Socioeconomic inequalities associated with mortality for COVID-19 in Colombia: a cohort nationwide study

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► Additional material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/jech-2020-216275).

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Received 17 December 2020
Revised 11 February 2021
Accepted 20 February 2021
Published Online First 4 March 2021

ABSTRACT

Background After 8 months of the COVID-19 pandemic, Latin American countries have some of the highest rates in COVID-19 mortality. Despite being one of the most unequal regions of the world, there is a scarce report of the effect of socioeconomic conditions on COVID-19 mortality in their countries. We aimed to identify the effect of some socioeconomic inequality-related factors on COVID-19 mortality in Colombia.

Methods We conducted a survival analysis in a nation-wide retrospective cohort study of confirmed cases of COVID-19 in Colombia from 2 March 2020 to 26 October 2020. We calculated the time to death or recovery for each confirmed case in the cohort. We used an extended multivariable time-dependent Cox regression model to estimate the HR by age groups, sex, ethnicity, type of health insurance, area of residence and socioeconomic strata.

Results There were 1 033 218 confirmed cases and 30 565 deaths for COVID-19 in Colombia between 2 March and 26 October. The risk of dying for COVID-19 among confirmed cases was higher in males (HR 1.68 95% CI 1.64 to 1.72), in people older than 60 years (HR 296.58 95% CI 199.22 to 441.51), in indigenous people (HR 1.20 95% CI 1.08 to 1.33), in people with subsidised health insurance regime (HR 1.89 95% CI 1.83 to 1.96) and in people living in the very low socioeconomic strata (HR 1.44 95% CI 1.24 to 1.68).

Conclusion Our study provides evidence of socioeconomic inequalities in COVID-19 mortality in terms of age groups, sex, ethnicity, type of health insurance regimen and socioeconomic status.

INTRODUCTION

The COVID-19 is the first pandemic caused by a human coronavirus, the SARS-CoV-2. The first cluster of patients with pneumonia of unknown origin was reported in Wuhan, China in January 2020.[1] As of 31 October 2020, there were more than 45.5 million confirmed cases and 1.1 million deaths affecting 188 countries around the world. The region of the Americas is the most affected region accounting for more than 20.3 million confirmed cases and 636 482 deaths.[2]

Recently, it has been declared that the situation due to COVID-19 corresponds to a syndemic since there is a combination between the epidemic due to the infection by SARS-CoV-2 and the epidemic due to chronic non-communicable diseases (NCDs) that interact in a social context of poverty and inequity.[3] There are three crisis affecting economies and societies in the region: the slow economic growth, the environmental emergency and the growing inequality.[4] The combination of these social crises with the endemic of NCDs and the current pandemic are disproportionately affecting the region. Latin America currently holds some of the highest COVID-19 death rates in the world and is facing a humanitarian crisis powered by the long-standing inequality of its countries.[5]

COVID-19 has been recognised by some governments and media as 'the great equaliser' due to its capacity to affect people of different age groups, socioeconomic conditions, or prestige.[6] While this is probably true in terms of the biological risk of infection, it is not the case for the observed risk of COVID-19 infection, severity and mortality. There is evidence of racial and socioeconomic disparities in the USA in terms of the population infected by and dying from COVID-19.[7] However, socioeconomic characteristics are not routinely collected or described in most COVID-19 analyses.[8] Therefore, there is a need for collecting and analysing data on socioeconomic determinants of health to monitor COVID-19 inequities, identify high-risk populations and guide the development of public health interventions within countries.

During the first wave of the pandemic by SARS-CoV-2 infection/COVID-19 in Colombia, South America, the national public health surveillance system early adapted and prepared for this new threat, being able to detect and follow-up the ongoing cases and their demographic and socioeconomic characteristics. To identify the effect of some demographic and socioeconomic inequality-related factors on COVID-19 mortality during the first 8 months of the epidemic in Colombia, we conducted a survival analysis (time to death for COVID-19) using individual data from a nationwide cohort.

METHODS

Study population

Colombia is located in the north corner of South America. According to the National Administrative Department of Statistics (DANE, for its initials in Spanish), the total population is projected by 2020 in 50 372 424 inhabitants.[9] The country is divided into 33 departments and districts which groups 1122 municipalities. Half of the population are women (51.2%), 77.1% of people live in urban areas and 68.2% of Colombians are between 15

► http://dx.doi.org/10.1136/jech-2021-216797

To cite: Cifuentes MP, Rodriguez-Villamizar LA, Rojas-Botero ML, *et al*. *J Epidemiol Community Health* 2021;**75**:610–615.

Table 1 Sociodemographic characteristics of COVID-19 confirmed cases and deaths in Colombia up to and including 26 October 2020

Characteristic	Total confirmed cases alive (N=1 002 653) (n, % for rows)	Total confirmed deaths (N=30 565) (n, % for rows)	Total confirmed cases (N=1 033 218) (n, % for columns)
Sex			
Male	500 820 (96.23)	19 613 (3.77)	520 433 (50.37)
Female	501 833 (97.86)	10 952 (2.14)	512 785 (49.63)
Age groups			
0–5 years	20 892 (99.82)	38 (0.18)	20 930 (2.03)
6–11 years	23 391 (99.95)	12 (0.05)	23 403 (2.27)
12–26 years	203 475 (99.54)	231 (0.11)	203 706 (19.72)
27–45 years	430 375 (99.54)	2000 (0.46)	432 375 (41.85)
46–59 years	193 142 (97.48)	5000 (2.52)	198 142 (19.18)
60 years or more	131 378 (84.95)	23 284 (15.05)	154 662 (14.97)
Ethnicity			
White, mestizo, other	942 712 (97.08)	28 366 (2.92)	971 078 (93.99)
African-Colombian	37 883 (96.38)	1421 (3.62)	39 304 (3.80)
Indigenous	22 011 (96.59)	776 (3.41)	22 787 (2.21)
Gipsy-Roman	34 (94.44)	2 (5.56)	36 (0.00)
Raizal	13 (100.00)	0 (0.00)	13 (0.00)
Area of residence			
Urban	861 071 (96.87)	27 844 (3.13)	888 915 (86.03)
Semirural (village)	44 586 (97.18)	1296 (2.82)	45 882 (4.44)
Sparse rural	25 002 (96.19)	991 (3.81)	25 993 (2.52)
Unknown area	71 994 (99.40)	434 (0.60)	72 428 (7.01)
Type of health insurance regime			
Contributory	646 670 (97.97)	13 415 (2.03)	660 085 (63.89)
Subsidised	146 290 (92.86)	11 250 (7.14)	157 540 (15.25)
Special	16 306 (97.24)	463 (2.76)	16 769 (1.62)
Exception	47 490 (97.44)	1247 (2.56)	48 737 (4.72)
Uninsured	18 447 (97.49)	474 (2.51)	18 921 (1.83)
Unknown or pending insurance	10 115 (97.41)	269 (2.59)	10 384 (1.01)
Non-registered insurance	117 335 (91.15)	3447 (2.85)	120 782 (11.69)
Socioeconomic strata			
1 very low	183 857 (95.51)	8 644 (4.49)	192 501 (18.63)
2 low	366 446 (96.80)	12 113 (3.20)	378 559 (36.64)
3 middle low	200 213 (97.43)	5 276 (2.57)	205 489 (19.89)
4 middle	35 339 (97.47)	918 (2.53)	36 257 (3.51)
5 middle high	11 857 (97.61)	290 (2.39)	12 147 (1.18)
6 high	6126 (96.73)	207 (3.27)	6333 (0.61)
Non-registered strata	198 815 (98.46)	3117 (1.54)	201 932 (19.54)

and 64 years old. The first case of infection for SARS-CoV-2 was confirmed on 6 March in Bogotá.

Study design and data sources

We conducted a survival analysis in a nationwide retrospective cohort study of confirmed cases of COVID-19 in Colombia from 2 March 2020 to 26 October 2020. The nationwide cohort was ensembled using individual data obtained from the national public health surveillance system (SIVIGILA, for their initials in Spanish). The National Institute of Health (INS, for its initials in Spanish) compiles, verifies and adds laboratory data and other criteria for confirm or discard cases and publishes anonymised and deidentified registries as open data (www.ins.gov.co). The first day of symptoms' onset for the first confirmed case was 26 February and there were 245 days elapsed till the end of the follow-up period.

Symptomatic and asymptomatic COVID-19 cases are confirmed in Colombia by using Reverse transcription PCR (RT-PCR). Starting on 23 July 2020, symptomatic cases can be also confirmed by using antigen-based validated tests. Deaths for COVID-19 are notified by healthcare services to SIVIGILA and DANE and then an individual analysis of the cases confirms, discards or keeps as suspected the reports of deaths due to COVID-19.

All procedures performed in this study followed the national and international ethical standards. Informed consent was not required due to the nature of the study and use of anonymised data from publicly available data sources.

Outcome and predictors assessment

The outcome event of interest for the study was COVID-19 death among confirmed cases. For deceased symptomatic cases, we computed the 'time to event' as the difference between the dates of symptoms onset and the date of death. For deceased asymptomatic cases, 'time to event' was calculated as the difference between the date of first medical appointment and the date of death. The follow-up time of symptomatic recovered cases was the difference between the date of symptoms' onset and date of recovering (registered as laboratory or clinical recovery). For asymptomatic recovered cases, the follow-up time was calculated as the difference between the date of the first medical appointment and the registered date of recovery. We defined censored cases as active cases for which no event (death or recovery) was confirmed by the last date of observation (26 October). For symptomatic and asymptomatic censored cases, we used the same calculation of the follow-up time described above taking into account the date of symptoms' onset or the date of the first medical appointment date, respectively (see online supplemental figure S1).

The exposure predictor variables of the model included the following individual demographic and socioeconomic variables that usually leads to health inequalities: age, sex, ethnicity, type of health insurance, area of residence and socioeconomic strata. In Colombia, ethnicity minorities include 'indigenous', 'African-Colombian descent', a special group of 'Raizales' which refers to descendants of the original enslaved Africans and 'Gipsy-Romany'. The type of health insurance is a proxy variable for health access. The 'Contributory' type refers to job-related health insurance, the 'Subsidised' type covers poor people without formal jobs which hold a subsidy paid by the government, the 'Special' health regimen covers few unionised workers, and the 'exception' regimen groups the army-related members. We included six age groups based on the Colombia's primary healthcare model classification for life-course categories: infants (0–5 years), children and school age (6–11 years), adolescents (12–26 years), young adults (27–45 years), adults (46–59 years) and seniors (60 or more years). The socioeconomic strata is a classification based on the stratification of residential properties used by DANE according to the socioeconomic resources of a census block that received public services. This classification divides houses (dwellings) into class levels, which range from one (very low) to six (high) being one the strata with higher

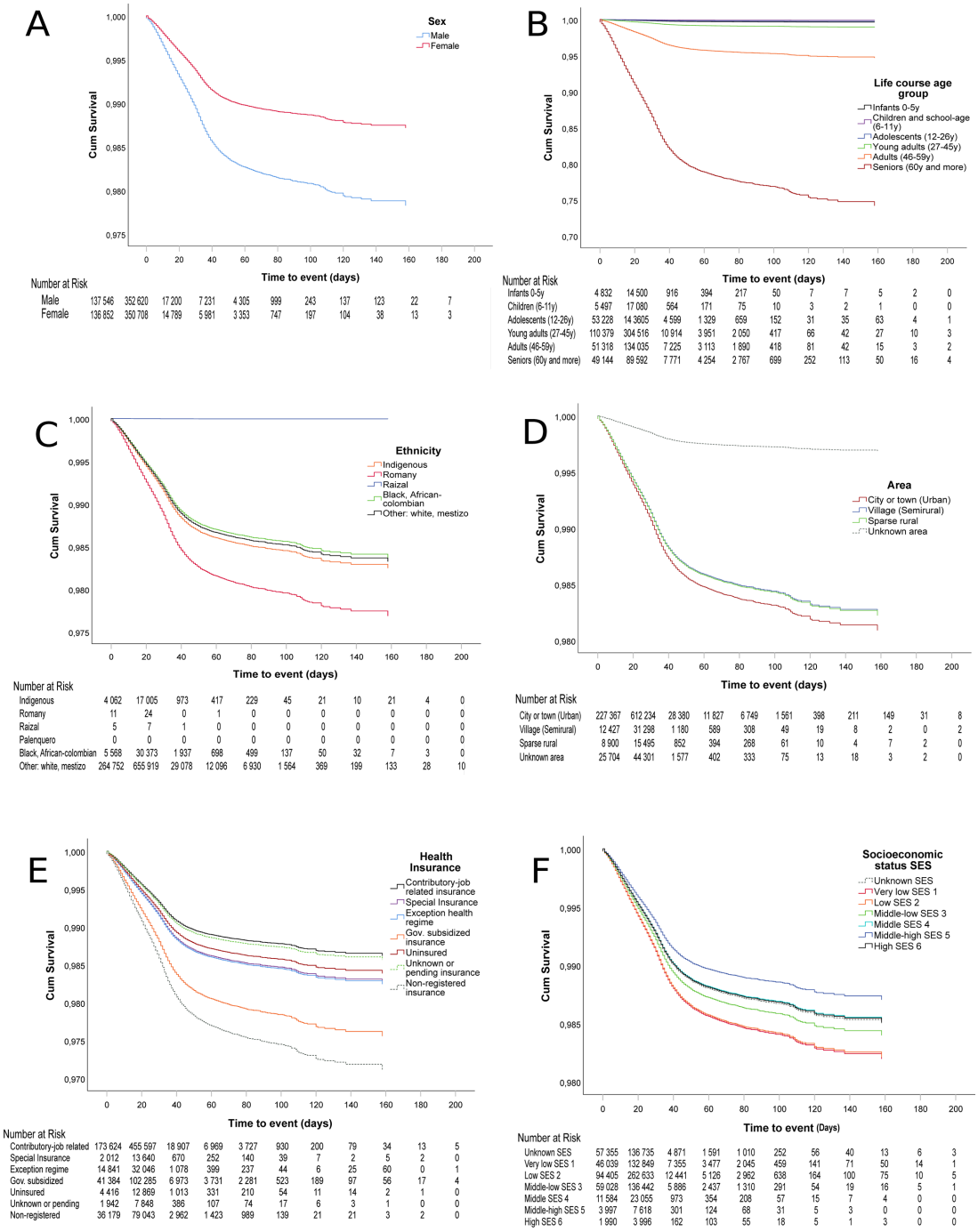

Figure 1 Survival curves for COVID-19 by socioeconomic conditions. (A) sex; (B) age groups; (C) ethnicity; (D) area of residence; (E) health insurance regime; (F) socioeconomic status (SES).

socioeconomic deprivation.[10] The socioeconomic strata is used as a proxy of socioeconomic status (SES) in this study and was obtained as a self-reported variable in SIVIGILA.

Statistical analysis

All confirmed COVID-19 cases were included in the analysis by using the national cohort's time to death and recovery. Exploratory customary descriptions for distributions of continuous time-to-death variable and all categorical predictors, for the different outcomes (dead, recovered and censored) included means, medians, frequencies and percentages. The modelling process included testing of proportional hazards assumption for all the predictors using hypothesis tests (p values of terms addressing time dependent factors) and graphs (Log minus log plots and partial residuals plots from models with no interaction terms). As all predictors but sex were dependent on time, we used an extended multipredictor time-dependent Cox regression model.[11] By using this extended model, it is possible to jointly evaluate the effect of multiple time-dependent variables and their role as potential confounders or effect modifiers. We included simple product interactions between these variables and the time to event to estimate an extended Cox regression model that allows non-proportional hazards. Survival functions were calculated using the Kaplan-Meier method. As our objective

was to obtain an explanatory model, we ran the multipredictor regression models by the Enter method, therefore, the resulting equation included all variables. We assessed the coefficient signs and significance by the Wald statistic, and associations expressed as HRs with 95% CIs. All tests with p<0.05 were considered statistically significant. We performed the statistical analysis using SPSS software V.26.

RESULTS

There were 1 033 218 confirmed cases and 30 565 deaths for COVID-19 in Colombia from the first day of notification, 2 March to 26 October. Table 1 summarises the characteristics of the cohort of COVID-19 confirmed cases. Most confirmed COVID-19 cases were male, between 27 and 45 years old, living in urban areas, with the contributory regime of health insurance, and living in residences that belong to the two lower levels of socioeconomic strata. Seven (0.02%) out of the 30 565 cases that end up in deaths were asymptomatic. From all 914 882 confirmed cases that end up in recovery, 11.2% were asymptomatic. The 12.1% of the 87 874 confirmed cases censored at the end of the follow-up time were asymptomatic (see online supplemental tables S1–S3).

Figure 1 shows the survival functions for each predictor in the model obtained from the multiple Cox Regression without time-dependent factors (see online supplemental table S4 for model details). As the assumption of proportional hazards did not hold for all predictors but sex (see online supplemental figure S2–S12), we fit the multipredictor Cox Regression for time dependent variables including the same predictors. This model was statistically significant (p<0.001). Table 2 presents the results of our final multipredictor time-dependent Cox regression model (see online supplemental tables S5–S6 for details). The instantaneous risk of dying for COVID-19 among confirmed cases is 59% higher in males compared with females, 27% higher in indigenous people compared with whites/mestizos, and 97% higher in people with subsidised health insurance regime compared with contributory. There was evidence of a dose–response pattern by life-course age groups and SES levels. The risk of dying for COVID-19 among confirmed cases for people over 60 years is extremely higher than the risk for infants. The instantaneous risk of death for people with confirmed diagnosis of COVID-19 living in the very low SES increases by 73% compared with the risk of people living in the high SES (HR 1.73 95% CI 1.48 to 2.04). In contrast, living in a sparse rural area decreased the risk of mortality for COVID-19 (HR 0.83 95% CI 0.76 to 0.91). Interactions terms between the time to the death and all the variables in the model were statistically significant (p<0.001).

Table 2 Risks of death for COVID-19 by some socioeconomic conditions in Colombia up to and including 26 October 2020

Socioeconomic condition	HR (95% CI)	P value
Sex (female as reference)	1.59 (1.53 to 1.65)	<0.001
Age groups (0–5 years as reference)		
6–11 years	0.42 (0.22 to 0.81)	0.009
12–26 years	1.16 (0.81 to 1.67)	0.414
27–45 years	5.67 (4.00 to 8.04)	<0.001
46–59 years	33.70 (23.59 to 48.14)	<0.001
60 years or more	214.31 (148.64 to 309.01)	<0.001
Ethnicity (white/mestizo as reference)		
Indigenous	1.27 (1.13 to 1.43)	<0.001
Gipsy-Roman	1.56 (0.39 to 6.25)	0.530
Raizal	0.00 (0.00 to 3.44)	0.913
African-Colombian	1.01 (0.96 to 1.08)	0.613
Area of residence (urban as reference)		
Semirural (village)	0.88 (0.82 to 0.93)	<0.001
Sparse rural	0.83 (0.76 to 0.91)	<0.001
Unknown area	0.14 (0.12 to 0.16)	<0.001
Type of health insurance regime (contributory regime as reference)		
Subsidised	1.97 (1.89 to 2.04)	<0.001
Special	1.29 (1.17 to 1.41)	<0.001
Exception	1.37 (1.29 to 1.45)	<0.001
Uninsured	1.34 (1.21 to 1.48)	<0.001
Unknown or pending insurance	1.22 (1.07 to 1.39)	0.002
Non-registered insurance	2.57 (2.41 to 2.73)	<0.001
Socioeconomic strata (high SES as reference)		
Very low	1.73 (1.48 to 2.04)	<0.001
Low	1.61 (1.38 to 1.87)	<0.001
Middle low	1.34 (1.16 to 1.56)	<0.001
Middle	1.16 (0.99 to 1.36)	0.059
Middle high	0.94 (0.79 to 1.13)	0.531
Unknown	1.54 (1.30 to 1.83)	<0.001

SES, socioeconomic status.

DISCUSSION

Our results provide evidence of socioeconomic and demographic inequalities in COVID-19 mortality in Colombia. In addition to the well documented differential risk of mortality related to older age groups and male sex, this study provides evidence of socioeconomic and ethnicity inequalities in COVID-19 mortality. We identified higher mortality risks for indigenous people, people in the subsidised health regime, and those living in areas classified as very low and low SES. The risks of mortality for age groups and SES levels followed a consistent dose–response pattern.

Our findings of association between COVID-19 mortality and older age (60 years or more) and male sex are consistent with previous reports.[12] The most plausible explanation for this finding is the age-related response to sepsis in older adults with decline in the immune cell function, reduced humoral immune function, and uncontrolled production of inflammatory cytokines.[13] Our study also found an increased risk of death in men which is consistent with previous results.[14] Sex differences in COVID-19 mortality are probably explained by the increased expression in men of the ACE-2, a key factor involved in the pathogenesis of COVID-19.[15]

Ethnicity disparities have been also reported in a variety of contexts. African American and Hispanic in the USA are more vulnerable to COVID-19 mortality than other ethnic groups.[7] In Brazil, after age, Pardo ethnicity was the second most important risk factor for death and probable explanations are differential access to healthcare or susceptibility to COVID-19 infection.[16] Our study found an increased risk of COVID-19 mortality among indigenous people. Leticia, the capital of the Amazonas department with a live frontier with Brazil, holds the highest COVID-19 mortality rate across departments in Colombia. It is estimated that at least 163 indigenous communities have been infected for the SARS-CoV-2 in Latin America. Poor living and sanitary conditions combined with the burden of previous infectious diseases and malnutrition impose a higher risk to the health of individuals and entire communities.[17]

There is evidence of historical socioeconomic inequalities in previous pandemics. During the 1918 Spanish influenza pandemic, there were reports that showed that mortality rates in some countries

of South America was 20 times higher compared with countries in Europe.[18] The case fatality rates across countries early in the current COVID-19 pandemic showed negative correlation with countries' gross domestic product and Human Development Index.[19 20] In the USA, the COVID-19 pandemic is accelerating the health inequities by disproportionately affecting people from the most disadvantaged groups such as immigrants, people with disabilities and people in prisons and jails.[21] Using a population-based and individual level data, there was evidence of increased mortality risk associated with people living in care homes in Stockholm.[22] In Brazil, income and education inequalities were positively associated with COVID-19 incidence and mortality rates.[23 24] Our results showed that living in areas of very low or low SES is associated with higher COVID-19 mortality risk with a consistent dose–response effect pattern. These results are consistent with a previous report of inequalities in mortality by SES levels among COVID-19 confirmed cases in Bogotá.[25] These findings are also consistent with results of a nationwide ecological study that showed increased risk of COVID-19 mortality associated with the municipalities' multidimensional poverty index.[26] Colombia has one of the largest income gaps in Latin America and income inequalities within the country differ widely by geographical region in relation to land property, work market and the effect of violence and armed conflict.[27] These baseline socioeconomic inequalities are translated into higher risk of exposure to and severity of COVID-19 affecting disproportionately to people in lower socioeconomic conditions in Colombia.

Social disruption stress producing pro-inflammatory gene expression has been described as a potential pathological mechanism to explain higher adverse health outcomes in populations with disadvantaged socioeconomic conditions.[28] However, the most possible explanation for the inequalities in COVID-19 mortality are the historical inequalities in terms of living and working conditions, and the unequal access to healthcare services. Inequalities in working conditions might explain an important part of the inequalities of COVID-19 infection and mortality. In our study, people in the subsidised health insurance regime represent people with unstable or informal work, or unemployed people who need subsidy from the government to get access to health services. Thus, the higher mortality risk observed in this group compared with the contributory health regime might be representing the social inequality related to working conditions in Colombia. People in the more disadvantaged working groups have lower-paid work and are more likely to work in key basic services (food, cleaning, delivery or public services) that require them to work in person and commute across the cities.[29] In contrast, people with higher-paid work are more likely to work from home with lower exposure to COVID-19 infection.[30]

Despite having an almost universal health insurance coverage, the Colombian health system is characterised by a strong fragmentation in the provision of healthcare services, an incipient primary healthcare, and differences in quality of healthcare services across regimes.[31] Therefore, differences between contributory and subsidised groups might be explained not only by underlying working conditions but also for chronic inequalities in access to high quality healthcare services. Limited healthcare services are provided in semirural and sparse rural areas. Our findings, however, found a potential protector effect for COVID-19 mortality for people living in those areas compared with people living in urban areas. The direction of this association might be explained by the SARS-CoV-2 transmission dynamics that started in urban areas and reached sparse rural areas later in time, having less exposed and tested people in rural areas during the study period.

The COVID-19 pandemic is occurring in the presence of a NCDs epidemic and within a context of historical inequalities in the social determinants of health, which is recognised as a syndemic.[30] There are complex connections among NCDs, COVID-19 transmission dynamics and living conditions that shape disparities with higher adverse effects for disadvantaged people. People from minority ethnic groups, people living in areas with higher socioeconomic deprivation, generally have a greater number of or more severe or uncontrolled coexisting NCDs.[32] These inequalities in chronic conditions are deepened by the way people live and work which make them also more exposed to COVID-19 infection and mortality. Therefore, there is a need to measure, analyse and report demographic and socioeconomic inequities for identifying groups at higher risk for COVID-19 mortality in order to guide tailored public health interventions in countries.[8]

Our study provides strong evidence of socioeconomic inequalities in COVID-19 mortality in Colombia by using data from a nation-wide cohort of confirmed cases during the first 8 months of the epidemic. However, conclusions should be carefully interpreted considering the limitations of the study. This study relies on data reported to SIVIGILA and it is possible that despite its national coverage, some degree of under-reporting might be present. The probability of under-reporting might be higher in the sparse rural areas (15% of total population), where most disadvantaged people live and therefore under-reporting, if present would have an attenuating effect of the effect measures. In Colombia, there is not a mass COVID-19 testing programme, but testing does occur as part of the surveillance system SIVIGILA and starting in August as part of the PRASS programme (testing, contact tracing, and isolation programme). The SARS-CoV-2 diagnosis relied exclusively on RT-PCR testing during the first 4 months of the epidemic and then the diagnostic capacity was expanded by introducing Antigen tests which allowed to cover diagnosis in areas with limited access to RT-PCR. In addition, during the first months the guidelines for testing were mainly symptoms-based and then additional criteria were added related to risk-of-contact which increase the testing access. Therefore, the probability of being tested changed over the study period in urban and rural areas but occur later in time in rural areas due to the COVID-19 transmission dynamics that started in the

What is already known on this subject

- Literature shows that COVID-19 mortality exhibits socioeconomic and demographic inequities.
- Most reports on socioeconomic disparities in COVID-19 infection and mortality belonged to the USA.
- Despite having some of the highest rates in COVID-19 mortality, there is a scarce report of the effect of socioeconomic conditions on COVID-19 mortality in Latin American countries.

What this study adds

- This is the first nationwide cohort study to examine socioeconomic and demographic disparities in time to COVID-19 mortality in Latin America.
- Being male, older than 60 years old, belonging to the subsidised health insurance regime, being indigenous and living in a residence in a very low or low socioeconomic strata shortened the time to death for COVID-19 among confirmed cases in Colombia.
- There was evidence of a dose–response pattern by age groups and socioeconomic strata.

largest urban areas. On the other hand, the distribution of SIVIGILA confirmed cases in very low and low SES categories is very close to the population's estimation by SES reported by the Census 2018 which suggests a low probability of selection bias related to SES in the analysis. Finally, our results are not controlled for the presence of chronic morbidities in confirmed cases so the effect of specific chronic diseases on COVID-19 mortality was not estimated and socioeconomic variables are not controlled for them.

In conclusion, our study provides evidence of demographic and socioeconomic inequalities in COVID-19 mortality in terms of age groups, sex, ethnicity, type of health insurance regimen and socioeconomic strata. Confirmed COVID-19 cases who are male, over 60 years old, indigenous, holding a government subsidised health insurance, and those living in areas classified in the lower socioeconomic strata have a higher risk of dying faster from COVID-19. Our results provide evidence to help support the prioritisation of public health interventions for COVID-19 prevention and detection in Colombia such as testing, contact tracing and vaccination directed to the more vulnerable groups according to the unequal mortality risks.

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Contributors MPC: methodology design, verification of the underlying data, data analysis, data interpretation, writing-original draft. LAR-V: literature research, data analysis, data interpretation, writing-original draft. MLR-B: verification of the underlying data, data analysis, data interpretation, writing-review and editing. CAA-M: data interpretation, writing-review and editing. JAF-N: conceptualisation, methodology design, data analysis, data interpretation, writing-review and editing.

Funding This study did have a specific funding grant. Study design, data collection, data analysis, data interpretation, and writing the report were conducted as part of the work of the Direction of Epidemiology and Demography of the Ministry of Health and Social Protection of Colombia.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available in a public, open access repository. Data used for the current study are publicly available as open data on the government website https://www.datos.gov.co/Salud-y-Protecci-n-Social/Casos-positivos-de-COVID-19-en-Colombia/gt2j-8ykr/data.

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