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Clinical Microbiology and Infection 27 (2021) 632.e1–632.e5

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Original article

COVID-19 and geographical area of origin

Francesca F. Norman*, Clara Crespillo-Andújar, José Antonio Pérez-Molina, Belén Comeche, Sandra Chamorro, Begoña Monge-Maillo, Santiago Moreno-Guillén, Rogelio López-Vélezon behalf of COVID-19 ID Team†

National Referral Unit for Tropical Diseases, Infectious Diseases Department, Hospital Ramón y Cajal, IRYCIS, Madrid, Spain

ARTICLE INFO

Article history:
Received 11 August 2020
Received in revised form
12 November 2020
Accepted 15 November 2020
Available online 25 November 2020

Editor: L. Leibovici

Keywords:
Coronavirus disease 2019
Immigrant
Severe acute respiratory syndrome coronavirus 2
In-hospital mortality
Pandemic

ABSTRACT

Objectives: To describe and compare the main clinical characteristics and outcome measures in hospitalized patients with confirmed coronavirus disease 2019 (COVID-19) according to geographical area of origin.

Methods: A retrospective analysis of patients hospitalized with confirmed COVID-19 at a referral centre in Madrid, Spain, during March–May 2020 was performed. Recorded variables (age, gender, intensive care unit (ICU) admission, outcome), and geographical area of origin were compared for Europeans and non-Europeans (Latin Americans, Asians and Africans).

Results: In total, 2345 patients with confirmed COVID-19 hospitalized during the study period were included in the study. Of these, 1956 (83.4%) were European and 389 (16.6%) were non-European (of whom over 90%, 354/389, were Latin American). Non-Europeans were significantly younger than Europeans (mean 54 (SD 13.5) versus 70.4 (SD 15.1) years, $p < 0.001$); the majority were male (1420/2345, 60.6%), with no significant differences in gender between Europeans and non-Europeans (1197/1956 (61.2%) male in the European group versus 223/389 (57.3%) male in the non-European group, p 0.15). In-hospital mortality overall was higher in Europeans (443/1956, 22.7%) than in non-Europeans (40/389, 10.3%) ($p < 0.001$), but there were no significant differences when adjusted for age/gender (OR 1.27, 95% CI 0.86–1.88). Non-Europeans were more frequently admitted to ICU (71/389, 18.3%) compared with Europeans (187/1956, 9.6%) ($p < 0.001$) and a difference in ICU admission rate was also found when adjusted for age/gender (OR 1.43, 95% CI 1.03–1.98).

Conclusions: No significant differences in mortality were observed between Europeans and non-Europeans (mainly Latin Americans), but an increase in ICU admission rate was found in non-Europeans. **Francesca F. Norman, Clin Microbiol Infect 2021;27:632.e1–632.e5**

Introduction

The current COVID-19 pandemic—caused by infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)—is having an unprecedented global impact at a human, social and economic level, precipitating escalating efforts by the scientific community to identify the exact pathogenesis of the infection and risk factors associated with morbidity and mortality. Recent studies in the UK and the USA have highlighted a possible association between more severe disease in patients from ethnic minorities, although whether this may be due to individual genetic factors or socio-economic differences remains unclear [1–4]. Most of these studies have included patients from non-Hispanic ethnic backgrounds and data for certain minority groups have been underrepresented. The objective of this study was to describe and compare the main clinical characteristics and outcome measures in hospitalized patients with confirmed COVID-19 according to geographical area of origin.

Materials and methods

A retrospective analysis was performed of all individuals hospitalized with confirmed COVID-19 (positive specific SARS-CoV-2 PCR test) at a large (1000-bed) tertiary referral centre in Madrid,

* Corresponding author: Francesca F. Norman, National Referral Unit for Tropical Diseases, Infectious Diseases Department, Ramón y Cajal University Hospital, IRYCIS, Madrid, Spain.
E-mail address: ffnorman@gmail.com (F.F. Norman).
† Members of COVID-19 ID Team are listed in Appendix A section.

https://doi.org/10.1016/j.cmi.2020.11.011
1198-743X/

Spain, during the period March–May 2020. Cases with a codified confirmed diagnosis of COVID-19 were identified from the hospital's electronic medical records. Recorded variables included age, gender, intensive care unit (ICU) admission, outcome (discharge or death), and country of birth/geographical area of origin. In a preliminary analysis, significant differences in the baseline characteristics of the patients depending on their geographical origin were evaluated. Characteristics for European and non-European patients were compared and analysed by age range. Co-morbidities (hypertension, diabetes mellitus, chronic pulmonary disease, chronic renal disease, cardiac disease, malignancy and immunosuppression) were recorded and analysed for non-European patients. The study was approved by the local Hospital Ethics Committee.

Qualitative variables were expressed as relative and absolute frequencies, and quantitative data were expressed as the mean and standard deviation (SD), and 95% CI were calculated. The χ^2 and Fisher exact tests were used when appropriate for comparison of categorical variables, whereas continuous variables were compared using Student's *t* test (when normally distributed) or the Mann–Whitney *U* test (when data were not normally distributed). Bivariable analysis was used to compare demographic characteristics. The threshold for statistical significance was a two-sided p value < 0.05. Univariable analysis was performed comparing in-hospital mortality and ICU admission between European and non-European individuals, followed by a multivariable analysis adjusted for age and gender.

A logistic regression multivariable model was performed to assess whether there were differences in mortality and ICU admission depending on the origin of patients (Europeans and non-Europeans). The independent variables considered for inclusion in the model were origin of patients, sex and age. The origin of patients was coded as a categorical variable (European 0; non-European 1), sex was included as a categorical variable (female 1; male 0), and age was included as a continuous variable. A bivariable analysis with the two dependent variables (mortality and ICU admission) and the three independent variables (origin of patients, age and sex) was performed followed by a multivariable model with mortality and another with ICU admission. STATA® version 15.1 (StataCorp LP, College Station, TX, USA) was used as statistical software.

Results

In total, 2345 individuals with confirmed COVID-19 hospitalized during the study period (March–May 2020) were included in the study. Of these, 1956 (83.4%) were European and 389 (16.6%) were of non-European origin. In the latter group, 354 (91%) patients were from Latin America (LA) (the majority from Ecuador, 108/354, 30.5%; Peru, 84/354, 23.7%; Colombia, 45/354, 12.7%; Venezuela, 30/354, 8.5%; Bolivia, 27/354, 7.6%), 19 (4.9%) were from Asia (AS) (mainly the Philippines, 6/19, 31.6%; India 3/19, 15.8%) and 16 (4.1%) were from Africa (AFR) (the majority from Morocco, 10/16, 62.5%).

The mean age in the study group was 67.7 years (SD 16), 70.4 years (SD 15.1) for Europeans, 54 years (SD 13.5) for non-Europeans (p < 0.001) (61 years (SD 15.3) for AFR, 52.5 years (SD 15.5) for AS, 53.8 years (SD 13.2) for LA, p < 0.001). The majority of patients were male (1420/2345, 60.6%), with no significant differences in gender between Europeans (1197/1956, 61.2% male) and non-Europeans (223/389, 57.3% male) (p 0.15).

In total, 258/2345 patients (11%) were admitted to ICU; 187/1956 (9.6%) Europeans and 71/389 (18.3%) non-Europeans (p < 0.001) (2/16, 12.5% of AFR patients; 3/19, 15.8% of AS patients; 66/354, 18.6% of LA patients were admitted to ICU; p < 0.001). The mean age for European patients who were admitted to ICU (62.2 years (SD 12.9)) was significantly higher compared with mean age in non-European patients who were admitted to ICU (54.7 years (SD 11.1)) (p < 0.001). Regarding ICU admission, univariable analysis showed ICU admission was more frequent in non-Europeans (OR 2.11, 95% CI 1.56–2.84), and this was also true when adjusted for age and gender (OR 1.43, 95% CI 1.03–1.98).

The in-hospital mortality rate in the study group overall was 20.6% (483/2345), and this was 22.7% (443/1956) in Europeans and 10.3% (40/389) in non-Europeans (p < 0.001) (1/16, 6.3% in AFR; 3/19, 15.8% in AS; 36/354, 10.2% in LA; p < 0.001). The mean age for European patients who died (79.5 years (SD 11)) was significantly higher compared with mean age in non-European patients who died (69.4 years (SD 12.5)) (p < 0.001). No differences were found regarding in-hospital mortality between groups when adjusted for age and gender (OR 1.27, 95% CI 0.86–1.88).

A descriptive analysis comparing ICU admission and in-hospital mortality rate for different age ranges was performed for Europeans and non-Europeans and these data and the main characteristics of hospitalized patients with confirmed COVID-19 according to geographical area of origin are described in Table 1.

Co-morbidities recorded in the non-European group included hypertension (23.9%), diabetes mellitus (13.4%), chronic pulmonary disease (11.8%), immunosuppression (9.2%; 1.3% human immunodeficiency virus-associated, 7.9% non-human immunodeficiency virus-related), cardiovascular disease (8%), chronic renal disease (6.2%) and malignancy (5.1%). When co-morbidities were compared in LA, AFR and AS patients, diabetes and cardiovascular disease were found to be significantly more frequent in the AFR group (p 0.015, p 0.002), and no significant differences were found regarding other co-morbidities.

The main characteristics in hospitalized non-European patients with confirmed COVID-19 according to age range (years) are described in Table 2. The main co-morbidities in hospitalized non-European patients with confirmed COVID-19 according to geographical area of origin are shown in Table 3.

Discussion

The present study analysed differences in adverse clinical outcomes (ICU admission and in-hospital mortality) in hospitalized patients with confirmed COVID-19 according to geographic area of origin, with a large representation of patients of Latin American origin. According to official 2020 statistics, around 9.7% of Madrid's registered population originate from a non-European Union country; hence, this series included data on a large proportion of foreign-born patients [5]. In this study, no significant differences in the in-hospital mortality when adjusted for age and gender were observed when Europeans and non-Europeans were compared. However, an increase in ICU admission rate was found in non-Europeans.

Around 16% of the study cohort were of non-European origin (over 90% of these were Latin American), and were significantly younger than the European patients (mean age 54 years for non-Europeans versus 70.4 years for Europeans), but with no significant differences in gender distribution (a predominance of males was found, as described in other European series, but this occurred both in the European and non-European groups) [6–8]. Other determining factors, such as the inability to maintain home isolation precautions on discharge because of overcrowding, may have prolonged hospital admission in younger foreign-born patients, and could be investigated in further analyses [9,10].

Regarding ICU admission (11% for the total group, which was within the 10%–18% range reported in other European series), this was significantly more frequent in the non-European group compared with the European group (18.3% versus 9.6%, respectively) [6,7,11,12]. This observed difference may have been due to

Table 1
Main characteristics of hospitalized patients with confirmed COVID-19 according to geographical area of origin at a referral centre in Madrid, Spain

Characteristic	Total	European, *n* (%)	Non-European, *n* (%)	p value
Number of participants	2345 (100%)	1956 (83.4%)	389 (16.6%) LA: 354 (91%) AS: 19 (4.9%) AFR:16 (4.1%)	
Age (years), mean (SD)	67.7 (16)	70.4 (15.1)	54 (13.5)	<0.001
Male gender	1420/2345 (60.6%)	1197/1956 (61.2%)	223/389 (57.3%)	0.15
ICU admission	258 (11%)	187 (9.6%)	71 (18.3%) LA: 66/354 (18.6%) AS: 3/19 (15.8%) AFR: 2/16 (12.5%)	<0.001
By age range (years)				
0–20		3/5 (60%)	0/3 (0%)	
21–40		4/69 (5.8%)	9/55 (16.4%)	
41–60		65/438 (14.8%)	42/224 (18.8%)	
61–80		110/845 (13%)	20/94 (21.3%)	
81–100		5/598 (0.8%)	0/13 (0%)	
101–120		0/1 (0%)	0	
In-hospital mortality	483 (20.6%)	443 (22.7%)	40 (10.3%) LA: 36/354 (10.2%) AS: 3/19 (15.8%) AFR: 1/16 (6.3%)	<0.001 (not significant when adjusted for age/gender)
By age range (years):				
0–20		0/5 (0%)	0/3 (0%)	
21–40		3/69 (4.4%)	0/55 (0%)	
41–60		28/438 (6.4%)	12/224 (5.4%)	
61–80		169/845 (20%)	21/94 (22.3%)	
81–100		242/598 (40.5%)	7/13 (53.9%)	
101–120		1/1 (100%)	0	

Abbreviations: AFR, Africa; AS, Asia; COVID-19, coronavirus disease 2019; ICU, intensive care unit; LA, Latin America.

Table 2
Main characteristics in hospitalized non-European patients (n = 389) with confirmed COVID-19 according to age range (years)

Age range (years)	Age (years) mean (SD)	Male gender *n* (%)	Area of origin *n* (%)	ICU admission *n* (%)	In-hospital mortality *n* (%)	Co-morbidity[a] *n* (%)
0–20	18.6 (0.5)	2/3 (66.7)	LA: 3/3 (100)	0	0	1/3 (33)
21–40	34.6 (5.2)	32/55 (58.2)	LA: 50/55 (90.9) AS: 3/55 (5.4) AFR: 2/55 (3.6)	9/55 (16.4)	0	11/55 (20)
41–60	51.4 (5.4)	134/224 (59.8)	LA: 206/224 (92) AS: 11/224 (4.9) AFR: 7/224 (3.1)	42/224 (18.7)	12/224 (5.3)	85/224 (37.9)
61–80	68.3 (5.4)	49/94 (52.1)	LA: 84/94 (89.4) AS: 5/94 (5.3) AFR: 5/94 (5.3)	20/94 (21.2)	21/94 (22.3)	61/94 (64.9)
81–100	87.2 (3.8)	6/13 (46.2)	LA: 11/13 (84.6) AFR: 2/13 (15.4)	0	7/13 (53.8)	12/13 (92.3)

Abbreviations: AFR, Africa; AS, Asia; COVID-19, coronavirus disease 2019; ICU, intensive care unit; LA, Latin America.
[a] Presence of at least one of the following: hypertension, diabetes mellitus, chronic pulmonary disease, chronic renal disease, cardiovascular disease, neoplasia or immunosuppression.

Table 3
Co-morbidities in hospitalized non-European patients (*n* = 389) with confirmed COVID-19 according to geographical area of origin

Co-morbidity	Latin America,*n* (%)	Asia,*n* (%)	Africa,*n* (%)	Total, *n* (%)
Total	354 (91)	19 (4.9)	16 (4.1)	
Diabetes mellitus	44 (12.4)	2 (10.5)	6 (37.5)	52 (13.4)
Hypertension	81 (22.9)	5 (26.3)	7 (43.8)	93 (23.9)
Chronic pulmonary disease	41 (11.6)	2 (10.5)	3 (18.8)	46 (11.8)
Chronic renal disease	20 (5.6)	2 (10.5)	2 (12.5)	24 (6.2)
Cardiovascular disease	25 (7.1)	1 (5.3)	5 (26.3)	31 (8)
Malignancy	19 (5.4)	1 (5.3)	0	20 (5.1)
Immunosuppression	30 (8.5)	3 (15.8)	3 (18.8)	36 (9.2)
HIV-associated	3 (0.8)	1 (5.3)	1 (6.3)	5 (1.3)
Non-HIV-related	27 (7.6)	2 (10.5)	2 (12.5)	31 (7.9)

Abbreviations: COVID-19, coronavirus disease 2019; HIV, human immunodeficiency virus.

the significant differences in age between Europeans and non-Europeans, if more elderly European patients with severe disease were not being considered for ICU admission, especially during the peak of the pandemic (included in the study period) when shortage of resources was observed [11]. In April 2020, ICU bed occupancy reached almost 300% in Madrid as intermediate-care beds and other designated critical-care beds were reconverted for COVID-19 ICU patients, and this collapse of the hospital system could have contributed to the low rates of ICU admission among elderly patients [13]. However, multivariable analysis showed ICU admission was more frequent in non-Europeans when adjusted for age and gender. This possible association should be explored further, and other factors such as co-morbidities should be investigated in detail. When different groups of non-Europeans were examined, Latin American patients had a significantly higher rate of ICU admission (18.6%) compared with African (12.5%) and Asian patients (15.8%), despite African patients being older (mean age 61 years) than Asian and Latin American patients (mean age 52.5 years and 53.8 years, respectively). However, because of the lower number of patients in the African and Asian groups, these results should be confirmed (or refuted) in further studies.

The overall in-hospital mortality rate (20%) was within the reported 15%–28% range for other series in Europe and was significantly higher in Europeans (22.7%) than in non-Europeans (10.3%); however, no significant differences were found between these groups when in-hospital mortality rates were adjusted for age and gender [6,11,12]. A significantly higher mean age was found in European patients who died compared with non-European patients who died, which supports previous findings that advanced age is a risk factor associated with mortality in COVID-19 (rather than geographical area of origin) [11,14]. The increased risk in mortality associated with male gender found in other studies was not observed in this series (in the overall group, nor when analysed in Europeans and non-Europeans separately) [1,12]. When subgroups were considered, in-hospital mortality was significantly higher in Asian patients (15.8%) compared with Latin Americans (10.2%) and Africans (6.3%), despite a mean age of 52.5 years in the Asian group, which was much lower than the cohort's mean age overall. A study examining factors associated with COVID-19 mortality in 17 million patients found both black and south Asian patients were at higher risk of death compared with people of white ethnicity even after adjustment for other factors [1]. However, as for the findings regarding ICU admission, the data in the current series should be interpreted with caution and investigated further with larger populations. Only diabetes and cardiovascular disease were found to be significantly more frequent in African patients, so presence of recorded co-morbidities did not appear to explain the observed higher rate of ICU admission in Latin American patients or the higher in-hospital mortality in Asian patients, despite African patients being older.

Recent studies have focused on the possible association between ethnicity and COVID-19, with a systematic review concluding that further investigation on the role of ethnic background in the evolution of the current pandemic should be prioritized [1,15]. Ethnicity refers to the shared genetic, cultural and social traits, among other factors, of a population group and has been previously found to be a determinant of outcome for other diseases [16,17]. Individuals from minority ethnic backgrounds may be at increased risk of infection from SARS-CoV-2 and adverse outcomes, although this association has not been firmly established, and whether this is mainly related to socio-economic rather than genetic factors and presence of risk co-morbidities remains unclear [1,2,15]. Traditional migrant routes from Latin America to Spain have been long-established, and over 90% of non-Europeans included in the study were of Latin American origin, with the majority having access to publicly funded health care. The absence of an association between mortality and geographical area of origin in this study population may support the important role of negative socio-economic factors as drivers of poor outcome in ethnic minorities with COVID-19 found in other published studies. The increased frequency of ICU admission in non-Europeans (with no demonstrated associated increase in the in-hospital mortality) should be investigated further. Although presence or absence of specific co-morbidities was not directly compared between groups, an increase in co-morbidities in the non-European group admitted to ICU should probably have led to worse outcomes and a higher mortality, which was not observed, suggesting that other determinants, such as genetic factors, may also be playing a role in outcome for these patients.

Limitations of the study include the under-representation of patients from certain geographical areas and the unavailability of data on the exact number of inhabitants from each geographical origin who are currently residing in Madrid (due to the presence of undocumented migrants and large mobile immigrant populations), to reliably calculate hospitalization and attack rates for different groups. Although a large representation of hospitalized patients from Latin America was included, Asian and African patients were under-represented. Possible underlying determinant factors such as differences in immune responses and angiotensin-converting enzyme 2 expression and/or polymorphism should be explored further in other studies [18,19]. Although it was not possible to establish whether patients of African origin truly had lower hospitalization rates, their ICU admission and in-hospital mortality rates were lower than for other non-European patients, despite older age and higher prevalence of some co-morbidities in Africans. A gene cluster on chromosome 3 has been identified as a risk locus for respiratory failure in patients with SARS-CoV-2 infection and is a major genetic risk factor for severe disease and hospitalization [20,21]. This risk has been shown to be associated with a specific genomic segment carried by around 50% of South Asians and 16% of Europeans, but is less frequent in Americans, Africans and East Asians [22].

As mentioned above, the complex association between higher ICU admission rates but no higher associated mortality in non-Europeans needs to be explored further. A more detailed investigation of co-morbidities, including other factors such as obesity (an identified risk factor for COVID-19 and other respiratory infections, such as influenza, and which has a higher prevalence in certain population groups) and genetic studies may help confirm or refute possible associations between geographic area of origin and outcome in COVID-19 [23,24].

Conclusions

No significant differences regarding in-hospital mortality (when adjusted for age and gender) were observed between Europeans and non-Europeans (mainly Latin Americans), although an increased rate of ICU admission in non-Europeans was found. Differences between ethnicity and COVID-19 outcome found in other studies may be the result of a higher burden of adverse socio-economic factors in certain populations. Investigation of genetic and immunological markers in patients of different geographical origin should aid the understanding of determinants of outcome in COVID-19.

Author contributions

FFN designed the study, analysed the data and wrote the paper. CCA provided support with data analysis. All authors contributed to clinical management of patients and reviewed the paper.

Transparency declaration

The authors declare that they have no conflicts of interest.

Support was provided by the Instituto de Salud Carlos III project 'RD16/0027/0020' Red de Enfermedades Tropicales, Subprograma RETICS del Plan Estatal de I+D+I.

Acknowledgements

Technical support was provided by Ms B. Gullón, Infectious Diseases Department and by A. Muriel, Clinical Biostatistics Unit, IRYCIS, Hospital Ramón y Cajal.

Appendix A. COVID-19 ID Team

Pilar Vizcarra, Francesca Norman, Clara Crespillo, José Pérez-Molina, Belén Comeche, Sandra Chamorro, Begoña Monge, Santiago Moreno, Rogelio López-Vélez, Maria Jesús Pérez-Elías, Jesús Fortún, Enrique Navas, Carmen Quereda, Fernando Dronda, Santos Del Campo, Javier Cobo Reinoso, José Luis Casado, Ana Moreno, Pilar Martín-Dávila, José Manuel Hermida, Vicente Pintado, Sergio Serrano-Villar, Matilde Sánchez-Conde, Rosa Escudero, Francesca Gioia, Sabina Herrera, Raquel Ron, Javier Martínez-Sanz, Mario Pons-Guillén, María Jesús Vivancos.

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