ORIGINAL RESEARCH

Comprehensive Geriatric Assessment in a Mexican Long-term Care Facility During a COVID-19 Outbreak

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Abstract

Objective: The Coronavirus disease-2019 (COVID-19) pandemic has greatly affected long-term care facilities worldwide. In Mexico, there are no studies that assess the impact between COVID-19 and the comprehensive geriatric assessment (CGA). This article aims to investigate the effect on the geriatric assessment before and after COVID-19 infection had in residents of a long-term care facility, as well as the factors that influenced the virus transmission and its associated mortality.

Materials and Methods: This is a prospective observational study that included 90 older adults during an outbreak of COVID-19 in a long-term care facility in Monterrey, Nuevo León, Mexico. Participants' geriatric assessments were designed using their history records, comorbidities and Barthel index, Folstein's mini-mental state examination, geriatric depression scale, mini nutritional assessment, and polypharmacy.

Results: When comparing the CGA before and after the COVID-19, Barthel index median was 90 vs 57.7 (p=0.001), the mini-mental state examination median was 23 vs 19 (p=0.001), the geriatric depression scale median was 4 vs 5 (p=0.007), the weight mean was 59.63 vs 56.95 (p=0.001), the body mass index mean was 23.9 vs 23.19 (p=0.009), and the mini nutritional assessment median was 23 vs 21.5 (p=0.001). Mortality in positive residents of COVID-19 was significantly higher in those with a polypharmacy >8 and mini-mental state examination <10 points.

Conclusion: This study highlights the vulnerability of older adults to COVID-19 infection associated with high mortality and their global deterioration in the post-infection stage. Likewise, mortality in our population was higher in those with polypharmacy and cognitive impairment. These results guide us to create preventive measures that improve the quality and survival of geriatric COVID-19 patients.

Keywords: COVID-19, comprehensive geriatric assessment, older adults, long-term care facilities

Introduction

Coronavirus disease-2019 (COVID-19) has had a devastating impact in Mexico, ranking among the top five countries most affected by the virus with 10.4% in an observed case-fatality ratio (vs 2.8% in the United States) and 65.56 deaths per 100,000 people (vs 64.74 per 100,000 in the United States) (1). By August 2021, Mexican government statistics have reported 1,637,836 excess deaths, from which it is estimated that 360,034 were caused by COVID-19; this represents an increase of 44.2% in the excess mortality (2). Of these deaths, 910,464 were found within the population over 65 years of age, resulting in an excess mortality of 41.2%. These data are similar to the ones reported in the State of Nuevo León (42.4%) and, unfortunately, a significant percentage of these deaths do not have a confirmatory test for a severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection (2).

In March 2020, the first COVID-19 case was confirmed in Monterrey, Mexico. By August 12, 2021, the State of Nuevo Leon statistics reported 138,406 accumulated cases and 11.780

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deaths due to COVID-19 (3). Of these, 138 infections in older adults occurred in multiple long-term care facilities (LTCF's) in Monterrey; nonetheless, data have not been updated in months. A potential reason is that most of these institutions are private and are afraid that the government regulatory bodies will close down the facilities (3).

Evidence has shown an exponential mortality increase in patients over 50 years; therefore, there has been an emphasis on protecting LCTF's residents since early in the pandemic (4). However, research on LTCF's is limited (5). In the United States, by May 21, 2021, over 35,000 deaths have been reported in LTCF's, representing 42% of total deaths due to COVID-19; LTCF's with more than 50 residents are the most affected (6). A study published in September 2020 reported that the mortality in 12 member countries of the organization for economic co-operation and development was 47.3% in LTCF's and 44.7% in older adults living in the community (7). In addition to the greater risk in the elderly population, it is extremely important to consider the frailty syndrome in this population, since mortality reaches up to 33.7% in frail adults infected by COVID-19 (8).

Literature on COVID-19 infections at LCTF's and their post-infection impact on the elderly measured by the comprehensive geriatric assessment (CGA) in Mexico is scarce. Therefore, this study aims to i) Describe the COVID-19 outbreak in a LTCF in Monterrey, ii) Recognize factors that could have influenced the transmission of the SARS-CoV-2 and the mortality caused by COVID-19, and iii) Measure geriatric assessments after residents re-entry to the LTCF.

Materials and Methods

An observational, prospective study was carried out in a LCTF in Monterrey, Mexico. The CGA was evaluated in two stages: 1) In May 2020, representing the period patients received a confirmatory COVID-19 active infection, and 2) After their readmission to the LTCF in July 2020. The SARS-CoV-2 infection was confirmed through a reverse transcription-polymerase chain reaction test. Nuevo Leon's Health Ministry collected and processed COVID-19 tests.

Residents' socio-demographic characteristics and medical history were collected from patients' health records. Participants' functional status was evaluated using the Barthel index (BI) to measure their performance on activities of daily life (ADLs) (9), cognitive status was evaluated with Folstein's mini-mental state examination (MMSE) (10), and emotional status was measured according to the geriatric depression scale (GDS) (11). Additionally, we evaluated the participants' nutritional status using the mini nutritional assessment (MNA), including their measurements to calculate their body mass index (BMI) (12). Polypharmacy was also evaluated and defined as patients receiving a prescription of 8 or more drugs (13).

Statistics

Statistical analysis was done by IBM SPSS v22 software. Continuous variables are presented as the median and interquartile range or mean ± standard deviation. Categorical variables are described as frequencies with their respective percentages (%). The distribution of numeric variables was measured with the Kolmogorov-Smirnov test. Differences between groups were evaluated using the Mann-Whitney U test for numeric variables without a normal distribution, while the student t-test for independent groups was used for numeric variables with a normal distribution. The Wilcoxon test and the paired t-test were used for numeric variables with a non-normal and normal distribution, respectively, to evaluate the differences before the outbreak and after the patients' readmission. Differences in proportions were evaluated with the chi-square test. A binary logistic regression was performed adjusting for age and sex and including all the variables with a p-value <0.1 in the bivariate analysis. Statistical significance was defined as a p-value <0.05.

Results

Ninety patients were examined prior to the COVID-19 outbreak. The mean age was 84.71±7.47, and the range was 67-101 years. Sixty-one (67.8%) were females and twenty-nine (32.2%) males. The median outcome of the BI evaluation was 80 (38.75-95), and 17 (18.9%) patients were classified as totally dependent. The cognitive evaluation resulted in a median MMSE of 21 (13-26); 29 (65.4%) patients had a degree of cognitive impairment. The median GDS score was 4 (2-6); 21 (23.3%) were classified as having depression. Finally, patients' nutritional status had a mean weight of 57.66±14.46 kg, with a mean BMI of 23.7±4.6 and a median MNA of 23 (19.25-25). 33 (36.7%) were underweight, 19 (21.1%) were overweight or obese, 39 (43.3%) were at risk of malnutrition, and 11 (12.2%) were malnourished.

The median of prescribed drugs was 6 (4-9) and 30 (33.3%) residents reported having polypharmacy. The most frequently prescribed drug groups were antidepressants in 52 (57.8%), acetylsalicylic acid in 35 (38.9%), and lipid-lowering drugs in 33 (36.7%) (Table 1). Regarding chronic degenerative diseases, 52 (57.8%) were hypertensive, 24 (27.7%) were diabetic, and 25 (27.8%) had hypercholesterolemia. Since March 2020, 49 (54.4%) residents have taken vitamin C 1.000 mg and zinc 50 mg daily.

On May 2, 2020, 5 people (two staff and three residents) reported fever. The following day, six additional residents reported fever, and health authorities were notified. On May 4, 10 residents had a positive test for COVID-19, and in the next 24 hours, over 50 COVID-19 tests from people within the LTCF were positive. Consequently, all residents were transferred to different healthcare facilities. On May 9, 2020, the staff positive

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Table 1. Baseline characteristics of residents before the outbreak

Socio-demographic features	N (%)
Age, mean ± SD, years	84.71±7.47
Sex, female	61 (67.8)
BI, median (IQR)	80 (38.75-95)
BI >90	36 (40)
BI 61-90	21 (23.3)
BI 21-60	16 (17.8)
BI <21	17 (18.9)
MMSE, median (IQR)	21 (13-26)
MMSE >24	31 (34.4)
MMSE 17-24	29 (32.2)
MMSE 10-16	15 (16.7)
MMSE <10	15 (16.7)
GDS, median (IQR)	4 (2-6)
GDS >5	21 (23.3)
MNA, median (IQR)	23 (19.25-25)
MNA 24-30	36 (40)
MNA 17-23.5	39 (43.3)
MNA <17	11 (12.2)
Weight, mean ± SD, kg	57.66±14.46
BMI, mean ± SD, kg/m²	23.7±4.6
BMI <18.5	9 (10)
BMI >24.9	33 (36.7)
Arterial hypertension	52 (57.8)
Type 2 diabetes mellitus	24 (27.7)
Hypercholesterolemia	25 (27.8)
Medications, median (IQR)	6 (4-9)
Polypharmacy	30 (33.3)
Antidepressants	52 (57.8)
Acetylsalicylic acid	35 (38.9)
Lipid-lowering agents	33 (36.7)
PPI	31 (34.4)
ACE inhibitors	26 (28.9)
Benzodiazepines	25 (27.8)
ARBs	23 (25.6)
Antipsychotics	22 (24.4)
Analgesics	20 (22.2)
Oral antidiabetics	16 (17.8)
Anti-dementia	15 (16.7)
Diuretics	12 (13.3)
Insulin	10 (11.1)
Antiprostatic hypertrophy agents	10 (11.1)
Beta-blockers	7 (7.8)
Oral contraceptives	3 (3.3)

SD: Standard deviation, BI: Barthel index, MMSE: Mini-mental state examination, GDS: Geriatric depression scale, MNA: Mini nutritional assessment, BMI: Body mass index, PPI: Proton-pump inhibitors, ACE: Angiotensin-converting enzyme, ARBs: Angiotensin II receptor blockers

for COVID-19 was isolated in a shelter, and the 90 residents were taken to different medical units, separating the positive cases from the negatives. As for the residents with a positive test for COVID-19, 41 (62.1%) were transferred to private centers, 22 (33.3%) to public centers, and 3 (4.5%) to their homes.

Out of the 90 residents (R), 66 (73.3%) had a positive test for COVID-19 (R+) and 24 (26.6%) a negative one (R-). When comparing both groups, the R+ group had a lower mean age, fewer women, and a lower vitamin C and zinc intake; however, none of these differences resulted in a statistically significant p-value (Table 2). Further, we found a BI median of 90 (50-100) in the R+ group and of 45 (16.25-92.5) in the R- group, suggesting that a greater independence in the ADLs, greater the risk for contagion (p=0.003). Similarly, when evaluating the cognitive status, we observed a median MMSE in the R+ group of 23 (15.75-27) and of 15 (1-23.75) in the R- group, suggesting that a higher cognitive performance, the greater the risk of infection (p<0.001). The nutritional assessment resulted in a median of MNA in the R+ group of 23.5 (21-25.5) and 18.5 (16.62-24) in the R- group, suggesting that a higher MNA result, greater is the risk of infection (p=0.006). The BMI was higher in the R+ group (23.9±3.81 vs 23.19±6.28); however, statistical significance was not reached (p=0.524). Nonetheless, a higher proportion of low-weight residents was found in the R- group (p=0.010). The GDS score and weight were higher in the R+; however, no statistically significant difference was observed. In addition, the proportions of residents with polypharmacy, hypertension, diabetes, and hypercholesterolemia were higher in the R+ group without reaching a statistically significant difference (Table 2).

Of the 90 residents, 26 (28.9%) died, 20 before returning to the LTCF, and six within the five months after returning. Out of the residents who died, the majority were women (57.7% vs 42.3%; p=0.192) and were R+ (80.8% vs 19.2%; p=0.309). Participants were most frequently admitted to a public medical centre (57.1% vs 42.9%), with patients treated in a private medical facility reporting fewer deaths (p=0.008).

From June 15, 2020, residents started to return to the LTCF. By October 1, 2020, there were 59 residents due to the relatives' decision of 5 (7.8%) not to return. Out of the 59 residents, 17 (28.8%) were R- and 42 (71.2%) R+; 41 (69.5%) women and 18 (30.5%) male. When evaluating participants with the CGA, we compared the results between the R+ survivors and those who died, 20% had an MMSE <10 (p=0.048), 60% had polypharmacy (p=0.030), and the rest of the variables were not statistically significant (Table 3). In addition, the CGA was compared with the assessment prior to the outbreak, finding that after readmission to the LTCF, there was a greater functional dependence in the ADLs (p<0.001), lower cognitive performance (p<0.001), a higher score on the GDS (p=0.007), a lower nutritional status (p<0.001) and a lower BMI (p=0.009) in the residents (Table 4).

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Table 2. Comparison of residents with a positive (R+) and negative (R-) test for SARS-CoV-2

	R+ (n=66)	R- (n=24)	p-value
Age	84.14±7.64	86.29±6.9	0.228
Sex, female	42 (63.6%)	19 (79.2%)	0.163
Vitamin C + zinc	35 (53%)	14 (58.3%)	0.655
BI	90 (50-100)	45 (16.25-92.5)	0.003*
BI >90	30 (45.5%)	6 (25%)	0.079
BI <21	7 (10.6%)	10 (41.7%)	<0.001*
MMSE	23 (15.75-27)	15 (1-23.75)	<0.001*
MMSE <10	7 (7.6%)	10 (41.7%)	0.101
GDS	4 (2-6)	4 (2-5)	0.694
GDS >5	18 (27.2%)	3 (12.5%)	0.142
Weight	58.86±10.62	54.55±21.44	0.217
BMI	23.9±3.81	23.19±6.28	0.524
BMI <22	19 (28.7%)	14 (58.3%)	0.010*
MNA	23.5 (21-25.5)	18.5 (16.62-24)	0.006*
MNA <17	5 (7.57%)	6 (25%)	0.025*
Number of prescribed drugs	7 (4-9)	4 (2.25-8.5)	0.113
Polypharmacy	24 (36.4%)	6 (25%)	0.312
Hypertension	40 (60.6%)	12 (50%)	0.368
Type 2 diabetes mellitus	21 (31.8%)	3 (12.5%)	0.067
Hypercholesterolemia	28 (42.4%)	9 (37.5%)	0.675

BI: Barthel index, MMSE: Mini-mental state examination, GDS: Geriatric depression scale, MNA: Mini nutritional assessment, BMI: Body mass index, SARS-CoV-2: Severe acute respiratory syndrome-coronavirus-2, *a p-value <0.05 is statistically significant

Table 3. Comparison between the residents with a positive COVID-19 who survived (R+ survivors) and died (R+ deceased)

	R+ survivors (n=48)	R+ deceased (n=15)	p-value
Age	83.79±7.82	85.2±7.02	0.536
Sex, women	31 (64.6%)	8 (53.3%)	0.434
Vitamin C + zinc	27 (56.3%)	5 (33.3%)	0.121
BI	90 (61.25-100)	80 (40-95)	0.148
BI >90	23 (47.9%)	6 (40%)	0.591
BI <21	4 (8.3%)	3 (20%)	0.209
MMSE	23 (18-27)	21 (11-25)	0.228
MMSE <10	2 (4.2%)	3 (20%)	0.048*
GDS	4 (2-5.5)	5 (2-9)	0.446
GDS >5	11 (24.4%)	6 (46.2%)	0.129
Weight	59.93±10.53	56.02±10.57	0.230
BMI	23.55±5.27	23.41±3.29	0.925
BMI <22	14 (31.1%)	4 (28.6%)	0.857
MNA	24 (21-25.5)	23 (20-24.25)	0.260
MNA <17	4 (8.9%)	1 (7.1%)	0.838
Number of prescribed drugs	7 (4-8.75)	9 (4-10)	0.150
Polypharmacy	14 (29.2%)	9 (60%)	0.030*
Hypertension	30 (62.5%)	9 (60%)	0.862
Type 2 diabetes mellitus	14 (29.2%)	6 (40%)	0.431
Hypercholesterolemia	20 (41.7%)	8 (53.3%)	0.427

COVID-19: Coronavirus disease-2019, BI: Barthel index, MMSE: Mini-mental state examination, GDS: Geriatric depression scale, MNA: Mini nutritional assessment, BMI: Body mass index, *a p-value <0.05 is statistically significant

Lastly, the binary logistic regression did not show a statistically significant value between the included variables and the risk for infection. However, having an MMSE <10 and reporting polypharmacy increased the risk of mortality in the R+ group by 11 and 4 times more, respectively (Table 5).

Discussion

To the authors' knowledge, this is the first study in Mexico that evaluates the impact of COVID-19 on LTCFs using the CGA and compares the physical, psycho-affective, mental, and nutritional status before and after a COVID-19 outbreak. The LTCF evaluation has been characterized by providing daily rehabilitation services to the patients from their admission to the unit, fostering the preservation and improvement of the physical, cognitive, and emotional health according to the individual resident's needs.

Among the residents of the LTCF, 66 of them were diagnosed with COVID-19, and 15 died, resulting in an attack rate of 73.3% and a fatality rate of 22.7%. Similar results were observed compared to studies in different European countries, where attack rates in nursing homes long stay due to COVID-19 outbreaks oscillated in 60% and the fatality rates have been between 15 and 34%

Table 4. Comparison of residents' performance prior to the outbreak and after their readmission to the LTCF

	Prior the outbreak	After readmission	p-value
BI	90 (45-100)	57.5 (10-95)	<0.001*
MMSE	23 (13-27)	19 (11-26)	<0.001*
GDS	4 (2-5)	5 (3-7)	0.007*
Weight	59.63±15.41	56.95±14.93	<0.001*
BMI	23.9±4.85	23.19±4.83	0,009*
MNA	23 (19.75-25.5)	21.5 (18.75-23.12)	<0.001*
Number of prescribed drugs	6 (4-9)	6.5 (4-8.25)	0.246

BI: Barthel index, MMSE: Mini-mental state examination, GDS: Geriatric depression scale, MNA: Mini nutritional assessment, BMI: Body mass index, *a p-value <0.05 is statistically significant, LTCF: Long-term care facilities

(14,15). This demonstrates the increase in mortality that has been described with increasing age (16).

A significantly higher incidence of COVID-19 cases was detected in older adults with low physical dependence in the ADLs, with a median BI of 90 (50-100) in residents with COVID-19. This could

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Table 5. Regression analysis of factors that increased the risk of transmission and mortality due to COVID-19			
	OR	95% CI	p-value
Variables related to an increased risk of COVID-19 infection			
BI <21	0.466	0.081-2.675	0.392
MMSE	1.051	0.971-1.137	0.217
BMI <22	0.621	0.157-2.466	0.499
MNA	1.026	0.816-1.292	0.824
Type 2 diabetes mellitus	2.142	0.489-9.386	0.312
Variables related to an increased risk of COVID-19 mortality			
MMSE <10	11.111	1.369-90.909	0.024*
Polypharmacy	4.651	1.218-17.765	0.025*

COVID-19: Coronavirus disease-2019, BI: Barthel index, MMSE: Mini-mental state examination, MNA: Mini nutritional assessment, BMI: Body mass index, CI: Confidence interval, OR: Odds ratio, *a p-value <0.05 is statistically significant

be related to the route of transmission of the virus: Mainly from person to person (staff-residents), and the increased social contact in adults with greater functionality. Compared to Spanish LTCF's, where residents with moderate to total dependence were more vulnerable to the risk of transmission of SARS-CoV-2, associated with closer physical contact between workers and residents, facilitating transmission (17). Likewise, significant results were found when evaluating the functionality in ADLs before and after the COVID-19 outbreak at the facility, finding a considerable 32.5 decrease in the BI median. This decrease might be the consequence of the length of stay, functional depression, and the need for restrictive mobility in most of them, thus increasing dependency (18).

A significant cognitive decline (4-point median MMSE score decrease) was found in COVID-19 positive older adults after readmission to the LTCF. It is important to emphasize that progress to a moderate cognitive impairment was observed in the vast majority of the residents. Moreover, higher mortality was found in residents with a positive test for COVID-19 and an MMSE <10 points. Post-acute manifestations have been described as associated with cognitive impairment with or without fluctuations, including memory problems manifesting as difficulty in concentration, memory, receptive language, and/or executive function (19). Furthermore, long-term cognitive impairment is well recognized after a critical illness occurring up to 20-40% of patients discharged from intensive care (20).

Regarding the affective mood behaviour, we found a significant change in the GDS-15 scale items of the residents evaluated after returning to the institution, resulting in an overall median increase of 4 to 5 points, considering that most of the residents before the pandemic did not report symptoms of depression. Our results coincide with studies where depression, measured with the same instrument, was exacerbated by up to 86.6% two weeks after being discharged from the hospital in patients aged 65 or older who survived COVID-19 (21). Demonstrating that

social disconnection and isolation are risk factors for presenting a depressive mood in older adults (22).

Concerning nutritional status of the residents, a significantly higher proportion of underweight and malnutrition was observed in the non-infected residents. This aligns with the explanation that the highly dependent population in the ADLs with a higher risk of sarcopenia has less mobilization and less social contact with other residents and staff; thus, reducing the risk of infection. Similarly, a significant change was observed in the decrease in residents' weight, BMI, and MNA after the COVID-19 outbreak. For these reasons, it is vital to identify and prevent a nutritional decline in hospitalizations and improve clinical outcomes in patients at nutritional risk. It has been found that the MNA-SF (short-form) scale predicted in a good way the worst clinical results after COVID-19 infection (23). On the other hand, when using the MNA scale in full version in patients with COVID-19, found a positive correlation between poor nutritional status and a prolonged stay in the intensive care unit (24).

It was observed that polypharmacy was significantly associated with higher mortality in residents who tested positive for COVID-19. Sixty percent of the residents who died had polypharmacy, and the regression analysis resulted in four times the risk of dying in this sub-group compared to the rest of the residents with COVID-19. Polypharmacy has unpredictable consequences as cohort studies reported that up to 50% of American older adults use at least five drugs, of which 1 in 2 have been found to have significant interactions with drugs tested for COVID-19, such as hydroxychloroquine (25). In the REACT-SCOT study, an evident association was found between the severity of COVID-19 and polypharmacy, mainly in using more than four drugs of different classes. In addition, it was found that the severity of the infection is strongly associated with antipsychotics, proton pump inhibitors, opioids, and gabapentinoids, since an increase in activity associated with pneumonia has been found by different routes, mainly anticholinergic and by mechanisms that increase the severity such as sedation, respiratory depression, and dyskinesia (26).

Among the chronic-degenerative diseases, we found a statistical trend between the presentation of COVID-19 and type 2 diabetes mellitus (27). This could be explained by the alterations in the expression of the surface receptors of the converting enzyme angiotensin 2, which has a binding region with a high affinity for the S protein of the SARS-CoV-2 virus (28). In addition, there is a dysregulation of the immune system due to the increase in interleukin-6 and the weakening of anti-inflammatory signals producing more significant damage to the affected organs (29). On the other hand, a meta-analysis found that hypertension and diabetes are highly associated with an increase in severity and mortality from COVID-19 of 2.3 and 2.5 times, respectively (30).

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Study Limitations

Our study had limitations worth mentioning: we do not know the evolution that the patients had during their infection and what could have influenced their outcome (e.g., clinical evolution, possible complications, laboratory findings, received treatment, and whether or not they received any rehabilitation). It is important to emphasize that a significantly lower mortality rate was found in private medical centers than public ones, which would be associated with better availability of human, pharmacological, and medical devices resources. Lastly, the results should be interpreted with caution due to the size of the study group.

Conclusion

The COVID-19 pandemic, as observed in other countries and Mexico, not being the exception, confirms the vulnerability in the functional, cognitive, emotional, and nutritional aspects of the elderly. An essential factor to consider is that most of the residents evaluated in this study who were positive cases were patients with a better global status in all indicators considered in the study, which would be associated with a greater risk of infection. In our population, we found higher mortality in residents with polypharmacy and with an MMSE <10 points. In addition, a significant change was found in functional dependence in the ADLs, cognitive impairment, emotional mood changes and nutritional status after the COVID-19 outbreak in the LTCF. Currently and with the growing information that we have about COVID-19, changes are needed in the CGA to provide measures that promote preventive, diagnostic, and therapeutic options to preserve and improve the quality of life and even decrease mortality in the elderly associated with COVID-19 infection.

Ethics

Ethics Committee Approval: The Ethics Committee of Asilo Luis Elizondo through its members of the Council formed by Fomento Moral y Educativo A.C. authorized the preparation of this manuscript entitled: Comprehensive Geriatric Assessment in a Mexican Long-Term Care Facility during a COVID-19 Outbreak.

Informed Consent: All the relatives and residents of the Asilo Luis Elizondo upon admission sign an informed consent on the use of their personal and clinical data to carry out clinical research work.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: F.C.F., J.D.D.G.R., L.E.F.G., J.V.G., Concept: F.C.F., J.D.D.G.R., L.E.F.G., J.V.G., Design: F.C.F., J.D.D.G.R., L.E.F.G., J.V.G., Data Collection or Processing: F.C.F., J.D.D.G.R., L.E.F.G., J.V.G., Analysis or Interpretation: F.C.F., J.D.D.G.R., L.E.F.G., J.V.G., Literature Search: F.C.F., J.D.D.G.R., L.E.F.G., J.V.G., Writing: F.C.F., J.D.D.G.R., L.E.F.G., J.V.G.

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