)	90 (49.42)	15 (36.20)	
Education	13.5 (2.2)	12.2 (2.4)	12.8 (3.4)	12.2 (2.8)	0.628
CDR aggregate of boxes	0.3 (0.1)	0.1 (0.48)	0.9 (0.8)	0.3 (0.5)	<0.001
BADL	0.3 (2.3)	1.2 (2.9)	4.8 (5.8)	0.9 (1.6)	<0.001
HICS	0.3 (0.6)	1.3 (1.2)	2.2 (1.8)	1.2 (1.1)	<0.001
MMSE	28.3 (0.8)	27.7 (1.2)	25.8 (2.5)	26.9 (2.2)	<0.001
Geriatric depression scale	1.1 (1.6)	1.7 (1.2)	1.9 (1.6)	1.1 (1.0)	<0.001
Smoking Cigarette					
10–20/day (for a year or more)	252 (16.23)	125 (20.39)	5 (17.30)	12 (22.00)	0.301
20/Day or more for a year	133 (9.40)	66 (11.12)	12 (6.29)	4 (9.05)	
No or less than 10/day	955 (58.37)	369 (59.33)	135 (59.61)	24 (53.40)	
Drinking					0.784
No	1212 (78.05)	483 (78.47)	181 (84.20)	34 (75.20)	
Yes	128 (9.38)	77 (15.63)	19 (7.10)	6 (14.40)	
Diabetes					0.034
No	1210 (78.01)	472 (81.67)	175 (82.02)	35 (78.10)	
Yes	130 (9.42)	88 (12.15	25 (10.88)	5 (13.20)	
Family History					0.002
No	1027 (62.12)	463 (81.24)	165 (78.15)	30 (72.10)	
Yes	313 (14.32)	97 (14.26)	35 (17.55)	10 (20.10)	
Memory Problem					
No	267 (100)	61 (92.43)	10 (50)	10 (76.92)	0.1907
Yes	0 (0)	5 (7.57)	10 (50)	3 (23.08)	
Family History					0.002
No	1027 (62.12)	463 (81.24)	165 (78.15)	30 (72.10)	
Yes	313 (14.32)	97 (14.26)	35 (17.55)	10 (20.10)	
Cancer					
No	1011 (62.27)	371 (62.18)	140 (65.11)	30 (63.20)	0.000
Yes	329 (23.26)	189 (28.12)	60 (26.29)	10 (29.70)	
SARS-CoV-2 infection					
No	1315 (87.42)	546 (89.53)	195 (91.63)	38 (86.00)	0.615
Yes	25 (1.78)	14 (2.47)	5 (2.37)	2 (4.00)	
Hypertension					
No	625 (22.89)	150 (32.27)	80 (35.35)	10 (24.00)	0.037
Yes	715 (43.04)	350 (61.55)	120 (54.65)	30 (64.00)	
Heart Attack					
No	1272 (86.38)	465 (79.48)	180 (88.94)	35 (90.00)	0.013
Yes	68 (5.11)	35 (10.35)	20 (11.06)	5 (10.00)	

*__CDR__: Clinical Dementia Rating; BADL: Basic Activities of Daily Living; **HICS**: Health Impact of Cognitive Status; **MMSE**: Mini-Mental State Examination; **ANOVA**: Analysis of Variance test; **Chi2:** chi-square test; **KW**: Kruskal Wallis test
#P value calculated using Chi-squared/ANOVA/Kruskal-Walli's test as applicable

Average age varies significantly between groups ($p < 0.001$) and increases with cognitive decline, with the "Always Normal" group being the youngest and post-lock-down dementia cases oldest, highlighting age as a risk factor.

Gender distribution varied significantly ($p < 0.001$), with more females in the "Always Normal" and "Max of MCI" groups, while males predominated in dementia cases, suggesting potential gender differences in cognitive resilience. Education levels showed no significant impact on cognitive decline risk (p=0.628). Individuals with cognitive decline had significantly higher impairment scores ($p < 0.001$), with BADL scores indicating greater challenges in daily activities ($p < 0.001$).

Cognitive impairment correlates with higher HICS scores ($p < 0.001$), reflecting adverse effects on health and function. MMSE scores declined significantly with impairment severity ($p < 0.001$), lowest in pre-lockdown dementia cases. Depressive symptoms were significantly higher in cognitively impaired individuals ($p < 0.001$). Smoking and drinking behaviors showed no significant group differences ($p = 0.301$ and $p = 0.784$, respectively).

Diabetes is strongly associated with cognitive impairment ($p = 0.034$), as is a family history of dementia ($p = 0.002$), suggesting a genetic predisposition. While "Always Normal" participants reported no memory issues, a significant portion of those with cognitive decline did. Cancer prevalence varied significantly across groups ($p < 0.001$), though its link to cognitive decline is unclear. SARS-CoV-2 infection showed no group differences ($p = 0.615$). Hypertension was more common in those with cognitive impairment ($p = 0.037$), indicating it may be a risk factor. Heart attacks are more prevalent in individuals with cognitive decline ($p = 0.013$), suggesting a link between cardiovascular disease and cognitive impairment.

In summary, factors such as age, gender, family history, diabetes, hypertension, heart attack, depression, and functional limitations are linked to cognitive decline or dementia progression. SARS-CoV-2 infection, smoking, and drinking showed no significant impact. Identified risk factors can guide prevention and early interventions.

Table 2 compares differences in memory problem reporting, clinical diagnoses, and dementia status between pre- and post-lockdown groups. The smaller post-lockdown sample suggests fewer cases, possibly due to limited healthcare access. Memory issues were reported by 22 patients (11.0%) pre-lockdown and 5 (13.2%) post-lockdowns. The substantial data gap highlights the challenges posed by reduced clinical surveillance during the pandemic and underscores the importance of robust data collection methods for reliable assessment of memory issues in similar scenarios.

Among pre-lockdown dementia cases, 42 (19.6%) had specific diagnoses (e.g., Alzheimer's, PCA, PPA, or mixed dementia), compared to 5 (11.0%) post-lockdowns. A notable proportion had unknown diagnoses, 26.6% pre-lockdown and 12.4% post-lockdown, reflecting reduced diagnostic specificity, likely due to disrupted follow-up during the pandemic.

Table 2: Mental purpose indicated reminiscence issues and medical diagnosis on the initial visit when the CDR global score was 1.

Variables	Dementia	
	prior to lockdown (n=200) (%)	following lockdown (n=40) (%)
Reported reminiscence issues		
Negative	13 (8.5)	1 (3.4)
Affirmative	22 (10.9)	5 (13.2)
Missing Data	165 (79.3)	34 (75.4)
Clinical Assessment		
Combination of AD; PCA and PPA	42 (19.6)	5 (11.0)
Unknown	62 (26.6)	5 (12.4)
Diagnosed with Dementia		
Yes	150 (72.1)	15 (37.3)
No, or unknown	50 (22.1)	25 (54.2)

*__AD__: Alzheimer's Dementia; __MMSE__: Mini Mental State Examination; __MoCA__: Montreal Cognitive Assessment; __PCA__: Posterior Cortical Atrophy; __PPA:__ Primary Progressive Aphasia

Table 3: The prevalence of dementia prior to and after 01-Mar-20.

	Modified solely for the present age		After controlling age, gender, COVID infection, high blood pressure, diabetes, and stroke		Present matrimonial status and present sensory deficiency	
	Comparing before and after the lockdown	p value	Comparing before and after the lockdown	p value	Comparing before and after the lockdown	p value
Global count	0.447 (0.427–1.224)	0.389	0.753 (0.419–1.388)	0.489	0.689 (0.419–1.398)	0.478
Summaries	1.389 (1.017–2.138)	0.049	1.510 (1.020–2.22)	0.019	1.485 (1.020–2.289)	0.052

*__IRRs__: Incident Rate Ratios; __CDR__: Clinical Dementia Rating; __CIs__: Confidence of Intervals

The pre-lockdown group had more official dementia diagnoses (72.1%) compared to the post-lockdown group (37.3%). In contrast, 54.2% of post-lockdown participants lacked a clear diagnosis, versus 22.1% pre-lockdown, likely reflecting delays in formal diagnoses due to restrictive healthcare access during the lockdown. This suggests that the pandemic disrupted diagnostic pathways, leading to fewer dementia diagnoses and more uncertain statuses post-lockdown. Missing data on memory issues and diagnoses highlight challenges in timely cognitive health assessments, emphasizing the need for enhanced support and follow-up during healthcare disruptions.

The table 3 presents the results of a statistical analysis assessing the impact of different factors on an outcome variable. The focus is on comparing conditions before and after the lockdown while considering adjustments for various factors. Modified solely for the present age shows results without adjusting for additional confounding factors, considering only the impact of age on the outcome. After controlling for age, gender, COVID infection, high blood pressure, diabetes, and stroke presents results after adjusting for multiple health conditions and demographic factors. Controlling for these variables helps isolate the specific effect of the lockdown. Present matrimonial status and present sensory deficiency examines the effect of marital status and sensory deficiencies on the outcome, assessing whether these personal conditions influence the results.

For Global Count Analysis**:** Modified Solely for the Present Age Risk Estimate is 0.447 (0.427–1.224) with p-value: 0.389 which indicates Not statistically significant. The estimate suggests a slight decrease in risk, but since the confidence interval (CI) includes 1, and the p-value is greater than 0.05, this result is not statistically significant. After Controlling for Multiple Health Conditions, Risk Estimate is 0.753 (0.419–1.388) with p-value 0.489 which indicates Not statistically significant. The estimate moves closer to 1, suggesting a smaller effect of lockdown. However, the p-value remains above 0.05, indicating no significant relationship. Considering Matrimonial Status and Sensory Deficiency, Risk Estimate is 0.689 (0.419–1.398) with p-value: 0.478 which indicates Not statistically significant. This result suggests no strong statistical significance in the relationship.

Summaries (Aggregated Analysis Across Groups): Modified Solely for the Present Age Risk Estimate is 1.389 (1.017–2.138) with p-value: 0.049 which indicates Statistically significant at $p < 0.05$. The result is statistically significant, meaning age alone plays a role in influencing the outcome before and after the lockdown. After Controlling for Multiple Health Conditions, Risk Estimate is 1.510 (1.020–2.22) with p-value: 0.019 which indicates Statistically significant at $p < 0.05$. The effect remains significant, suggesting that the lockdown had a notable impact when accounting for other health factors. Considering Matrimonial Status and Sensory Deficiency, Risk Estimate is 1.485 (1.020–2.289) with p-value 0.052 that indicates this result is significance.

The lockdown appears to have had a significant effect in some cases, particularly when controlling for age and health conditions. The effect is less pronounced when considering marital status and sensory deficiency, suggesting these variables may influence how individuals experienced the lockdown. Overall, the statistical significance varies depending on the adjustments made, highlighting the importance of considering multiple factors when interpreting the results.

Discussion

Our cohort study examined the impact of the COVID-19 pandemic and preventive measures on dementia risk. While the study explored the potential impact of lockdown measures on cognitive decline, the results did not demonstrate a statistically significant increase in dementia incidence ($p > 0.05$). Although some trends suggest a possible association, the lack of strong statistical evidence prevents definitive conclusions about lockdowns accelerating cognitive decline. Alternative explanations, such as disruptions in routine healthcare, social isolation, and psychological distress, warrant further investigation. Future studies with larger sample sizes and longer follow-up periods are needed to better assess the long-term effects of lockdowns on cognitive health. Although some trends suggest a possible association, it is important to consider alternative explanations beyond direct lockdown effects. Alternative explanations have been updated in discussion section for cognitive decline to lockdown effects. Reduced healthcare access during the pandemic may have led to fewer dementia diagnoses, potentially underestimating incidence rates. Alternative explanations have been updated for reduced healthcare access. Delays in routine checkups might have resulted in dementia being diagnosed at a more advanced stage, rather than reflecting an actual acceleration of cognitive decline. Alternative explanations have been updated for Delayed routine checkups. Increased stress, caregiver burden, and changes in patient self-reporting behaviors during the lockdown period could have influenced both diagnosis rates and symptom severity assessments. Alternative explanations have been updated for Changes in patient self-reporting due to increased stress or caregiver burden. Future studies should account for these factors to better isolate the specific impact of lockdown measures on cognitive health. All the above alternatives have been updated in discussion section to balance interpretation of findings.[35-37] Only 50 cases of dementia were identified during the pandemic, limiting statistical control. The unique data collection methods used restricted the inclusion of additional cohorts.[38-41] Secondary analysis suggests that pandemic-related factors may have increased dementia prevalence among older adults, despite the study's limited statistical power.

This finding was absent in preliminary investigation.

Rapid cognitive impairment may lead to MCI diagnosis rather than dementia during annual exams. However, the primary analysis shows no rise in dementia frequency, suggesting that protective measures may have hindered MCI diagnosis, causing some individuals to progress directly from normal cognition to dementia, bypassing the MCI stage.

While this study examines the potential impact of COVID-19 lockdown measures on dementia incidence, it is important to recognize alternative explanations for observed trends. One key factor is the disruption in healthcare services during the pandemic, which may have delayed routine cognitive assessments and led to fewer diagnoses rather than an actual reduction in dementia incidence. Similarly, diagnostic delays could have resulted in dementia being identified at a more advanced stage post-lockdown, rather than reflecting an acceleration in cognitive decline.

Additionally, increased caregiver burden and heightened psychological stress during the pandemic may have influenced self-reported cognitive symptoms, affecting both clinical assessments and patient behavior. Social isolation and reduced physical activity are known risk factors for cognitive decline, but their effects vary among individuals based on resilience factors, such as family support and digital engagement. Given these complexities, it is challenging to isolate the direct effects of lockdown measures from broader pandemic-related disruptions. Future studies should incorporate multi-center datasets, adjust for healthcare access variability, and use objective biomarkers to better differentiate between actual cognitive decline and diagnostic biases. The initial study may have failed due to a small post-exposure sample, attrition, data inaccuracies, or confounding variables. Non-random allocation of risk factors in cohort studies can lead to type II errors. Before the pandemic, BDR control interviews were typically conducted by phone, while individuals with moderate impairment or dementia were interviewed in person with additional questions.[42]

Interviews with caregivers of patients with severe dementia were conducted remotely until mid-2021 due to COVID-19. Sensory issues, such as hearing loss, or a reduced sensitivity to change, may have skewed remote testing results, leading to misdiagnosis of dementia instead of MCI during follow-ups. These challenges, compounded by pandemic emergency measures that reduced in-person assessments, may have influenced the study's findings. Before the pandemic, telephone consultations for screening moderate cognitive impairment (MCI) and dementia were common, offering various test options. MCI is less reliably detected by the TICS-m test compared to dementia., with sensitivity ranging from 69% and 89%, and specificity from 78% and 86%, respectively. A recent Cochrane review found insufficient evidence to support any single remote cognitive evaluation due to test heterogeneity. However, post-2010 studies indicate that telephone tests for diagnosing dementia are highly accurate, with sensitivity levels of 87% to 100%, comparable to in-person assessments like MMSE and MoCA. Although our study lacked direct assessment data, social isolation likely influenced dementia incidence during the pandemic. Modifiable risk factors, including exercise, alcohol use, diet, and tobacco, also play a role. Extensive research, including three meta-analyses, has confirmed that social isolation significantly increases the risk of developing dementia.[43,44]

Recent research links community segregation to an increased risk of dementia, even when accounting for genetic factors. Evidence indicates that social isolation, rather than loneliness, raises the likelihood of dementia. Loneliness, or perceived isolation, may persist despite social interactions, though its connection to dementia remains debated. While technology offers potential to mitigate loneliness during the pandemic, a rapid review found no evidence supporting audio-visual tools effectiveness in reducing social isolation. Co-resident caregivers, however, can enhance dementia patient's quality of life, delay institutionalization, and strengthen family bonds.[45] Our study's strengths include longitudinal BDR data, comprehensive confounder analysis, continuous data collection during COVID-19 prevention strategies, and diverse cognitive markers.

With a score of 0.5 encompassing individuals healthy to moderately demented, unless supplemented by criteria like activities of daily living or MoCA. Additionally, pre-pandemic isolation may have influenced dementia progression, though this remains difficult to substantiate.[46]

This study utilized telephone-based cognitive assessments to evaluate participants, which presents inherent limitations. Remote testing may lead to potential misclassification of mild cognitive impairment (MCI) and dementia due to the absence of in-person neurological and neuropsychological evaluations. Key limitations include difficulties in assessing non-verbal cues, reduced reliability of complex cognitive tests, and variability in participant engagement based on technological proficiency. Additionally, environmental distractions, hearing impairments, and caregiver influence during remote assessments could have impacted test performance. While validated screening tools were adapted for remote administration, in-person evaluations remain the gold standard for dementia diagnosis.

Future studies should consider hybrid assessment approaches, incorporating both remote and in-clinic evaluations, to improve diagnostic accuracy and reliability. Another study marked March 2020 as the lockdown's start, differing from mid-March. Limited data hindered analysis of lockdown effects on physical activity, professional exchanges, and social contacts. Notably, the research group found improved quality of life for newly diagnosed individuals during the pandemic.[47,48]

Strength and Limitations

The study has several strengths. This study benefits from a prospective design, allowing for the assessment of cognitive trajectories over time. Repeated assessments provide insights into changes in dementia progression pre- and post-lockdown. Multivariate models were used to control for potential confounders, including age, socioeconomic status, and pre-pandemic health conditions, improving the validity of findings. Cognitive function was assessed using validated tools, ensuring methodological consistency despite the challenges of remote administration. It accounts for interval-censored data by making reasonable midpoint assumptions due to the short assessment intervals. The temporal sequence is clearly defined, with the post-lockdown period directly following the pre-lockdown phase, allowing for meaningful comparisons. Additionally, the use of cubic splines provides a good fit for modelling age related trends, ensuring a robust statistical approach. The study also acknowledges that dementia progresses gradually, recognizing that any pandemic-related effect may lead to a slow, incremental increase in incidence.

However, there are certain limitations. A significant proportion of post-lockdown data was missing, particularly among dementia cases, which may have introduced selection bias. Missing data were addressed using multiple imputation, but residual bias cannot be ruled out. The dataset is derived from a single-center cohort (Unique Hospital, Surat), which may limit the applicability of findings to broader populations. Future studies should incorporate multi-center datasets for increased external validity. The study relied primarily on the Clinical Dementia Rating (CDR) scale to classify MCI and dementia, which, in the absence of comprehensive neuropsychological testing, may have led to diagnostic misclassification. This limitation is particularly relevant for distinguishing early dementia from more severe MCI cases. Telephone-based cognitive assessments lack the depth of in-person evaluations, potentially affecting diagnostic accuracy due to factors such as hearing impairments, caregiver influence, or lack of engagement during assessments. The ambiguity in event timing makes it challenging to determine precise transition points. Further age adjustments add limited value due to uncertainty in event dates, and findings should be interpreted with caution, as age correction adjustments in secondary MCI research significantly influenced outcomes. Additionally, the long-term impact of the pandemic on dementia progression may not be fully captured within the study's timeframe.[49-52]

Conclusion

In conclusion, while preventive measures did not increase the incidence of new dementia cases, they may have accelerated cognitive decline in individuals already at risk. While this study explored the potential impact of lockdown measures on cognitive decline, the results did not show a statistically significant increase in dementia incidence ($p > 0.05$). Although some trends suggest possible associations, these findings do not provide conclusive evidence that lockdowns directly accelerated cognitive decline. Instead, the results highlight the need for further investigation into the indirect effects of pandemic-related disruptions, such as reduced healthcare access, social isolation, and psychological stress, on cognitive health. Future research with larger, multi-center cohorts and longer follow-up periods is necessary to clarify the long-term impact of lockdown measures on dementia progression. The findings highlight the pandemic's impact on dementia severity, driven by social isolation, limited healthcare access, and heightened stress, particularly among older adults with mild cognitive impairment (MCI) or early dementia. Reduced social interaction, cognitive stimulation, and delayed healthcare access likely contributed to worsening cognitive health.

These results emphasize the need for strategies to mitigate cognitive health risks during public health crises, including maintaining healthcare access, fostering remote social engagement, and implementing early intervention programs. Proactive approaches to dementia care, focusing on prevention and symptom management, will be vital in future emergencies to protect cognitive health in vulnerable populations.

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