



ORIGINAL ARTICLE

Case fatality of COVID-19 in patients with neurodegenerative dementia



J.A. Reyes-Bueno^{a,*}, N. Mena-Vázquez^b, T. Ojea-Ortega^c, M.M. Gonzalez-Sotomayor^c, P. Cabezudo-García^c, N.L. Ciano-Petersen^c, G. Pons-Pons^c, M.V. Castro-Sánchez^c, P.J. Serrano-Castro^c

^a Unidad de Gestión Clínica de Neurociencias, Servicio de Neurología, Hospital Regional Universitario de Málaga, Málaga, Spain

^b Unidad de Gestión Clínica de Reumatología, Hospital Regional Universitario de Málaga, Málaga, Spain

^c Unidad de Gestión Clínica de Neurociencias, Servicio de Neurología, Hospital Regional Universitario de Málaga, Málaga, Spain

Available online 7 October 2020

KEYWORDS

COVID-19;
SARS-CoV-2;
Dementia;
Case fatality

Abstract

Introduction: The elderly population is the group most threatened by COVID-19, with the highest mortality rates. This study aims to analyse the case fatality of COVID-19 in a cohort of patients with degenerative dementia.

Methods: We conducted a descriptive case-control study of a sample of patients diagnosed with primary neurodegenerative dementia.

Results: Twenty-four of the 88 patients with COVID-19 included in the study died: 10/23 (43.4%) patients diagnosed with dementia and 14/65 (21.5%) controls; this difference was statistically significant.

Discussion: Our results suggest that case fatality of COVID-19 is significantly higher among patients with primary degenerative dementia than in other patients with similar mean ages and comorbidities.

© 2020 Sociedad Española de Neurología. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

PALABRAS CLAVE

COVID-19;
SARS-Cov-2;
Demencias;
Letalidad

Análisis de letalidad por COVID-19 en pacientes con demencia neurodegenerativa

Resumen

Introducción: La población anciana es la más amenazada por COVID-19, con mayores tasas de mortalidad. El objetivo de este trabajo es analizar la letalidad en una cohorte de pacientes de COVID-19 con demencia degenerativa.

Please cite this article as: Reyes-Bueno JA, Mena-Vázquez N, Ojea-Ortega T, Gonzalez-Sotomayor MM, Cabezudo-García P, Ciano-Petersen NL et al. Análisis de letalidad por COVID-19 en pacientes con demencia neurodegenerativa. Neurología. 2020;35:639–645.

* Corresponding author.

E-mail address: jareybu@gmail.com (J.A. Reyes-Bueno).

2173-5808/© 2020 Sociedad Española de Neurología. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Métodos: Hicimos un estudio descriptivo de casos-control de una muestra de pacientes diagnosticados con demencias neurodegenerativas primarias.

Resultados: De los 88 pacientes incluidos en el estudio, 24 pacientes con COVID-19 fallecieron: 10/23 (43,4%) eran pacientes con diagnóstico de demencia y 14/65 (21,5%) pacientes del grupo control, una diferencia estadísticamente significativa.

Discusión: La letalidad entre los pacientes con demencia degenerativa primaria por COVID-19 es significativamente mayor en comparación con otros pacientes con edades medias y comorbilidades similares, según nuestro estudio.

© 2020 Sociedad Española de Neurología. Publicado por Elsevier España, S.L.U. Este es un artículo Open Access bajo la licencia CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

On 11 March 2020, the WHO declared the outbreak of SARS-CoV-2 a pandemic. The virus is lethal and highly dangerous, and is similar to the SARS-CoV virus that emerged in 2003.^{1,2} As of 23 April 2020, there are estimated to be 2 544 792 confirmed cases worldwide, with 175 694 deaths recorded in 213 countries.¹

This novel coronavirus belongs to the group of beta-coronaviruses, for which bats constitute the main reservoir and origin. They present high pathogenicity and infectivity, leading to high mortality rates.³ Clinical presentations of COVID-19 include a syndrome of respiratory insufficiency and pneumonia, with a clinical spectrum ranging from banal flu-like symptoms or even asymptomaticity to acute cases of highly fatal respiratory failure.⁴ SARS-CoV-2 is thought to infect the nervous system through the angiotensin-converting enzyme 2 (ACE2) receptor and the transmembrane protease serine 2 (TMPRSS2), both of which are necessary for the virus to enter cells and are present in neurons, glial cells, and respiratory epithelial cells.⁵

The elderly population is the group most threatened by COVID-19, with the highest mortality and fatality rates, especially among individuals who live in retirement or nursing homes, as shown by mass media and government data. Furthermore, some studies report that up to one-third of the elderly population living in nursing homes have primary degenerative dementia (PDD).⁶ In Spain, Ministry of Health data (consulted 23 April 2020) indicate that 36% of the 148 069 reported cases corresponded to individuals older than 70 years; this age group accounts for 86% of deaths from the disease.⁷ The proportion of individuals with primary degenerative dementia is known to be much higher in this age group (up to 9.4% in patients older than 70 years⁸); while the presence of primary degenerative dementia does not in itself increase the risk of developing COVID-19, it does increase the risk of complications and death.

Case fatality in this age group is higher than in the general population. A Chinese study reports case fatality rates of 8% in patients aged between 70–79 years and 14.8% in patients older than 80 years.⁹ However, to our knowledge, little evidence is available on case fatality rates in patients with primary dementias. The aim of this study is to analyse a series of patients with primary degenerative dementia and COVID-19 who were treated at our hospital, considering their clinical status, prognosis, and treatment. Our hypothesis is that presence of degenerative dementia increases case fatality rates among patients with COVID-19.

Material and methods

Design

We conducted a descriptive case-control study of a sample of patients with PDD at the Málaga Institute of Biomedical Research and the neurology department at Hospital Regional Universitario de Málaga (HRUM).

Study group

After reviewing emergency department admissions between 14 March 2020 and 15 May 2020, inclusive, using the Diraya electronic history system, we included patients admitted to the emergency department at HRUM with suspected COVID-19. Patients with dementia were diagnosed at the memory units at HRUM and Hospital Virgen de la Victoria (Málaga). We also included patients with mild cognitive impairment of probable neurodegenerative origin. We excluded patients with vascular dementia due to stroke, dementia, or cognitive impairment due to another cause and patients with active neoplasia.

Control group

To compare the case fatality of COVID-19 in patients with primary dementias, we also analysed a group of patients with COVID-19 without dementia from our hospital. We excluded patients with a final aetiological diagnosis other than COVID-19.

Study protocol

We selected patients meeting the inclusion criteria and admitted to the HRUM emergency department's COVID-19 unit. The unit is an independent area dedicated to the assessment of patients presenting biological hazard. It includes a consultation area, a critical care room, and a dedicated radiology team. All patients with signs and symptoms compatible with SARS-CoV-2 infection were admitted through this pathway. Patients were assessed by a physician who requested a laboratory analysis and radiological and microbiological studies, in line with the recommendations of the Spanish Ministry of Health.¹⁰

We included patients with acute respiratory infection compatible with COVID-19, as Spain was considered to present community transmission. RT-PCR testing was performed in all patients with moderate-severe symptoms or mild cases presenting some risk fac-

tor for severe COVID-19. Diagnosis was clinical in patients with mild symptoms and no risk factors; these were considered "possible cases."¹¹ RT-PCR testing was performed at least once in all hospitalised patients. Those patients with clinical/radiological signs compatible with COVID-19, negative RT-PCR results, and no other likely aetiology were considered "probable cases," in accordance with the guidelines of the Spanish Ministry of Health. Patients with positive RT-PCR results were considered confirmed cases. In our study, clinical history data were systematically recorded using a predefined form.

Objectives

The main aim of this study was to estimate case fatality. Case fatality was estimated according to the number of deaths occurring during the recruitment period. We included a similar control group of patients with COVID-19 and without primary dementia from the same hospital, to test the hypothesis of a higher case fatality rate of COVID-19 in the group with primary dementia.

Sample characteristics

COVID-19 was diagnosed according to the classification of the Spanish Ministry of Health: confirmed cases (patients with positive RT-PCR results for SARS-CoV-2) and probable cases (patients with a severe acute respiratory infection requiring hospitalisation and with clinical and radiological characteristics compatible with COVID-19, in the absence of RT-PCR confirmation). We recorded all the treatments administered for COVID-19: azithromycin, hydroxychloroquine/chloroquine, lopinavir/ritonavir, remdesivir, anti-IL-6, anti-IL-1, steroids, and intravenous immunoglobulins.

Other variables

We collected data on the following variables: age; sex; institutionalisation in retirement or nursing homes (patients dependent for such everyday tasks as getting dressed, eating, walking, or hygiene); and cardiovascular risk factors, including history of smoking, hypertension, type 2 diabetes mellitus, heart disease (ischaemic heart disease, congestive heart failure, or significant arrhythmic events [atrial fibrillation]), and pulmonary disease (chronic obstructive pulmonary disease, pulmonary fibrosis, or active asthma). Regarding dementia, we collected the following data from patients diagnosed with primary dementia at the memory unit: type of degenerative dementia (Alzheimer disease, Lewy body dementia, frontotemporal dementia, corticobasal syndrome, progressive supranuclear palsy, Parkinson's dementia), and degree of dementia according to the Hughes Clinical Dementia Rating scale (CDR 0.5 = questionable dementia; CDR 1 = mild cognitive impairment; CDR 2 = moderate cognitive impairment; CDR 3 = severe cognitive impairment). We also recorded data on treatment with acetylcholinesterase inhibitors, memantine, and antipsychotics.

Data availability

Any unpublished anonymised data will be available to qualified researchers upon request.

Statistical analysis

We first used the chi-square test and *t* test or the Mann-Whitney *U* test to compare the main characteristics between patients with dementia and matched controls without dementia, as well as to compare the main characteristics of patients with dementia according to vital prognosis. Qualitative variables are expressed as absolute frequencies and percentages and quantitative variables as mean (SD) or median (IQR), according to whether they present

normal distribution. Normal distribution for continuous variables was confirmed using the Kolmogorov-Smirnov test. We conducted 2 stepwise logistic regression models: one to analyse which variables are independently associated with case fatality and another to identify the variables associated with case fatality in patients with dementia. This analysis only included variables with statistical significance or clinical interest. A *P*-value < .05 was considered statistically significant in all analyses. Data were analysed using the R 2.4.0 statistical software.

Results

Characteristics of patients with COVID-19

The sample included a total of 23 cases and 65 controls. Table 1 includes the main characteristics of both groups. Most patients were men (60%), and mean age was 79 years. Hypertension was the most frequent comorbidity, followed by diabetes mellitus and heart disease. Regarding epidemiological characteristics, we found no significant differences between cases and controls, except in the percentage of institutionalised patients, which was higher among patients with dementia (39.1% vs 3.1%; *P* < .001).

Most patients presented Alzheimer-type dementia (73.9%), which was moderate or severe in most cases (56.5%). Eighteen patients were under treatment with anticholinesterase inhibitors and/or memantine and 9 were receiving antipsychotics.

Regarding COVID-19 characteristics, 16 cases (69.6%) were confirmed by RT-PCR testing and 7 were considered probable cases. A higher percentage of patients than controls had poor prognosis (52.2% vs 24.6%; *P* = .015), or died (43.5% vs 21.5%; *P* = .042). Table 1 shows the treatments administered.

Factors associated with case fatality in patients with COVID-19

Twenty-four of the 88 patients included in the study died: 10 patients with dementia (43.4%) and 14 controls (21.5%).

Table 2 shows the multivariate logistic regression analysis (dependent variable: case fatality) in patients with COVID-19. Arterial hypertension, diabetes mellitus, and dementia were independently associated with case fatality in patients with COVID-19.

Factors associated with case fatality in patients with COVID-19 and dementia

In the bivariate analysis (Table 3), patients with heart disease presented significantly higher case fatality rates (60% vs 15.4%; *P* = .026). Furthermore, patients living in nursing homes showed a trend towards higher case fatality than that recorded in non-institutionalised patients (60% vs 23.1%; *P* = .072). We found no other differences between these groups.

Table 4 shows the multivariate logistic regression analysis (dependent variable: case fatality of COVID-19) in patients with dementia. Heart disease was associated with a twofold increase in the risk of death due to COVID-19 in patients diagnosed with dementia.

Discussion

The prevalence of cardiovascular comorbidities and chronic respiratory disease was considerable in both groups, with no significant differences between patients with primary dementia and controls. Primary dementia probably increases the risk of death, in comparison with individuals without degenerative dementia. A Spanish

Table 1 Characteristics of cases and controls.

Variables	Dementia (n = 23)	Controls (n = 65)	P
Epidemiological			
Age in years, mean (SD)	79.1 (9.7)	78.5 (7.4)	.743
Men, n (%)	14 (60.9)	39 (60.0)	.942
Institutionalised, n (%)	9 (39.1)	2 (3.1)	< .001
Smoking, n (%)	6 (31.6)	18 (29.0)	.832
Hypertension, n (%)	18 (78.3)	52 (80.0)	.859
Diabetes mellitus, n (%)	8 (34.8)	28 (43.1)	.487
Heart disease, n (%)	8 (34.8)	25 (38.5)	.754
Pulmonary disease, n (%)	5 (21.7)	23 (35.4)	.227
Chronic kidney disease, n (%)	6 (26.1)	9 (13.8)	.180
Cancer, n (%)	0 (0.0)	7 (10.8)	.101
Characteristics of dementia, n (%)			
<i>Type of dementia</i>			
Alzheimer disease	17 (73.9)	—	
FTD	1 (4.3)	—	
Lewy body dementia	2 (8.7)	—	
Other	3 (13.0)	—	
<i>Treatment</i>			
Anticholinergics	11 (47.8)		
Memantine	7 (30.4)		
Antipsychotics	9 (39.1)		
Diagnosis of COVID-19, n (%)			
Probable	7 (30.4)	9 (13.8)	.076
Confirmed	16 (69.6)	56 (86.2)	
Clinical characteristics of COVID-19, n (%)			
Hospital admission	20 (87.0)	39 (95.1)	.243
ICU admission	0 (0.0)	2 (4.9)	.304
Poor prognosis	12 (52.2)	16 (24.6)	.015
Death	10 (43.5)	14 (21.5)	.042
Treatment for COVID-19, n (%)			
Azithromycin	6 (27.3)		
Other antibiotic	11 (47.8)		
Lopinavir/ritonavir	1 (4.5)		
Hydroxychloroquine/chloroquine	17 (77.3)		
IL-1 inhibitors	1 (4.5)		
IL-6 inhibitors	1 (4.5)		
Glucocorticoids, n (%)	11 (50.0)		

Statistically significant differences are shown in bold. FTD: frontotemporal dementia; ICU: intensive care unit.

Table 2 Multivariate analysis of case fatality in patients with COVID-19.

Variable	Univariate, OR (95% CI)	Multivariate OR (95% CI) ^a	P
Age (years)	1.04 (0.97–1.10)		
Female sex	1.11 (0.42–2.89)		
Institutionalised	1.98 (0.66–5.92)		
Hypertension	3.93 (1.07–14.41)	4.53 (1.17–13.51)	.028
Diabetes mellitus	2.10 (0.81–5.45)	3.81 (1.21–11.02)	.022
Heart disease	1.00 (0.37–2.63)		
Pulmonary disease	1.82 (0.68–4.85)		
Dementia	2.80 (1.01–7.72)	3.45 (1.14–10.48)	.028

The variables included in the equation were: sex, age, arterial hypertension, diabetes mellitus, and dementia.

^a Naglerke $R^2 = 0.204$.

Table 3 Characteristics of patients with dementia and COVID-19.

Variables	Death, n = 10	Survival, n = 13	P
Epidemiological			
Age in years, mean (SD)	78.3 (11.7)	79.8 (8.4)	.716
Men, n (%)	5 (50.0)	9 (69.2%)	.349
Institutionalised, n (%)	6 (60.0)	3 (23.1)	.072
Smoking, n (%)	3 (37.5)	3 (27.3)	.636
Hypertension, n (%)	8 (80.0)	10 (76.9)	.859
Diabetes mellitus, n (%)	5 (50.0)	3 (23.1)	.179
Heart disease, n (%)	6 (60.0)	2 (15.4)	.026
Pulmonary disease, n (%)	3 (30.0)	2 (15.4)	.400
Chronic kidney disease, n (%)	3 (30.0)	3 (23.1)	.179
Characteristics of dementia, n (%)			
Type of dementia			.384
Alzheimer disease	9 (90.0)	8 (61.5)	
FTD	0 (0.0)	1 (7.7)	
Lewy body dementia	0 (0.0)	2 (145.4)	
Other	0 (0.0)	2 (15.4)	
Treatment			
Anticholinergics	5 (50.0)	6 (46.2)	.855
Memantine	4 (40.0)	3 (23.1)	.382
Antipsychotics	4 (40.0)	5 (38.5)	.940
Diagnosis of COVID-19, n (%)			
Probable	4 (40.0)	3 (23.1)	
Confirmed	6 (60.0)	10 (76.9)	
Clinical characteristics of COVID-19, n (%)			
Hospital admission	9 (90.0)	11 (84.6)	.704
ICU admission	0 (0.0)	0 (0.0)	1.000
Treatment for COVID-19, n (%)			
Azithromycin	6 (66.7)	10 (76.9)	.595
Other antibiotic	4 (40.0)	7 (53.8)	.510
Lopinavir/ritonavir	1 (11.1)	0 (0.0)	.219
Hydroxychloroquine/chloroquine	7 (77.8)	10 (76.9)	.962
IL-1 inhibitors	0 (0.0)	1 (7.7)	.394
IL-6 inhibitors	0 (0.0)	1 (7.7)	.394
Glucocorticoids, n (%)	3 (33.3)	8 (61.5)	.193

Statistically significant differences are shown in bold. FTD: frontotemporal dementia; ICU: intensive care unit.

Table 4 Multivariate analysis of case fatality in patients with dementia and COVID-19.

Variable	Univariate, OR (95% CI)	Multivariate, OR (95% CI) ^a	P
Age (years)	0.98 (0.90–1.07)		
Female sex	2.25 (0.40–12.40)		
Institutionalised	2.353 (0.82–22.46)		
Heart disease	2.11 (1.15–29.00)	2.11 (1.15–29.01)	.036

All variables were included in the equation.

^a Naglerke R² = 0.190.

study showed a population attributable risk of 11.3%; however, epidemiological data on COVID-19-associated mortality rates are limited, and we are yet to determine the effect on vital prognosis of such important variables as the use of certain drugs (eg, antipsychotics), comorbidities, and age.⁸

According to published case series,^{9,12} patients with COVID-19 and presenting such comorbidities as arterial hypertension, heart diseases, diabetes, or history of such respiratory diseases as chronic obstructive pulmonary disease present greater risk of complications and case fatality. Up to 80% of deaths due to COVID-19 are recorded

in patients older than 80 years, with some comorbidity recorded in up to 80% of cases; diabetes presents the greatest effect on mortality.¹²

An Italian study conducted in May 2020 reported a mortality rate of 62.2% (51/82) in patients with primary dementia, with higher rates associated with more severe dementia (83.9% in patients with severe dementia).¹³ These results are similar to our own: we found a COVID-19-associated case fatality rate of 43.4% in patients with dementia; this was significantly higher than the rate in the control group. The case fatality rate was higher in older patients, in those with more severe dementias, and in institutionalised patients. Arterial hypertension, diabetes mellitus, and dementia were independently associated with case fatality in the analysis of all patients with COVID-19. Heart diseases were more prevalent in the group of patients with primary degenerative dementia, and were associated with a statistically significant increase in the mortality rate.

We should be aware of the prevalence of primary dementia in patients older than 80 years, which amounts to 9.4%.⁸ Considering these data, it seems probable that degenerative dementia increases the risk of death in patients with COVID-19, although there is not yet sufficient evidence supporting this hypothesis. Another significant factor is that patients with moderate or severe dementia are not usually admitted to intensive care units, especially during the specific circumstances of this pandemic. This results in higher mortality due to SARS-CoV-2 infection in patients with dementia in general. In our study, no patient from the study group was admitted to the ICU.

Furthermore, patients living in nursing homes in Spain present a high mortality rate. In 2019, there were 5417 centres in Spain, with approximately 271 696 residents. Mortality rates associated with COVID-19 in these centres are alarming: up to 10 719 residents had died as of 16 April, due to the precarious situation of the health-care system and the lack of healthcare resources in many of these residences.¹⁴ Our study shows that case fatality was higher among previously institutionalised patients (66.6% vs 28.5%), although this was not a significant factor for case fatality. One of the main causes for institutionalisation is the onset of moderate or severe dementia. Up to 76% of patients presented some degree of cognitive impairment (probably underdiagnosed in many cases), and a third were diagnosed with dementia, with a mean age of 81.2 (10.2) years.⁶

Mortality due to COVID-19 in nursing homes is not currently well-established, and data provided by Spanish government agencies are not rigorous.

The care provided to patients with dementia during this pandemic should not be neglected. The increased workload due to the pandemic may reduce care and quality of life in this group of patients,¹⁴ especially those living in retirement or nursing homes.¹⁵

It is also important to acknowledge the neuroinvasive potential of SARS-CoV-2, which may impact progression or give rise to neuropathological changes leading to neurodegenerative disease, such as Alzheimer disease; therefore, in the short or medium term we may find ourselves facing a "delayed pandemic."¹⁶

The limitations of our study include the small number of cases, and a possible selection bias, as patients were retrospectively selected from the group of patients who attended the emergency department at our hospital; those who died at another hospital or at a nursing home were not considered. The case fatality rate among institutionalised patients is significantly higher, which may represent an additional confounding factor; therefore, the effect of dementia on the case fatality rate of COVID-19 in this group of patients may be overestimated.

Conclusion

Our study suggests that the case fatality of COVID-19 is significantly higher in patients with primary degenerative dementia than among other patients with similar ages and comorbidities. Several fac-

tors influence this trend: these patients are not usually admitted to intensive care units; they present greater limitations on the use of advanced and aggressive treatments; they present a higher rate of cardiovascular and respiratory comorbidities; and lastly, a significant percentage of this group is institutionalised. Future studies with larger samples of patients with dementia and COVID-19 are needed to confirm our results and to identify other possible risk factors associated with the severity of COVID-19 in patients with dementia.

Funding

This study was funded by the COVID-19 fund from Institute of Health Carlos III, Spain (project no. COV20/00157).

Conflicts of interest

The authors have no conflicts of interest to declare.

References

1. WHO (2020) Coronavirus disease (COVID-19) Pandemic. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>. (accessed 2020 Apr 23).
2. Li Q, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *N Engl J Med*. 2020;382(13):1199–207, <http://dx.doi.org/10.1056/NEJMoa2001316>.
3. Weiss SR, Leibowitz JL. Coronavirus pathogenesis. *Advances in Virus Research*. 2011;81:85–164.
4. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study [published correction appears in *Lancet Respir Med*. *Lancet Respir Med*. 2020;8(5):475–81, [http://dx.doi.org/10.1016/S2213-2600\(20\)30079-5](http://dx.doi.org/10.1016/S2213-2600(20)30079-5).
5. Li YC, Bai WZ, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. *J Med Virol*. 2020;92(6):552–5, <http://dx.doi.org/10.1002/jmv.25728>.
6. Gutiérrez Rodríguez J, Jiménez Muela F, Alonso Collada A, de Santa María Benedit LS. Prevalencia y manejo terapéutico de la demencia en centros residenciales para la tercera edad del Principado de Asturias [Prevalence and therapeutic management of dementia in nursing homes in Asturias (Spain)]. *Rev Esp Geriatr Gerontol*. 2009;44(1):31–3, <http://dx.doi.org/10.1016/j.regg.2008.10.002>.
7. Instituto de salud Carlos III (2020). Ministerio de ciencia en Innovación. Available from: <https://www.isciii.es/QueHacemos/Servicios/VigilanciaSaludPublicaRENAVE/EnfermedadesTransmisibles/Paginas/InformesCOVID-19.aspx>. (accessed 2020 Apr 2).
8. Garre-Olmo J. Epidemiología de la enfermedad de Alzheimer y otras demencias [Epidemiology of Alzheimer's disease and other dementias]. *Rev Neurol*. 2018;66(11):377–86.
9. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention [published online ahead of print, 2020 Feb 24]. *JAMA*. 2020, <http://dx.doi.org/10.1001/jama.2020.2648>.
10. Ministerio de Sanidad CyBS. Información científico-técnica, enfermedad por coronavirus, COVID-19; 2020.

11. Ministerio de Sanidad CyBS. Procedimiento de actuación frente a casos de infección por el nuevo Coronavirus (SARS-CoV-2); 2020.
12. Shahid Z, Kalayanamitra R, McClafferty B, Kepko D, Ramgobin D, Patel R, Aggarwal CS, Vunnam R, Sahu N, Bhatt D, Jones K, Golamari R, Jain R. COVID-19 and Older Adults: What We Know. *J Am Geriatr Soc.* 2020;68(5):926–9, doi: 10.1111/jgs.16472. Epub 2020 Apr 20. PMID: 32255507; PMCID: PMC7262251.
13. Bianchetti A, Rozzini R, Guerini F, et al. Clinical Presentation of COVID19 in Dementia Patients. *J Nutr Health Aging.* 2020;24(6):560–2, <http://dx.doi.org/10.1007/s12603-020-1389-1>.
14. Rada AG. Covid-19: the precarious position of Spain's nursing homes. *BMJ.* 2020;369:m1554, doi: 10.1136/bmj.m1554. Erratum in: *BMJ.* 2020 Apr 21;369:m1586. PMID: 32312710.
15. Wang H, Li T, Barbarino P, Gauthier S, Brodaty H, Molinuevo JL, et al. Dementia care during COVID-19. *Lancet.* 2020;395(10231):1190–1, [http://dx.doi.org/10.1016/S0140-6736\(20\)30755-8](http://dx.doi.org/10.1016/S0140-6736(20)30755-8).
16. Serrano-Castro PJ, Estivill-Torrús G, Cabezudo-García P, Reyes-Bueno JA, Ciano Petersen N, Aguilar-Castillo MJ, et al. Influencia de la infección SARS-CoV-2 sobre enfermedades neurodegenerativas y neuropsiquiátricas: ¿una pandemia demorada? *Neurologia.* 2020;35(4):245–51. English, Spanish. doi: 10.1016/j.nrl.2020.04.002.