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Coronavirus disease 2019 population-based prevalence, risk factors, hospitalization, and fatality rates in southern Brazil

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ABSTRACT

Objectives: To assess population-based prevalence, risk factors, hospitalization, and infection fatality rates (IFR) associated with COVID-19.
Methods: We conducted two household surveys among the non-institutionalized adult population from May 30 to June 17, 2020, in Lajeado, an 84,000-inhabitant industrial city in southern Brazil. Primary outcome was prevalence of SARS-CoV-2 infection. Secondary outcomes were COVID-19-related hospitalizations and deaths occurring up to June 20, 2020. We summarized prevalence rates across surveys with meta-analysis. We assessed age-range IFR and hospitalization rate and regressed these rates over age strata using nonlinear (exponential) coefficients of determination (R^2).
Results: Summarized overall prevalence was 3.40% (95% CI, 2.74–4.18), 34% lower in older adults ≥60 years. Prevalence was 14.3 and 5.4 times higher among household contacts and meat-precessing plant (MPP) workers, respectively. IFR ranged from 0.08% (0.06–0.11) to 4.63% (2.93–7.84) in individuals 20–39 years and ≥60 years, respectively. R^2 for hospitalization rate and IFR over age were 0.98 and 0.93 (both p-values <0.0001), respectively.
Conclusions: This is the first population-based study in Brazil to estimate COVID-19 prevalence, hospitalization, and fatality rates per age stratum. Rates were largely age-dependent. Household contacts and MPP workers are at higher risk of infection. Our findings are valuable for health-policy making and resource allocation to mitigate the pandemic.

Introduction

Brazil, a complex country with 210 million inhabitants, the fifth largest population in the world, has been enduring the novel coronavirus disease 2019 (COVID-19) pandemic since late February. Nationwide, up to mid-July, there were more than 2.1 million confirmed cases, with substantial geographic disparities, 80,000 COVID-19-related deaths, and a case fatality ratio (CFR) of 3.8% (Ministério da Saúde do Brasil, 2020a). Brazilian CFR is in line with other developing nations, such as in countries of Southeast Europe, for which a CFR of 3.6% has been reported (Puca et al., 2020).

Nevertheless, confirmed cases are just a fraction of the symptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-infected individuals who sought medical assistance. Hence, asymptomatic infections and the bulk of mild infections go by undetected, leading to biased hospitalization and death rates (Li et al., 2020). Thus, population-based studies are needed to estimate the true number of infected persons in order to calculate hospitalization and infections fatality rates (IFR) – crucial statistics for policy-making (Pearce et al., 2020). Such studies are also useful to identify potential risk factors for infection (Lipsitch et al., 2015).

Small and mid-size cities are home to 2 billion people globally and are being affected by the COVID-19 pandemic (United Nations, 2018; Piccininni et al., 2020). We investigated the municipality of Lajeado, an industrial city with 84,014 inhabitants in Rio Grande do Sul, the southernmost state of Brazil. The first case of COVID-19 in

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Lajeado was reported on March 20, 2020. By May 30, Lajeado had 1319 confirmed cases, ranking first in case count in the state (Secretaria Estadual da Saúde do Rio Grande do Sul, 2020). Regional economy relies heavily on Lajeado's meat-processing plants (MPP), with >4200 employees. In April, the State Health Department had pinpointed two MPP as sources of COVID-19 outbreaks (Governo do Estado do Rio Grande do Sul and Centro Estadual de Vigilância em Saúde, 2020). Here, we aimed to assess COVID-19 prevalence, hospitalization, and IFR, as well as risk factors, in the general adult population of Lajeado.

Methods

Study design and setting

This is a cross-sectional study comprised of two household surveys designed to assess the prevalence of SARS-CoV-2 infection. Surveys were carried from May 30 to June 4 (Survey 1) and from June 13 to 17 (Survey 2), 2020.

The population of Lajeado is 89% percent white. Its population density is 917 inhabitants/km^2 (Instituto Brasileiro de Geografia e Estatística, 2020). The current adult (≥18 years) population is estimated to be 64,000 individuals.

Participants

The target population was the 64,000 adults residing in Lajeado. The study population was the non-institutionalized adults of the target population.

Inclusion and exclusion criteria

Both surveys followed identical inclusion and exclusion criteria. All the non-institutionalized adults from the target population were deemed eligible. Individuals <18 years were not eligible. Sampled adults were included after signing the informed consent form approved by the Universidade do Vale do Taquari (UNIVATES) institutional Ethics Review Board and by the Brazilian National Committee for Research Ethics on May 27, 2020 (CAAE 32029520.9.0000.5310). If a participant tested positive for SARS-CoV-2 antibodies, all of her/his adult household contacts were included in the study after signing informed consent forms. Participants who refused or withdrew consent were excluded.

Sample size and sampling

For Survey 1, the calculated sample size was 1500 adults assuming an intracluster correlation coefficient (ρ) of 0.034 and a design effect (DEFF) of 2 (Killip, 2004). Other parameters were a target population of 64,000, an expected crude prevalence of 2%, a 1% margin of error with 95% confidence interval, and 52 primary sampling units (PSU). In Survey 1, the actual observed ρ was 0.017 and DEFF was 1.45. This allowed us to use a DEFF of 1.50 for Survey 2 and hence a sample size of 1100 adults. In Survey 2, the observed ρ and DEFF were 0.023 and 1.49, respectively.

We performed separate multi-stage cluster samplings for each survey (Kalton, 1983). In the first stage, we selected 52 census sectors (out of 120) as PSU through simple random sampling (SRS). Next, we selected city blocks (secondary sampling units; SSU) within a census sector using SRS. Field researchers followed a predetermined random sequence of SSU until the target number of participants per PSU was attained. Tertiary sampling units (TSU) were households within a block, selected by the field researchers on site through systematic sampling of one in every three households. Finally, we randomly selected one adult present at the household via SRS. If the sampled adult refused to participate or withdrew consent, the household was excluded and the next available TSU was selected.

Procedures

Lateral flow immunoassay

We tested all participants for specific anti-SARS-CoV-2 antibodies in capillary blood using Wondfo lateral flow immunoassays (LFIA; Guandzhou Wondfo Biotech Co., Ltd, Guanzhou, China). If a sampled participant tested positive for SARS-CoV-2, we tested all adult household contacts with LFIA immediately or on the next day if not present.

Wondfo LFIA detects IgM and IgG class antibodies and the cassette displays the result as a single test band, not discriminating IgM from IgG. Compared to RT-PCR, Wondfo LFIA has a reported near-perfect specificity of 99.57% (Guandzhou Wondfo Biotech, 2020) and, after more than five days since symptoms onset, a sensitivity of 76.24% (Whitman et al., 2020).

Real-time polymerase chain reaction

To detect current active infection, we performed RT-PCR testing in all participants who had two consecutive invalid LFIA, sampled participants who were LFIA-negative and reported fever, anosmia, or dysgeusia with onset on the past seven days, and all LFIA-negative household contacts (deemed as possible false-negatives). Following study protocol, agents of the Municipal Epidemiological Surveillance Authority (MESA) performed nasopharyngeal swabs for RT-PCR the day after the survey visit.

UNIVATES' Clinical Analysis Laboratory carried out all RT-PCR. Two target genes, including open reading frame 1ab (ORF1ab) and nucleocapsid protein (N), were simultaneously amplified and tested during the RT-PCR assay. Target 1 (ORF1ab): forward primer CCCTGTGGGTTTTACACTTAA; reverse primer ACGATTGTGCATCAGCTGA; and the probe 5′-VIC-CCGTCTGCGGTATGTGGAAAGGTTATGG-BHQ1-3'. Target 2 (N): forward primer GGGGAACTTCTCCTGCTAGAAT; reverse primer CAGACATTTTGCTCTCAAGCTG; and the probe 5′-FAM-TTGCTGCTGCTTGACAGATT-TAMRA-3′.

Data collection

Participants were interviewed at home using pretested electronic questionnaires to assess demographics, adherence to social distancing recommendations, and recent-onset influenza-like symptoms. We evaluated age, sex (as in participants' IDs), self-reported skin color, adherence to social distancing recommendations, schooling years, household's average monthly income, and participant's occupation–particularly employment status in any of the local MPP.

We measured adherence to specific social distancing recommendations through five-point Likert-scale questions and global adherence to social distancing both with a five-point Likert-scale and a zero-to-ten-point visual analogue scale (zero = no adherence; ten = perfect adherence). To minimize memory bias, assessment of adherence to social distancing was restricted to the past 30 days. Previous *bacillus* Calmette-Guérin (BCG) vaccination was evaluated by the presence of the unmistakable round scar on participants proximal right arm, the standard injection site in Brazil.

Predictive and confounding variables

Household contacts and MPP workers were explored as risk factors for infection. BCG vaccine was evaluated as a potential protector. Age, sex, income, and schooling were regarded as confounding.

Outcomes

The primary outcome was past or current SARS-CoV-2 infection. We employed only data from probabilistically sampled participants, not from the household contacts, to estimate population prevalence.

We rated participants as positive for infection if any of the following criteria were met: (i) positive LFIA (past infection); (ii) if LFIA-negative, had nasopharyngeal RT-PCR with detectable SARS-CoV-2 particles (current active infection); or (iii) if LFIA-negative, had either a prior immunoassay report or a prior respiratory tract RT-PCR report positive for SARS-CoV-2 (previous documented infection).

Secondary outcomes were COVID-19-related deaths, hospitalizations, and need for intensive care unit (ICU) and invasive mechanical ventilation (IMV). Using official records provided by the MESA, we accounted for all laboratory-proven COVID-19-related hospital admissions and deaths among the Lajeado resident population that took place anywhere in Brazil from March 15 to June 20, 2020. Given the retrospective nature of serological diagnosis and the median time from symptoms onset to death being 11 days in Brazil (Ministério da Saúde and Secretaria de Vigilância em Saúde, 2020b), we considered June 20 to be an adequate end-date for the assessment of lethality. We crosschecked MESA records with the records from Hospital Bruno Born, Lajeado's sole general hospital.

Data analysis

We calculated surveys response rates as the number of participants included in the analyses divided by the number of households approached by field researchers: $\frac{N^{\underline{o}}\ participants\ included}{N^{\underline{o}}\ households\ approached}$.

Using the equation proposed by Diggle and assuming a perfect (100%) specificity, we corrected seroprevalence rates for LFIA sensitivity dividing the crude LFIA-positive rate by 0.7624: $\frac{\frac{N^{\underline{o}} positive LFIA}{N^{\underline{o}} sampled participants tested}}{0.7624}$ (Diggle, 2011). We attained final SARS-CoV-2 infection prevalence by adding the corrected seroprevalence rate to the rate of current active infection and the rate of previous documented infection. We also adjusted infection prevalence for DEFF by attributing weights inversely proportional to participants' selection probability (Zou et al., 2020).

Overall and age-stratified IFR and hospitalization rates were ratios of the number of laboratory-proven COVID-19-related deaths and hospital admissions over the estimated number of SARS-CoV-2 infections overall and per age-stratum: $\frac{N^{\underline{o}} COVID-19-related deaths or admissions}{N^{\underline{o}} infected persons}$. We used Lajeado population

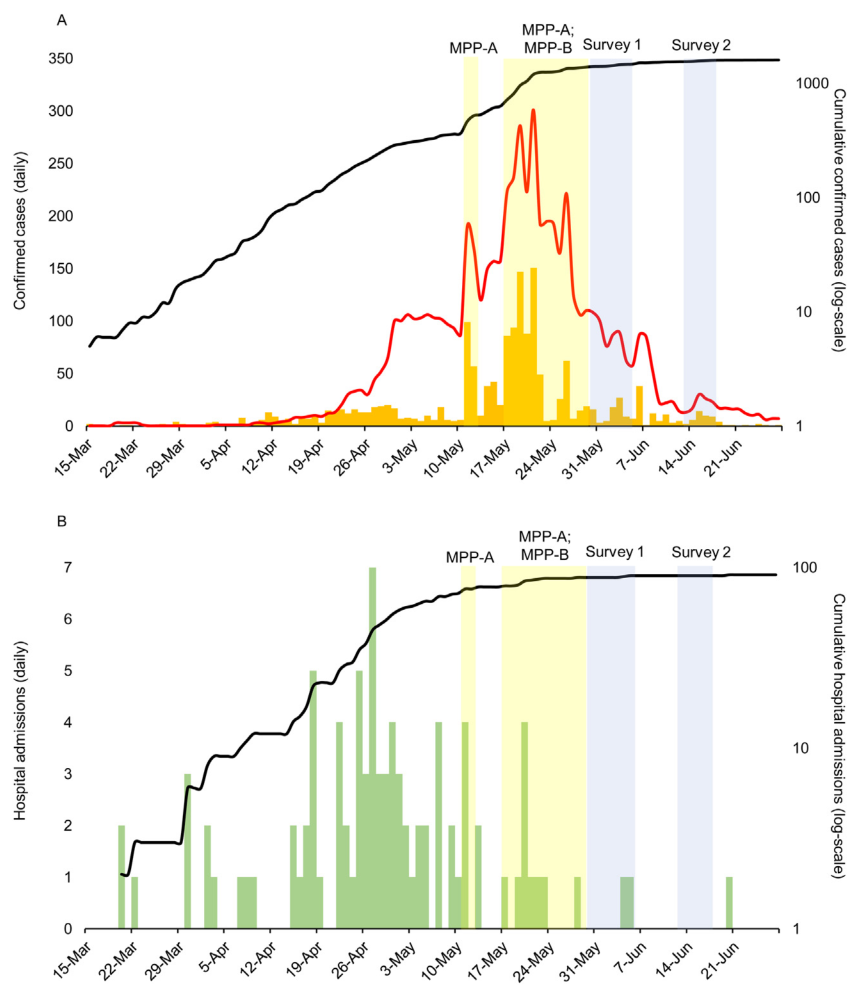


Figure 1. Daily confirmed COVID-19 cases, active cases per day, and cumulative case counts (A), and daily COVID-19 hospital admissions and cumulative hospital admissions counts (B) from March 15 to June 27, 2020.
Black lines are cumulative confirmed case counts (A) and cumulative hospital admissions (B). Yellow columns are daily confirmed cases. Red line is active cases per day. Green columns are daily hospital admissions. Yellow shading shows periods when meat processing plants A and B (MPP-A and MPP-B, respectively) performed mass screening for anti-SARS-CoV-2 antibodies on employees. Blue shading shows periods of data collection of Survey 1 and 2.

pyramid to estimate the number of infections per age stratum (Instituto Brasileiro de Geografia e Estatística, 2020). We aggregated participants into three age groups: 20–39, 40–59, and ≥60 years of age. We regressed IFR and hospitalization rates over age group using nonlinear (exponential) coefficients of determination (R^2) (Kva°Lseth, 1983). The equations for R^2 ($y = ae^{bx}$) are provided.

We performed binary logistic regression, stratified by survey, using MPP workers and household contacts as predictors and SARS-CoV-2 infection status as dependent variable. Models' covariates, selected for their epidemiological relevance, were sex, age, schooling, and household's average monthly income. We converted the predictors' odds ratios into prevalence ratios (PR) using the formula describe by Zhang and Yu (1998).

We summarized overall and age-stratified prevalence rates and PR across surveys with meta-analyses. We chose to pool data with meta-analysis because each survey is a separate study on its own (with independent samples), the overall corrected prevalence of infection was not significantly different between Survey 1 and 2 ($P = 0.051$), and DEFF-adjusted confidence intervals for crude prevalence of infection were very similar to unadjusted intervals. As the target population was the same in both surveys, we used fixed-effect models to summarize the corrected prevalence of infection, assuming that all between-study variance was due to sampling error (Borenstein, 2009).

Proportions, medians, and means were compared using Fisher's exact test, Mann–Whitney's *U* test, and Student's *t*-test, respectively. Two-sided *P* values <0.05 were considered significant. Statistical analyses were performed on SPSS version 18.0. Meta-analyses were performed on SciStat (www.scistat.com).

Results

The peak of daily confirmed cases occurred in early May but was somewhat "artificial" due to mass serological screening performed at MPP. Most detected infections were already cured at the time of mass screening. Daily hospital admissions, daily confirmed cases, and active cases rapidly declined after the end of Survey 1 (Figure 1).

Survey response rates were very high: 84.8% and 88.7% on Survey 1 and 2, respectively. Eighty percent of the households' adults were at home and therefore available for sampling selection.

In both surveys, we selected 2631 individuals, but 54 (2.1%) participants randomly had missing data due to a glitch in the electronic data collection forms. Thus, we included 2577 participants in the final analysis. Standardized mean difference meta-analyses showed that SARS-CoV-2-positive participants were poorer ($p = 0.049$) and less educated ($p < 0.001$). Skin color was not associated with SARS-CoV-2 infection on adjusted logistic regressions (*P*-values of 0.931 and 0.056 in Surveys 1 and 2, respectively). Prevalence of infection was similar between sexes. SARS-CoV-2-positive and negative participants reported similar adherence to social distancing recommendations (Table 1).

Summarized overall prevalence was 3.40% (95% CI, 2.74–4.18). Prevalence was significantly lower in older adults ≥60 years: 2.26 (95%; CI 1.34–3.58) (Figure 2). The total estimated number of infections in the Lajeado adult population was 2178 (95% CI, 1752–2673).

During the study period, there were 79 laboratory-proven COVID-19-related hospitalizations, with 29 patients requiring ICU

Table 1
Samples characteristics by survey and SARS-CoV-2 infection status.

	Survey 1 (n = 1450)			Survey 2 (n = 1127)		
	SARS-CoV-2			SARS-CoV-2		
	Positive	Negative	*P*	Positive	Negative	*P*
SARS-CoV-2-positive crude case count, No. (%)	46 (100)	NA	NA	23 (100)	NA	NA
Lateral flow immunoassay	40 (87.0)	NA	NA	20 (87.0)	NA	NA
RT-PCR	2 (4.3)	NA	NA	1 (4.3)	NA	NA
Previously documented infection	4 (8.7)	NA	NA	2 (8.7)	NA	NA
Active COVID-19 cases[a], No. (%)	5 (10.9)	NA	NA	2 (8.7)	NA	NA
Crude prevalence of infection[b]						
Unadjusted for DEFF, % (95% CI)	3.17 (2.32–4.23)	NA	NA	2.04 (1.29–3.06)	NA	NA
Adjusted for DEFF, % (95% CI)	3.17 (2.22–4.52)	NA	NA	2.04 (1.23–3.35)	NA	NA
Corrected prevalence of infection[c], % (95% CI)	4.03 (3.08–5.18)	NA	NA	2.59 (1.75–3.70)	NA	NA
Resident adults per household, mean (SD)	2.4 (1.0)	2.2 (0.9)	0.170	2.2 (1.0)	2.1 (0.9)	0.610
Resident adults present per household, mean (SD)	1.8 (0.9)	1.6 (0.8)	0.082	1.5 (0.8)	1.7 (0.8)	0.312
Female, No. (%)	28 (63.6)	924 (65.8)	0.749	18 (78.3)	705 (63.9)	0.190
Age, median (IQR)	49.9 (31.1)	49.9 (26.9)	0.376	45.4 (24.8)	49.6 (27.8)	0.365
White skin, No. (%)	32 (69.6)	1150 (81.9)	<0.0001	12 (52.2%)	911 (82.5)	<0.0001
Monthly household income[d], mean (SD)	1285 (1172)	1999 (2217)	0.046	1491 (359)	1949 (1916)	0.301
Schooling years, median (IQR)	8 (6)	11 (8)	0.002	8 (10)	11 (8)	0.329
Meat-processing plant worker, No. (%)	8 (18.2)	53 (3.8)	<0.0001	7 (30.4)	33 (3.0)	<0.0001
BCG vaccinated, No. (%)	34 (77.3)	1193 (85.0)	0.197	19 (90.5)	940 (85.1)	0.756
Social distancing recommendations, median (IQR)						
Global adherence[f]	8 (2)	8 (2)	0.274	8 (3)	8 (2)	0.304
Global adherence[e]	4 (1)	4 (0)	0.185	4 (0)	4 (0)	0.200
Adherence to shelter-in-place[e]	4 (2)	4 (2)	0.273	4 (3)	4 (3)	0.798
Avoidance of social gatherings at home[e]	5 (1)	4 (1)	0.627	4 (1)	4 (1)	0.800
Days per week out of home[e]	3 (6)	2 (4)	0.133	3 (5)	2 (4)	0.185

Abbreviations: IQR, interquartile range; SD, standard deviation; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; RT-PCR, real-time polymerase chain reaction; COVID-19, coronavirus disease 2019; DEFF, design effect; 95% CI, 95% confidence interval; NA, not applicable; BCG, *bacillus* Calmette-Guérin.

[a] Following Brazilian Ministry of Health's most current definition of active COVID-19.
[b] Uncorrected for lateral flow immunoassay sensitivity.
[c] Corrected for lateral flow immunoassay sensitivity of 76.24%.
[d] US dollars corrected by OECD purchasing power parity.
[e] One-to-five Likert scale: 1 = very poor adherence; 5 = very good adherence.
[f] Zero-to-ten visual analogue scale: zero = no adherence; ten = perfect adherence.

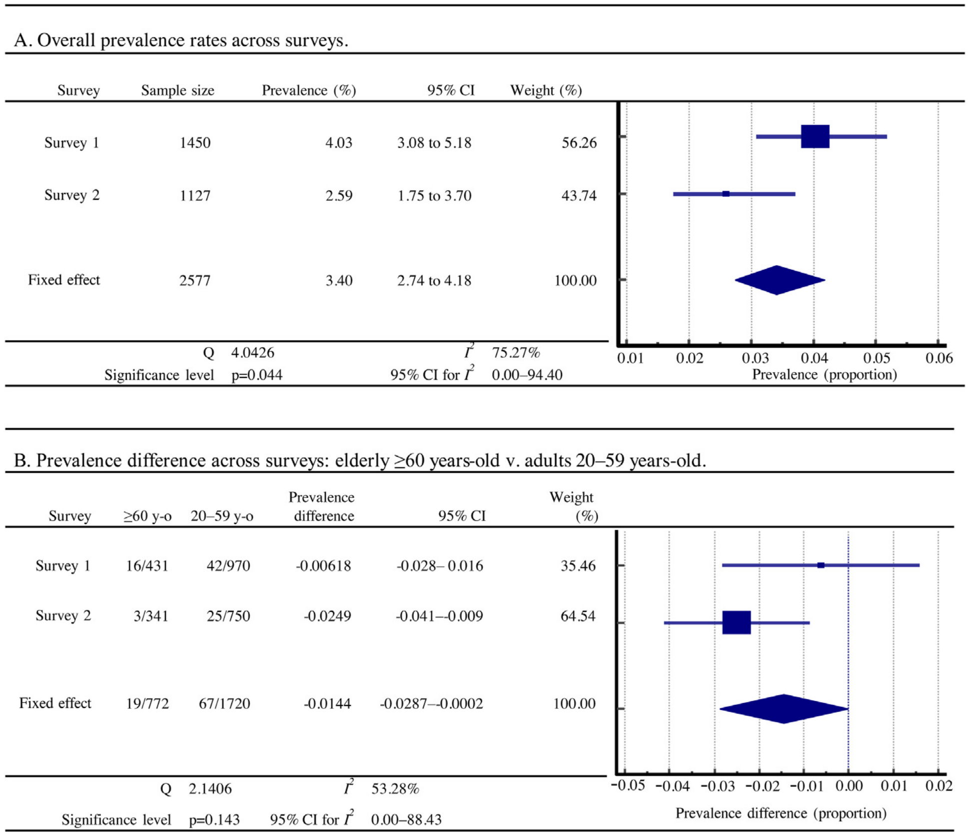


Figure 2. Forest plots of overall corrected prevalence of SARS-CoV-2 infection (A) and corrected prevalence difference between older and younger adults (B).
(A) Overall prevalence rates across surveys.
(B) Prevalence difference across surveys: older adults ≥60 years vs. adults 20–59 years.

beds and 14 needing IMV. There were no hospitalizations or deaths in adults aged 18–19 years. Among the institutionalized population, 12 older adults (ranging 74–90 years of age) living in three different nursing homes were hospitalized, and eight of them died.

Rates per age group are seen in Table 2. Overall IFR, hospitalization rate, and need for ICU and IMV rates were 0.60% (95% CI, 0.49–0.74), 3.63% (95% CI, 2.96–4.51), 1.33% (95% CI, 1.08–1.66), and 0.64% (95% CI, 0.52–0.80), respectively. IFR and morbidity rates were exponentially higher in older adults (Figure 3), with very high R^2 values (Table 2).

Among MPP workers, prevalence of infection was 11.91% (95% CI 6.36–19.78), which was 5.4 times higher than in non-workers (Figure 4A). Until June 26, MESA records showed 1052 confirmed COVID-19 cases and one death (a 37-year-old morbidly obese male) among Lajeado-resident MPP workers, that is, 48.3% (95% CI, 39.4–

Table 2
Population size, estimated number of infections, infection prevalence, hospitalization, and fatality rates in the non-institutionalized general population.

	20–39 years		40–59 years		≥60 years		
	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	R^2; equation for nonlinear (exponential) regression[a]
Population size, No	29,857	NA	22,055	NA	9542	NA	NA
Infections, No	1245	875 to 1712	834	577 to 1164	216	128 to 341	NA
Corrected prevalence, %	4.17	2.93 to 5.73	3.78	2.62 to 5.28	2.26	1.34 to 3.58	NA
Prevalence ratio	Refence	NA	0.91	0.57 to 1.45	0.61	0.35 to 1.05	NA
Hospitalization rate, %	1.69	1.23 to 2.40	3.60	2.58 to 5.20	12.96	8.21 to 21.95	0.9783; $y = 0.0056e^{1.0195x}$
Number of infections per hospitalization, No[b]	59	42 to 81	28	19 to 39	8	5 to 12	NA
Need for ICU, %	0.64	0.47 to 0.91	1.2	0.86 to 1.73	5.09	3.22 to 8.62	0.9499; $y = 0.002e^{1.0349x}$
Number of infections per ICU bed needed, No[b]	156	110 to 213	83	58 to 116	20	12 to 31	NA
Need for IMV, %	0.24	0.18 to 0.34	0.72	0.52 to 1.04	2.31	1.47 to 3.92	0.9996; $y = 0.0008e^{1.1311x}$
Number of infections per IMV needed, No[b]	417	294 to 556	139	96 to 192	43	26 to 68	NA
Infection fatality rate, %	0.08	0.06 to 0.11	0.24	0.17 to 0.35	4.63	2.93 to 7.84	0.9339; $y = 0.00008e^{2.0269x}$
Number of infections per death[b]	1250	909 to 1667	417	286 to 588	22	13 to 34	NA

[a] R^2 *P*-values are all <0.0001; in equations, x is age group, wherein 20–39 y-o = 1, 40–49 y-o = 2, and ≥60 y-o = 3.
[b] Rounded count to the closest integer.

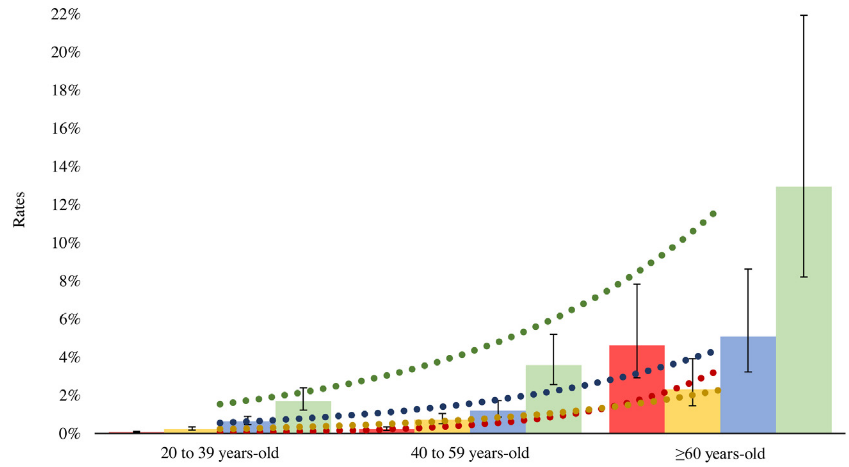
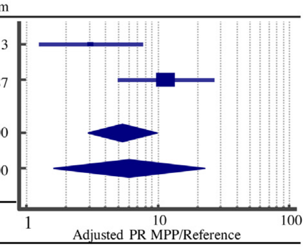


Figure 3. COVID-19 IFR, hospitalization rate, and need for ICU and IMV in the non-institutionalized general population.
Columns are rates. Red columns are infection fatality. Yellow columns are need for IMV. Blue columns are need for ICU. Green columns are hospitalization. Red, green, blue, and yellow doted lines are exponential trends for IFR, hospitalization, ICU, and IMV rates, respectively. Bars are 95% confidence intervals for rates.

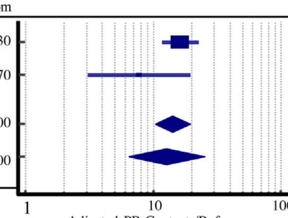
A. Adjusted prevalence ratios for meat processing plant (MPP) workers v. non-MPP workers.

Survey	MPP worker	Reference	Prevalence ratio	95% CI	P	Weight (%) Fixed	Weight (%) Random
Survey 1	4/61	36/1389	3.08	1.24–7.65		46.00	49.13
Survey 2	6/40	16/1087	11.50	4.96–26.68		54.00	50.87
Fixed effect	10/101	52/2476	5.37	2.94–9.82	<0.001	100.00	100.00
Random effects	10/101	52/2476	6.02	1.60–22.68	2.65	0.008	100.00
Q	4.5792	I^2	78.16%				
Significance level	p=0.032	95% CI for I^2	4.85–94.99				



B. Adjusted prevalence ratios for household contacts v. general population.

Survey	Contacts	Reference	Prevalence ratio	95% CI	P	Weight (%) Fixed	Weight (%) Random
Survey 1	30/47	57/1450	16.19	22.62–22.55		88.61	67.30
Survey 2	4/21	29/1127	7.75	3.08–19.54		11.39	32.70
Fixed effect	34/68	86/2577	14.26	10.42–19.52	<0.001	100.00	100.00
Random effects	34/68	86/2577	12.73	6.39–25.33	<0.001	100.00	100.00
Q	1.8543	I^2	46.07%				
Significance level	p=0.173	95% CI for I^2	0.00–0.00				



C. Unadjusted prevalence ratios for BCG vaccinated v. non-vaccinated.

Survey	BCG vaccine	Reference	Prevalence ratio	95% CI	P	Weight (%) Fixed	Weight (%) Random
Survey 1	43/1229	12/221	0.60	0.33–1.11		81.24	66.85
Survey 2	23/961	2/166	1.58	0.45–5.59		18.76	33.15
Fixed effect	66/2190	14/387	0.77	0.45–1.33	0.347	100.00	100.00
Random effects	66/2190	14/387	0.83	0.34–2.04	0.687	100.00	100.00
Q	2.2319	I^2	55.19%				
Significance level	p= 0.135	95% CI for I^2	0.00–89.11				

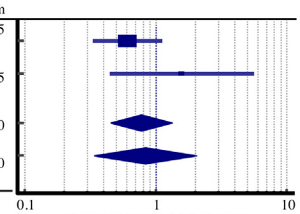


Figure 4. Forest plots of sex-, age-, income-, and schooling-adjusted prevalence ratios for infection.
(A) Adjusted prevalence ratios for meat-processing plant (MPP) workers v. non-MPP workers.
(B) Adjusted prevalence ratios for household contacts vs. general population.
(C) Unadjusted prevalence ratios for BCG vaccinated vs. non-vaccinated.

60.0%) of all estimated infections in the target population. Across surveys, SARS-CoV-2-positive participants had 88 adult household contacts. Sixty-eight (77.3%) contacts were studied and 31 (crude count) were positive for SARS-CoV-2–summarized corrected prevalence 61.33% (95% CI, 48.93–72.74). Three LFIA-negative contacts had detectable SARS-CoV-2 on RT-PCR, and two of them were asymptomatic. Adjusted prevalence among household contacts was 14 times higher than the general population (Figure

4B). Prevalence of infection was similar between BCG vaccinated and unvaccinated participants (Figure 4C).

Discussion

To our knowledge, this is the first study to provide population-based estimates of SARS-CoV-2 IFR and hospitalization rate per age stratum. Another survey from Rio Grande do Sul reported statewide overall IFR of up to 0.38% (95% CI, 0.21–0.80), within range of our overall 0.60% IFR (Silveira et al., 2020). We detected striking age-dependent morbidity and lethality, disfavoring the older adult population. Population-based IFR and hospitalization rate were, respectively, 57.9 and 7.7 times higher in older adults than younger adults. This corroborates the age-dependent severity and lethality of COVID-19 observed in health care settings (Onder et al., 2020; Williamson et al., 2020). Accordingly, nursing homes are a critical issue in the current pandemic as older adults living in long-term care facilities are probably the subpopulation most vulnerable to COVID-19 adverse outcomes (American Geriatrics Society, 2020; Bigelow et al., 2020). In Lajeado, 13% and 38% of all COVID-19-related hospitalizations and deaths, respectively, occurred among older adults living in nursing homes, which is a small segment of the general population. Despite the lower prevalence of infection among older adults, they carry most of the disease burden (American Geriatrics Society, 2020; Stringhini et al., 2020).

In this study, the combination of very high response rates, fully probabilistic selection of participants, relatively large sample size (4% of the entire target population), and high availability of individuals for SRS assured populational representativeness. The majority of prevalence studies to date have had either low response rates (33.7% in Iceland) (Gudbjartsson et al., 2020), did not use fully probabilistic sampling (Geneva and Rio Grande do Sul) (Silveira et al., 2020; Stringhini et al., 2020), or evaluated convenience samples (Los Angeles County and 10 US sites) (Havers et al., 2020; Sood et al., 2020). On the other hand, a large well-designed household survey with fully probabilistically sampling estimated a nationwide seroprevalence of 5.0% in Spain, but with considerable variability across provinces, ranging from 0.5% to 13.0% (Pollán et al., 2020). Similarly, the 3.4% prevalence observed in Lajeado was 15 times higher than the Rio Grande do Sul statewide seroprevalence of 0.22% estimated in early May (Silveira et al., 2020).

In Geneva, the first wave of SARS-CoV-2 epidemic apparently subsided after a 10.8% seroprevalence (Stringhini et al., 2020). We observed an important decrease in new confirmed COVID-19 cases and hospital admissions after the prevalence reached 3.4%. Higher frequency of pre-existing immunity (Grifoni et al., 2020), less transmissible viral strain (Zhang et al., 2020), lower population density (Baker et al., 2020), higher usage of face masks (Chu et al., 2020), earlier depletion of the more susceptible subpopulation, or differences in population age structure (Gomes et al., 2020) are among several plausible explanations for the seemingly more favorable unfolding in Lajeado. The influence of climate in the current pandemic remains incompletely understood, but might have played a role (Baker et al., 2020).

BCG vaccine has been a part of the Brazilian National Immunization Program for many decades (Ministério da Saúde do Brasil, 2020b). The vaccine has been hypothesized as a potential protector against SARS-CoV-2 infection due to its modulatory properties on the immune system (Arts et al., 2018; O'Neill and Netea, 2020). Unfortunately, BCG vaccination was not associated with lower prevalence of infection. Likewise, SARS-CoV-2-positive individuals showed similar adherence to social distancing recommendations in the last 30 days as their negative counterparts. It is possible that infections occurred before the adoption of said measures considering that most SARS-CoV-2-positive participants were asymptomatic in the past 14 days.

This is the first study to estimate the excess risk of infection among MPP workers. In the US and Brazil, MPP have been known sources of COVID-19 outbreaks since mid-April (Dyal et al., 2020; Governo do Estado do Rio Grande do Sul and Centro Estadual de Vigilância em Saúde, 2020). In Lajeado, MPP workers account for almost half of all estimated infections, which lead to the high adjusted PR observed in this subpopulation. This allows two conclusions: (i) MPP were indeed SARS-CoV-2 "hot spots", warranting further etiological investigation; and (ii) infections remained relatively contained among MPP workers and their close contacts at least until early June. The observed difference in prevalence rates would not have been so stark if a more homogeneous viral spread across the general population had occurred. Long working hours involving close proximity to each other, low socioeconomic status, and the sharing of transportation to and from work are some of the plausible explanations for COVID-19 outbreaks involving MPP workers (US Bureau of Labor Statistics, 2020; Dyal et al., 2020).

The prevalence of infection among household contacts was much higher than in randomly selected participants of the general population, reinforcing the known risk associated with domestic contacts (Chan et al., 2020; Guan et al., 2020; Wang et al., 2020). The same was observed in Spain, where prevalence in household members ranged from 15.1% to 37.4% (Pollán et al., 2020). Low prevalence of infection in the general population and high PR associated with household contacts and MPP workers suggest a pattern of transmission highly dependent on prolonged exposure to close contacts, as previously reported (Yong et al., 2020).

Limitations

A third survey could have been undertaken but would not change our prevalence, IFR, and hospitalization rates as new confirmed cases and hospital admissions sharply decreased after Survey 1. Analyzed samples were predominately female. However, SARS-CoV-2 seroprevalence was similar between sexes in other surveys (Pollán et al., 2020; Stringhini et al., 2020); thus, the predominance of women in our sample probably did not bias our results.

Forty percent of asymptomatic individuals may become seronegative eight weeks after infection (Long et al., 2020). Therefore, if delayed, surveys that rely solely on seroprevalence may underestimate the true prevalence of infection due to insensitive measure bias (CEBM University of Oxford, 2019), which is a limitation that this study attempted to circumvent by contemplating previous documented infection. Furthermore, low plasma concentrations of anti-SARS-CoV-2 antibodies (Robbiani et al., 2020) and memory T cells (Sekine et al., 2020) can still provide effective immunity to the host, further limiting the value of belatedly-performed serosurveys. Fortunately, this study was timely considering Lajeado's cumulative case and hospital admission counts.

At the time of study planning, Wondfo's LFIA was the only COVID-19 point-of-care rapid test approved by the Brazilian Sanitary Authority (Ministério da Saúde and Secretaria de Vigilância em Saúde, 2020a). The test's accuracy for detecting asymptomatic and mild infections is unknown as the LFIA was only validated for patients with moderate and severe COVID-19, but this is a limitation of all available serological assays (Deeks et al., 2020; Lisboa Bastos et al., 2020; Whitman et al., 2020). Moreover, seroprevalence is just an approximation of the true prevalence of infection. Thus, to minimize underestimation of prevalence, we ascertained infection status using three endpoints, including RT-PCR and previous documented infection.

We assessed adherence to social distancing solely through questioning. The use of geographic information systems probably would have increased accuracy, but was not considered feasible (Kamel Boulos and Geraghty, 2020).

The decision to not investigate individuals <18 years was grounded on a growing body of evidence indicating that children and adolescents are less susceptible to infection (Munro and Faust, 2020; Pollán et al., 2020; Stringhini et al., 2020). Moreover, persons <20 years comprised <4% of confirmed cases in Lajeado during study planning (Secretaria Municipal de Saúde de Lajeado, 2020).

Conclusions

Despite our efforts, it is possible that the reported prevalence rates are underestimated due to residual insensitive measure bias, which therefore resulted in overestimating hospitalization rates and IFR. Nonetheless, it is clear that older adults are at a substantially higher risk of adverse clinical outcomes and that MPP warrant deeper etiological studies to prevent future outbreaks. Our findings are valuable for health-policy making and resource allocation to mitigate the pandemic in other cities of similar size. Considering the possibility of a future second wave of COVID-19, data presented here can be used for disease modelling.

Author contributions

RVP and IC conceived the study. RVP drafted the first versions of the manuscript. IC, MM, AAS, GL, and GCD contributed to the manuscript. RVP did data analyses. RVP, IC, MM, AAS, GL, and GCD supervised data collection. LFFH, MC, BRG, and LLA participated in study planning, data collection, and supervision. All authors contributed to the interpretation of data and read and approved the final manuscript.

Conflict of interests

The authors declare no competing interests.

Role of the funding source

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