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Journal of Infection and Chemotherapy 29 (2023) 333–338

Contents lists available at ScienceDirect

Journal of Infection and Chemotherapy

journal homepage: www.elsevier.com/locate/jic

Original Article

An epidemiological evaluation of COVID-19 in La paz, Bolivia

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ARTICLE INFO

Keywords:
COVID-19
SARS-CoV-2
Epidemiology
La paz
Bolivia

ABSTRACT

Introduction: The Plurinational State of Bolivia (Bolivia) has experienced four major waves of coronavirus disease 2019 (COVID-19) so far. Although the ministry of health has been tracking morbidity and mortality through each wave, epidemiology of COVID-19 in Bolivia is not well defined, despite a need for more accurate measurement of the number of cases and deaths to allow for forecasting of the pandemic. This study examined prevalence of COVID-19 at community level, determinants of its occurrence and vaccine effectiveness.

Methods: We conducted a cross-sectional study in La Paz city on 2,775 individuals between March 2020 and February 2022. A structured questionnaire was used to collect data on COVID-19 morbidity, mortality and vaccination status.

Results: Of the 2,775 participants, 1,586 (57.1%) were infected with COVID-19, and 187 (6.7%) were suspected cases. The mortality rate was 2.9%. Sinopharm, Johnson & Johnson, Gamaleya, Pfizer-BioNtech, Moderna and AstraZeneka vaccines are in use, and all vaccines have demonstrated effectiveness in reducing the risk of onset. Risk for mortality was significantly lower in the vaccinated group with an odds ratio of 0.037 (95% confidential interval: 0.01–0.10, *p*-value: <0.001).

Conclusions: Actual prevalence of COVID-19 in La Paz (the prevalence rate: 63.8%, including suspected case) was higher than that reported by the Ministry of Health and Sports in Bolivia (7.5%). In addition, vaccination has contributed significantly to the control of the COVID-19 epidemic in Bolivia. We believe that our report will be useful for COVID-19 prevention strategies in Bolivia for the future.

1. Introduction

The novel coronavirus disease 2019 (COVID-19), which originated in Wuhan, China at the end of 2019, has spread worldwide with more than 500 million cumulative infections and 6 million deaths as of June 2022 [1]. The new coronavirus, named SARS-CoV-2, is known to have immune escape properties that it achieves by mutating its spike proteins, and continues to cause pandemics in various areas of the world intermittently even after vaccine introduction [2].

The Plurinational State of Bolivia (Bolivia) has experienced four major waves of infection since the first case of COVID-19 was reported on March 12, 2020 [3]. The first wave occurred in July 2020. It was the most severe, causing a large number of fatalities and resulting in the collapse of healthcare system throughout the country [4]. According to the Ministry of Health and Sports in Bolivia (MoH), more than 900,000 cumulative infections and 20,000 deaths have been reported so far [5]. The burden of COVID-19 in Bolivia is however likely to be higher than portrayed in official reports. There is a potentially large number of

Abbreviations: COVID-19, Coronavirus disease 2019; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; BMI, Body mass index; Bolivia, Plurinational state of Bolivia; MoH, Ministry of health and sports in Bolivia.

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https://doi.org/10.1016/j.jiac.2022.12.009
Received 4 August 2022; Received in revised form 23 November 2022; Accepted 19 December 2022

Available online 25 December 2022
1341-321X/© 2023 Japanese Society of Chemotherapy, Japanese Association for Infectious Diseases, and Japanese Society for Infection Prevention and Control. Published by Elsevier Ltd. All rights reserved.

patients who are asymptomatic carriers and others who cannot be tested for COVID-19 due to economic impediments. Healthcare provision is also limited with, patients unable to receive necessary medical care due to shortage of medical supplies and health care workers, which has been discouraging health-care seeking during the pandemic. Further, health-care seeking among the locals is generally poor. Many Bolivians fail or delay to seek care due to traditional beliefs or negative attitude towards the health care system.

The clinical pathologic features of COVID-19 ranges from mild symptoms such upper respiratory tract inflammation to severe disease complicated with pneumonia and thrombosis, among others [6,7]. In addition, occurrence of asymptomatic carriers has been demonstrated, who are a major factor in transmission of COVID-19 [8,9]. New variants and subvariants are still emerging, causing fresh surges of COVID-19 infections around the world. Monitoring morbidity and mortality as well as vaccine uptake and efficiency is therefore crucial, in order to continuously inform control and prevention measures.

This article reports an epidemiological survey conducted in La Paz, Bolivia with the aim of determining prevalence of COVID-19 at community level, mortality rates and determinants of mortality, and vaccine effectiveness. This is the first report of a well-defined assessment of the actual situation of COVID-19 in Bolivia.

2. Patients and methods

2.1. Study design

We conducted a community-based cross-sectional study in the province of La Paz from January 2022 to February 2022. The study population was persons of all ages drawn from staff of Embassy of Japan in Bolivia and their contacts, individuals from MoH and other international and public organizations including the international airport and police service, and persons attending the city's vocational schools and some main recreational squares in La Paz. Both paper-based and web-based structured questionnaires were used to collect data.

2.2. Data collection

A structured questionnaire was used for collecting data. Each participant provided demographic information including age, sex and Body Mass Index (BMI), smoking history, pregnancy, underlying health conditions, occupation and geographical location of their residence. Participants were also asked to provide a history of COVID-19 infection, including whether they had been infected with COVID-19 since March 2020 to February 2022, test used to confirm COVID-19 infection, contact with a confirmed case and their vaccination history. Information on deceased cases was obtained from participants who reported a death due to COVID-19 within their family. We defined a suspected case as a person with a history of intensive contact with a confirmed COVID-19 case and who had experienced COVID-19-specific symptoms (general fatigue, fever, sore throat, running nose and congestion, cough and anosmia etc), following contact.

2.3. Statistical analysis

Pearson's chi-square or Fisher's exact test was used to compare the categorical variables, and the Student's test was used to compare the continuous variables. Multiple logistic regression analysis was performed to identify factors significantly associated with mortality. Confounders such as BMI≧25, pneumonia, symptoms, vaccination, sex, diabetes, chronic kidney disease, chronic heart failure, age≧50, non-smoking history, malignancy, and hospital admission were included in the multivariate model, and adjusted odds ratios were calculated. Spearman's rank correlation analysis was used to assess multi collinearity. Statistical analyses were performed using SPSS statistics software version 23.0 (IBM Japan, Tokyo, Japan).

2.4. Ethical consideration

This study was approved by the Ethics Committee of Kawasaki Medical University (Okayama, Japan. Approval No: 2020–1818), Hokuto Social Medical Corporation (Hokkaido, Japan. Approval No: 1094) and Nanzan University (Aichi, Japan. Approval No: 21–004). We conducted informed consenting according to the ethical principles of the Declaration of Helsinki.

3. Results

This study recruited 2,775 participants (Fig. 1). Of these, 1,586 (57.1%) were infected with COVID-19 at least once, of whom 876 were confirmed positive by Real-time RT PCR using nasal swab specimens, 604 by rapid nasal antigen test, 224 were clinically diagnosed by a physician and 81 by serum antibody test. Of the 1,189 participants without COVID-19 infection events, 187 (6.7%) were suspected cases. Surges in number of cases were observed from June to August 2020, December 2020 to February 2021, May to August 2021 and December 2021 to February 2022, which coincided with the four waves reported by the MoH (Fig. 2).

Median age of the participants was higher among the infected cases (including suspected cases) (36.3 $\pm$ 13.7) compared to non-infected persons (30.9 $\pm$ 14.6) (Table 1). Slightly more males; 50.4% were infected and only 2.2% of the infected females were pregnant. There were more participants with BMI $\geq$25 and a history of smoking among the cases compared to the non-infected persons. The most common underlying condition among the participants was diabetes mellitus, and there were more infected cases; 3.9% presenting with diabetes mellitus compared to non-infected persons; 2.6%. Most of the infected cases were closed office space workers (26.5%), students (27%) and counter office workers (20.1%). There were more students (36.2%) among non-infected persons compared to infected persons. There were more residents of central area among the infected compared to non-infected persons. About 51 (2.9%) deaths were reported.

Table 2 shows the results of univariate and multivariate analysis of risk factors related to mortality in the infected group. Risk for mortality increased with increasing age, with persons aged 50 years and above having a significantly higher odds of mortality (OR 7.31, 95% CI; 2.97–17.98). Complication of COVID-19 infection with pneumonia yielded a significantly higher risk for mortality with an odds ratio of 29.67 (95% confidential interval [CI]: 13.04–67.45, p-value: $<$0.001), while the mortality risk was significantly lower among vaccinated persons (OR 0.037, 95% CI; 0.01–0.10).

Table 3 shows the efficacy of vaccination in preventing COVID-19 stratified by each vaccine supplier. Only the cases who had received two doses each vaccine except Johnson & Johnson (JJ) and whose events occurred in the month following the second dose were included in vaccine uptake and efficacy analysis. Sinopharm (SP) was the most commonly used vaccine, followed by JJ and Gamaleya (GM) [Fig. 3]. Most of the infected cases; 31.4% had received JJ. Efficacy of vaccination in preventing COVID-19 was stratified by vaccine supplier. Non-vaccinated cases were used as the control group. All vaccines significantly reduced the odds of infection. AstraZeneka (AZ) reduced the odds of infection more than all the other vaccines (OR 0.24, 95% CI; 0.09–0.63). JJ showed the least reduction in odds of infection (OR 0.66, 95% CI; 0.49–0.88).

4. Discussion

Bolivia is a multi-ethnic country located in the center of the South American continent, with an area of 1.1 million square kilometers. It consists of the Altiplano, which is a region of the Andes Mountains at an altitude of about 4,000 m, the Llano which is a tropical Amazon region and the Valle, a middle highland region [10]. It has a population of 12 million. The seat of national government La Paz, is located in the

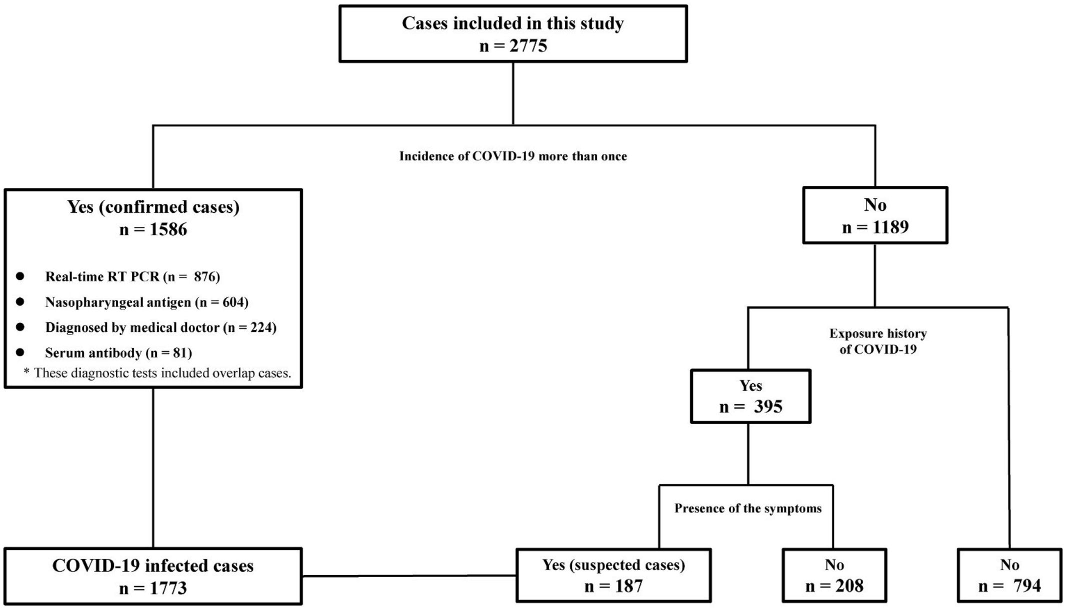

Fig. 1. Flowchart representing the number of cases background in this study.
Total 1,773 cases were included in this study as COVID-19 infected cases.

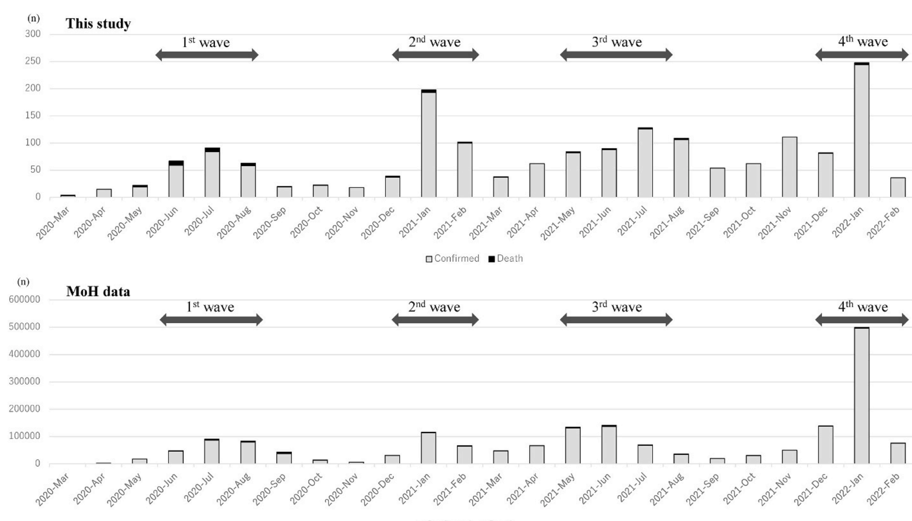

Fig. 2. Comparison of the number of new infected and death cases per month in this study and in the MoH.
The two graphs show similar trends.
MoH: Ministry of Health and Sports in Bolivia.

Altiplano, and its population is approximately 3.05 million [11]. The urban area of the La Paz province is divided into the city of La Paz, where the diplomatic corps and the wealthy reside, and the rest of the province. We conducted the survey in La Paz city center, targeting members of the diplomatic corps, government agencies and public authorities, as well as residents visiting the main square and persons attending vocational schools in the city.

According to official report from MoH as at March 2, 2022, there were 893,330 cumulative positive COVID-19 cases (7.5% of the population) and 21,432 cumulative deaths (2.4%) [5]. Our data shows a higher morbidity rate of 63.9% and a mortality rate of 2.9%. One of the reasons for the discrepancy in morbidity rates is that MoH only considered cases confirmed positive by RT-PCR. Our data shows that more than half of the infected cases were determined using rapid nasal antigen tests or by clinical diagnosis, suggesting potential underestimation in the MoH data. Secondly, Bolivia is a multi-ethnic country, with diverse cultures including indigenous practices that encourage traditional medicine. It is likely that there are a number of cases who did not seek health care upon infection with COVID-19 due to traditional or religious beliefs/beside economic considerations. Moreover, during the first wave, high incidence coupled with limited medical resources overwhelmed the health care system and many patients were unable to receive medical attention, that may not be considered in the cumulative tally [4]. Our data also shows that after the second wave, after which medical resources were secured, there were still 187 (6.7%) cases with a history of contact with COVID-19, who had symptoms but did not receive medical attention or undergo tests, supporting tendency to avoid seeking health care. COVID-19 is also known to have asymptomatic carriers, and it is likely that a significant portion of the 208 cases shown on Fig. 1 were also COVID-19 infected [8,9].

The study observed that there were more persons who were older than 50 years, male, obese (BMI ≥25), with a smoking history, with

Table 1
Characteristics of the cases in this study.

Factor	COVID-19 (%) n = 177	Non-COVID-19 (%) n = 1002	*P* value
Age (median), range	36.3 ± 13.7, 0-95	30.9 ± 14.6, 0-90	<0.001
≥50 years	230 (13.0)	103 (10.3)	0.038
Sex (female)	880 (49.6)	555 (55.4)	0.004
Pregnancy	19/880 (2.2)	20/555 (3.6)	0.101
BMI (≥25)	756 (43.5)	321 (32.5)	<0.001
Smoking history	512 (28.9)	215 (21.5)	<0.001
Underlying disease			
Malignancy	4 (0.2)	4 (0.2)	0.470
Diabetes mellitus	69 (3.9)	26 (2.6)	0.071
Chronic respiratory disease	14 (0.8)	1 (0.1)	0.017
Chronic heart disease	31 (1.7)	15 (1.5)	0.618
Chronic renal disease	6 (0.3)	2 (0.2)	0.719
Occupation			
Healthcare worker	36 (2.0)	14 (1.4)	0.228
Transport	75 (4.2)	43 (4.3)	0.939
Housework	201 (11.3)	137 (13.7)	0.071
Counter office worker	356 (20.1)	153 (15.3)	0.002
Closed space office worker	469 (26.5)	179 (17.9)	<0.001
Student	479 (27.0)	363 (36.2)	<0.001
Living area			
Central	875 (49.4)	414 (41.3)	<0.001

Data are presented as mean ± standard deviation or number (%).
BMI, body mass index.

chronic respiratory disease, and were counter and closed space office workers among the cases compared to the non-infected persons, suggesting higher susceptibility among such persons. Although determinants of COVID-19 infection in various settings around the world have been established, epidemiologic and clinical profile of COVID-19 cases in Bolivia is not well defined [12–14]. This finding therefore provides valuable information for management of COVID in Bolivia and other similar settings.

A mortality rate of 2.9% was observed in this study, which was slightly higher than that reported in the national data. The national data was collected through health facilities, hence only deaths that occurred within the health system were captured. Given the poor health seeking practices characteristic of this population coupled with weak civil registration system, some deaths might have occurred at home, that were possibly not reported and might therefore not be included in the national tally. Mortality rate observed in this study could therefore be a more accurate representation of the actual situation, and suggests greater mortality due to COVID-19 than portrayed in the national data.

Moreover, 78.4% of the cases reported a complication of COVID-19 with pneumonia that has been shown to increase the risk of death among COVID-19 patients [15]. Complication with pneumonia in this study too significantly increased the odds of mortality, implying a greater likelihood of death among COVID-19 cases. Additionally, altitude of La Paz is 3,700 m and its residents are constantly in a state of chronic hypoxemia, that might have further complicated COVID-19 infections [16]. And the study conducted in El Alto city, La Paz, at 4150 m above sea level, showed a higher mortality rate in COVID-19 cases with low erythropoietin and hemoglobin levels [17]. It is therefore likely that COVID-19 infections were severe in this population, with greater tendency of mortality.

Circulating SARS-CoV-2 mutant strain has also been shown to substantially impact mortality rate [5,18]. According to national data, mortality rate from the first to the fourth wave was 6.2%, 2.7%, 2.7% and 0.7% respectively. Molecular analysis of SARS-CoV-2 isolates causing the first and second waves in Bolivia was carried out outside the country but characterization of isolates causing subsequent waves was conducted by Instituto Nacional de Laboratorios de Salud Bolivia. The results showed that the main isolates of each wave were α strain, β strain, γ strain, δ and ο strain BA1 respectively, with lower mortality rates in δ and ο strains, as previously reported [18]. Strain distribution suggests higher mortality at the beginning of the pandemic, some of which might not have been captured in the national tally.

Vaccination in Bolivia began in January 2021 and as of June 2022, approximately half of the population had been vaccinated twice, with a total of 14 million doses administered. SP, JJ and GM were the most commonly used vaccines among participants in this study. High uptake of SP and GM was tentatively because the Bolivian Government

Table 3
Efficacy of vaccination in preventing COVID-19 stratified by vaccine supplier.

Vaccine supplier	All cases	Infected cases (%)	Odds ratio[a]	95% confidence interval	*P* value
Sinopharm	356	96 (27.0)	0.53	0.34–0.66	<0.001
Johnson & Johnson	287	90 (31.4)	0.66	0.49–0.88	0.006
Gamaleya (Sputnik-V)	242	60 (24.8)	0.47	2.11–3.44	<0.001
Pfizer-BioNtech & Moderna	88	22 (25)	0.48	0.29–0.80	0.004
AstraZeneka	35	5 (14.3)	0.24	0.09–0.63	0.002

[a] The odds ratio was calculated using the 512 non-vaccinated cases (included 235 infected cases) as comparators.

Table 2
Risk factors related mortality using logistic regression in the multivariate model in COVID-19 cases.

Risk factor	Univariate			Multiple logistic regression		
	Survived (n = 2724)	Death (n = 51)	p-value	Odds ratio	95% confidence interval	p-value
Age (≥50 years)	302 (11.1%)	31 (60.8%)	<0.001	7.31	2.97–17.98	<0.001
Sex (female)	1413(51.9%)	22(43.1%)	0.216	–	–	
BMI[a] (≥25)	1058(39.6%)	19(37.3%)	0.740	0.35	0.13–0.91	0.031
Smoking history	2016(74.0%)	32(62.7%)	0.070	–	–	
Vaccination	2197(80.7%)	6(11.8%)	<0.001	0.037	0.01–0.10	<0.001
Underlying diseases						
Malignancy	8(0.3%)	0(0.0%)	>0.99	–	–	
Diabetes mellitus	81(3.0%)	14(27.5%)	<0.001	5.37	1.80–16.06	0.003
Chronic respiratory disease	12(0.4%)	3(5.9%)	<0.002	–	–	
Chronic heart disease	41(1.5%)	5(9.8%)	0.001	–	–	
Chronic renal disease	8(0.3%)	0(0.0%)	>0.99	29.67	13.04–67.45	<0.001
Complications after onset						
Hospital admission	154(5.7%)	37(72.5%)	<0.001	–	–	
Specific symptomatic[b]	522(19.2%)	34(66.7%)	<0.001	5.26	2.31–11.96	<0.001
Pneumonia	132(4.8%)	40(78.4%)	<0.001	29.67	13.04–67.45	<0.001

[a] BMI, body mass index.
[b] At least one of the following; general fatigue, fever, sore throat, running nose and congestion, cough and anosmia.

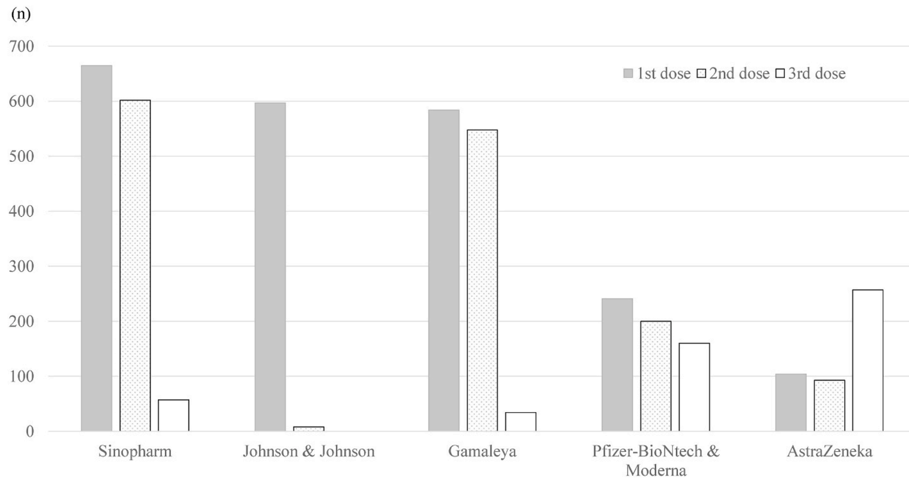

Fig. 3. Number of vaccinated cases per each supplier in this study. Sinopharm is the most commonly inoculated, followed by Johnson & Johnson and Gamaleya.

introduced more SP and GM vaccines from the outset due to its strong relations with China and Russia. Prominence of JJ in this population may be possibly due to its efficacy relative to SP beside its ease in use, being a one-dose vaccine [19]. In vitro neutralization studies have indicated that SP is inferior to the other vaccines in inducing immune response [20], which coincides with our preliminary data that showed a similar outcome when we measured serum SARS-CoV-19 RBD IgG in cases vaccinated with SP (data not shown). However, interestingly SP and GM were still shown to be effective in reducing the risk of infection and mortality in this study. There are several reports about vaccine efficacy from various countries, therefore our study will provide important data to inform decisions on additional vaccination protocols in Bolivia for the future [21,22].

Our study has some limitations that might affect interpretation of its findings. The questionnaire was administered in a wealthy area of La Paz, which may have introduced some bias in the target population. However, the study included a substantial number of local public officers and the public from public squares which lowered bias and increased representativeness of the study. Moreover, the annual morbidity trend of our data is similar to that reported in the MoH data, implying that our data sufficiently reflect the epidemic situation in Bolivia. Further, although the study utilized self-reported data which may have biased the results, the sample size was large enough to minimize bias. Additionally, because the subjects were common people who were not health care professionals, clinical questions could not be administered due to lack of authenticity. Therefore, we were not able to assess the severity of the disease or the effectiveness of the treatment. However, the population in La Paz has been adversely affected by COVID-19 pandemic, making them more willing to actively participate in mitigation measures, which might have encouraged honest responding.

We presented an epidemiological study of COVID-19 in Bolivia in this report. A high morbidity rate was observed in the study population that was higher than the national average, and a mortality rate that was within national average. Vaccine coverage is sub-optimal and herd-immunity is yet to be fully achieved. Human behavior, vaccination and virus evolution are important drivers of the pandemic in this population. The problem is that until now, MoH has simply tabulated the number of cases and vaccinations, but has not analyzed the trends or the effectiveness of the vaccine. The findings of this study provide evidence to support continued surveillance of COVID-19 in this population in order to inform control and management measures. We believe that accumulating and presenting such national data will contribute to improving health welfare and further increasing vaccination coverage in Bolivia.

Authorship statement

Kimito Kondo, Tomonari Nagata, Freddy Armijo Subieta, German Crespo and Hisashi Shoji were responsible for organization and coordination of the study. Ryota Ito, Masayuki Maeda, Yumiko Takehara, Go Diego Komori and Yoshito Nishi coordinated data collection, analysis and interpretation. All authors contributed to the writing of the final manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

The authors thank Betty Muriithi (NUITM-KEMRI Project, Nairobi, Kenya) for her editorial advice during preparation of this article.

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