IJID Regions 2 (2022) 74–81

Contents lists available at ScienceDirect

IJID Regions

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

Burden of COVID-19 and case fatality rate in Pune, India: an analysis of the first and second wave of the pandemic

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ARTICLE INFO

Keywords:
COVID-19
burden
case fatality rate
mortality
pandemic waves
India

ABSTRACT

Objective: To assess trends in case incidence and fatality rate between the first and second waves, we analyzed programmatic COVID-19 data from Pune city, an epicenter of COVID-19 cases in India.

Method: The trends of cases incidence, time-to-death and case fatality rate (CFR) were analyzed. Poisson regression models adjusted for age and gender were used to determine the independent effect of pandemic waves on mortality.

Results: Of 465 192 COVID-19 cases, 162 182 (35%) were reported in the first wave and 4146 (2.5%) deaths, and 275 493 (59%) in the second wave and 3184 (1.1%) deaths ($P<0.01$). The overall CFR was 1.16 per 1000 person-days (PD), which declined from 1.80 per 1000 PD during the first wave to 0.77 per 1000 PD in the second. The risk of death was 1.49 times higher during the first wave (adjusted CFR ratio (aCFRR)1.49; 95% CI: 1.37–1.62) and 35% lower in the second wave (aCFRR 0.65; 95% CI: 0.59–0.70).

Conclusion: The burden of COVID-19 cases and deaths was more significant in the second wave; however, the CFR declined as the pandemic progressed. Nevertheless, investigating new therapies and implementing mass vaccination against COVID-19 are urgently needed.

Key points

Question: What is the epidemiology of COVID-19 through the first and second waves in Pune city, one of the epicenters of India's COVID-19 cases?

Findings: The trend of COVID-19 cases in Pune city followed a pattern similar to India's pandemic. The burden of COVID-19 cases and deaths was more significant in the second wave in Pune, India; however, overall, the case fatality rate was 1.16 and declined as the pandemic progressed from the first wave to the second wave.

Meaning: The absolute case and mortality burden of the COVID-19 pandemic, particularly in India's second wave, underscores the urgent need to devise strategies to better manage disease outbreaks in resource-limited settings.

Introduction

Global COVID-19 cases exceeded 171 million as of 31 May 2021, leading to the loss of more than 3.69 million human lives (Dong et al., 2020). Data to date suggest that older men and those with comorbidities are at higher risk for poor clinical outcomes, including mortality, during and after acute SARS-CoV-2 infection (Mesas AE. et al., 2020). India shares approximately 16% of the reported global burden of COVID-19 cases and ranks second in the total cumulative COVID-19 cases. The first wave of the COVID-19 pandemic commenced with increased detection of cases in January–March 2020; after the September 2020 peak, cases declined by the end of October 2020. We have previously reported that the national lockdown in India delayed the peak of the first wave of the pandemic by approximately 8 weeks (Mave et al., 2021). Subsequently, a low COVID-19 incidence period occurred between November 2020 and mid-February 2021. However, the recent second wave in India in April–May 2021 placed an unprecedented burden on Indian health sys-

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https://doi.org/10.1016/j.ijregi.2021.12.006
Received 7 October 2021; Received in revised form 8 December 2021; Accepted 14 December 2021

tems, with 47% of single-day case incidence in the world during its peak (Ministry of Health and Family Welfare, 2021). Limited data exist on the epidemiology of the progression of the COVID-19 pandemic from the first wave through to the second wave in India.

With 334 608 COVID-19 related deaths to date, India ranks third globally in the total number of deaths (Dong et al., 2020). Interestingly, the observed case fatality ratio at 1.2% is the lowest among the top 20 highest-burden countries (Mortality Analysis, Johns Hopkins Coronavirus Resource Center, 2021). In general, the lower COVID-19 case fatality ratio reported in India can be attributed to the younger demographic profile of the population compared with other high-income countries (Samaddar et al., 2020). However, the explanation may be far more complex given the data collection and reporting structures, prevalence of comorbid diseases, testing strategy, sex differences and attribution of deaths to COVID-19 infections (Price-Haywood et al., 2020, and Samaddar et al., 2020). While emerging evidence from western countries supported the use of glucocorticoids, antivirals, monoclonal antibodies and optimal critical care illness management of COVID-19 (Goldman et al., 2020, Horby et al., 2021, and Tomazini et al., 2020), limited data exist on its impact in resource-limited countries at a programmatic level. As Pune city in India has a system of reporting detailed mortality data, we sought to describe an epidemiological analysis of COVID-19 burden and mortality data comparing the first and second wave in this city, one of the epicenters of India's COVID-19 cases.

Methods

Between 1 March 2020 and 31 May 2021, we conducted a retrospective analysis of COVID-19 mortality data from Pune city, India. As part of the COVID-19 surveillance program, the public and private hospitals under the jurisdiction of Pune Municipal Corporation in Pune city, India, shared daily reports of COVID-19 incident cases and related deaths with Pune Municipal Corporation. The data included age, sex and date of diagnosis for all incident cases. For those who died, the date of death was available. Aggregate daily data on the number of SARS-CoV-2 tests, new diagnoses, active cases and critical care cases were compiled at the city level. The individual hospital-level data on deaths were collected centrally, and the cause of death remarks was curated to elicit the comorbidities from the remarks. The details of programmatic management of the pandemic in India, including lockdowns during the early phases, have been described elsewhere (Laxminarayan et al., 2020, and Mave et al., 2021).

In brief, a nationwide lockdown was implemented between 25 March and 31 May 2020, and a regional lockdown of 2 weeks was implemented in the Pune region in July 2020. During the second pandemic wave, a regional lockdown in Maharashtra state, including Pune, was implemented in April–May 2021. In the early phases of the first wave, COVID-19 testing was available only for symptomatic close contacts of laboratory-confirmed cases and international travelers with a history of travel to COVID-19 affected countries who developed respiratory symptoms (Testing strategy for COVID-19 testing in India, 2020). However, in the last week of March 2020, testing expanded to symptomatic healthcare workers, all hospitalized patients with severe acute respiratory illness and the asymptomatic direct and high-risk contacts of confirmed cases (ICMR strategy for COVID Testing in India, 2020). Subsequently, the Indian Council of Medical Research devised a strategy to increase accessibility and availability of testing by engaging with government and private laboratories to add the optimum number of testing centers in the country (Revised ICMR strategy for COVID Testing in India, 2020). Rapid antigen testing was added to the testing strategy in April 2020 to test the symptomatic in hotspot areas (Advisory to start rapid antibody based blood test for COVID-19, 2020). In the later months of the pandemic, rapid antigen tests and reverse transcription-polymerase chain reaction (RT-PCR) were suggested to test all individuals residing in the containment zones as part of community surveillance. During the second wave, RT-PCR was advised for all symptomatic testing negative on rapid antigen test.

Home isolation for mild/pre-symptomatic patients was permitted starting 27 April 2020; hospitalization was only recommended to those with moderate and severe COVID-19 illness. Moderate disease was defined as the presence of breathlessness, respiratory rate of ≥24/min or oxygen saturation of <93% on room air; severe disease was defined as the presence of breathlessness, respiratory rate of >30/min or oxygen saturation of <90% on room air. The local authorities compiled the mandated data on testing and death outcomes among cases from individual facility level-testing centers, laboratories, hospitals and care centers and shared these nationally.

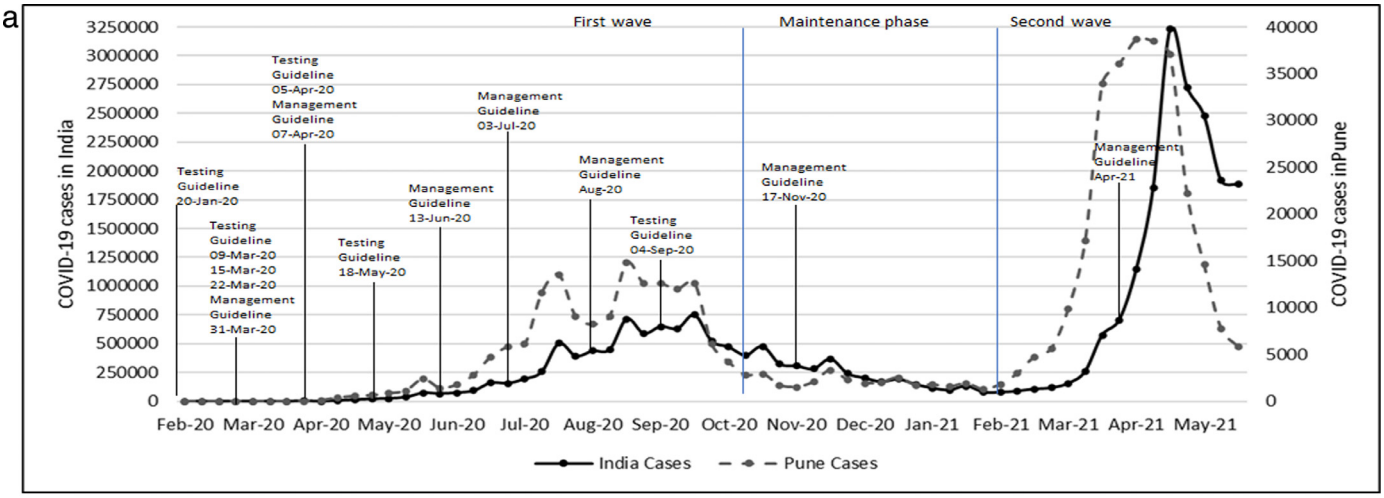
COVID-19 management

The Ministry of Health and Family Welfare (MoHFW) issued guidelines on clinical management of COVID-19 starting 17 March 2020 and subsequently revised them based on the available evidence (Ministry of Family Health and Welfare Resources on COVID-19, 2020). Initially, the treatment strategies were primarily based on early supportive therapy with supplemental oxygen, empirical antimicrobials and management of acute respiratory distress syndrome with non-invasive mechanical ventilation or invasive mechanical ventilation, if required. Glucocorticoids were also recommended for a short period (3–5 days) in deteriorating patients. Hydroxychloroquine was repurposed and indicated as an off-label treatment for COVID combined with azithromycin among patients with severe illness requiring intensive care unit admissions. In subsequent months, treatment strategies evolved, and the indicated use of hydroxychloroquine shifted from severe to milder cases or at-risk populations such as healthcare workers. On 13 and 27 June, MoHFW revised guidelines and recommended a 0.1–0.2 mg/kg dose of dexamethasone or its equivalent glucocorticoid among patients with increasing oxygen requirements. In addition, multiple investigational therapies were advised as ad-hoc, including remdesivir (an antiviral agent), convalescent plasma therapy, and tocilizumab (an anti-interleukin-6 monoclonal antibody) as off label treatment for COVID-19 for moderate disease.

Statistical analysis

For this analysis, we divided the COVID-19 pandemic into 3 phases based on the trend of incident cases and test positivity rates in Pune: the first phase representing the first wave of the pandemic from 9 March to 31 October 2020; followed by the maintenance phase from 1 November 2020 to 15 February 2021, a period when case detection decreased to a level when it became steady (test positivity below 10%) until it rose again; and the last phase, starting 16 February 2021, which represents the second wave currently ongoing in the country. Our analysis was censored for 31 May 2021, for incident cases (Supplementary Table 1). Characteristics of COVID-19 cases in the first wave, maintenance phase and second wave were summarized using frequencies and compared with a chi-squared test. The overall case burden for India abstracted from publicly available data was plotted over the study period. The test positivity rates were derived and plotted from the aggregated daily public reports. The case fatality ratio was measured by dividing the total deaths by total diagnosed cases. The ratio of critical care cases to daily active cases was plotted. COVID-19 deaths were censored for 7 June 2021. The case fatality rate (CFR) overall and for age groups, sex and the 3 pandemic phases were calculated as the total number of deaths divided by total cases diagnosed per 1000 person-days (PD). Cumulative time to death was estimated using the Kaplan-Meier product-limit estimator and compared within the risk groups using a log-rank test. Univariable and multivariable Poisson regression was used to assess the effects of sex, age categories and the 3 pandemic phases on mortality for the overall pandemic and stratified by the 3 pandemic phases. Furthermore, we compared the CFR before and after the national guidelines for intravenous steroids and their impact on mortality

a



Sr No.	Dates	Guidelines for COViD-19 Testing
1	20-Jan-20	Guidelines for specimen collection, packaging and transportation for COVID-19
2	09-Mar-20	Testing for only symptomatic close contact of confirmed cases or symptomatic international travelers with history of visit to high risk COCID-19 affected country
3	15-Mar-20	Added all symptomatic with SARI, symptomatic healthcare workers, asymptomatic close contacts of confirmed cases
4	22-Mar-20	Guidelines for Private labs
5	05-Apr-20	Strategy for use of Rapid Testing
6	18-May-20	Added testing for frontline workers, hospitalised patients with ILI (fever >38C and cough)
7	04-Sep-20	Routine surveillance in containment area and algorithm for RAT & RT PCR

Sr No.	Dates	Guidelines for COVID-19 Management
1	31-Mar-20	Early supportive therapy, empirical antimicrobials, supplemental oxygen, Oral glucocorticoid, HCQ in severe cases
2	07-Apr-20	Triaging of cases
3	13-Jun-20	HCQs for mild/moderate cases, Investigational therapies - Remdesevir, Convalescent plasma, Tocilizumab (off label)
4	03-Jul-20	Use of Remdesevir and CPT for moderate cases and Tocilizumab in severe cases
5	Aug-20	Management of comorbidities - Diabetes
6	17-Nov-20	Discouraged use of CPT
7	Apr-21	Specific instructions for use of Remdesivir & Tocilizumab. Inj Methylprednisolone as a main therapy for moderate/severe cases.

Figure 1a. The trajectory of weekly incident COVID-19 cases in India and Pune Municipal Corporation from 30 January 2020 to 31 May 2021. The weekly cases in Pune city are shown on the secondary axis.

Table 1
Characteristics of COVID-19 incident cases and deaths in the first wave, maintenance phase, and second wave in Pune, India.

Characteristics	Total Cases		First Wave		Maintenance phase		Second Wave	
	Cases n (%)	Deaths n (%)	Cases n (%)	Deaths n (%)	Cases n (%)	Deaths n (%)	Cases n (%)	Deaths n (%)
Overall	465192	7920 (2)	162182 (35)	4146 (3)	27517 (6)	590 (2)	275493 (59)	3184 (1)
Median Age, IQR	38 (28 – 52)	65 (54 – 73)	38 (27 – 52)	65 (55 – 73)	41 (30 – 55)	66 (55 – 75)	38 (28 – 52)	64 (52 – 73)
Age categories								
0 – 17	43859 (9)	37 (0)	17577 (11)	28 (0)	2105 (8)	1 (0)	24177 (9)	8 (0)
18 – 29	92218 (20)	82 (0)	31304 (19)	29 (0)	4708 (17)	14 (0)	56206 (20)	39 (0)
30 – 44	155588 (33)	726 (1)	51228 (32)	306 (1)	8601 (31)	51 (1)	95759 (35)	369 (0)
45 – 64	123015 (26)	3015 (3)	45115 (28)	1618 (4)	8594 (31)	196 (2)	69306 (25)	1201 (2)
65 – 85	47991 (10)	3755 (8)	16287 (10)	2026 (12)	3359 (12)	300 (9)	28345 (10)	1429 (5)
>85	2521 (1)	305 (12)	671 (0)	139 (21)	150 (1)	28 (19)	1700 (1)	138 (8)
Gender								
Female	199446 (43)	2729 (1)	68089 (42)	1342 (2)	11661 (42)	201 (2)	119696 (43)	1186 (1)
Male	265623 (57)	5185 (2)	94071 (58)	2799 (3)	15855 (58)	389 (3)	155697 (57)	1997 (1)

The first wave of the pandemic is between March 09th,2020, and October 31st, 2020; the maintenance phase is between November 01st,2020, and February 15th, 2021. The second wave is between February 16th,2021, and May 31st, 2021, and this analysis was censored for May 31st, 2021, for incident cases and June 07th, 2021, for deaths.

using logistic regression analysis. The Indian Institute of Science Education and Research ethics committee, Pune, India, approved this analysis of the public health monitoring program.

Results

COVID-19 in the first wave, second wave and maintenance phase

During the study period, 465 192 COVID-19 cases were diagnosed in Pune city; 162 182 (35% of total cases) in the first wave, 27 517 (6%) in the maintenance period, and 275 493 (59%) in the second wave. The trends in COVID-19 case detection in Pune city and India are shown in Figure 1a. The peak of the second wave was delayed by 12 days for India compared with Pune city. Overall, the test positivity of cases was 19%; it was highest at 22% (P<0.01) during the first wave, followed by 19% (P<0.01) in the second wave and 8% (P=0.18) in the maintenance period (Supplementary Figure 1). As shown in Table 1, the 30–45 year age group (P<0.01) and men (P<0.01) contributed most to COVID-19 cases across all 3 phases of the pandemic. The largest increase in the proportion of weekly cases was observed among those aged 30–44 years (P<0.01), followed by 45–64 (P=0.02), then 65–85 years (P=0.003) (Figure 1b). The ratio of critical care cases to active cases (Figure 1c) was 6% in the first wave, 8% in the maintenance phase and 3% in the second wave (P<0.01).

Death characteristics and time to death

Of 465 192 cases, 7920 (1.7%) died. The median age of those who died was 65 (interquartile range (IQR), 54–73) years; with almost half of the deaths, 3755 (47%), in patients 65–85 years of age, and 5185

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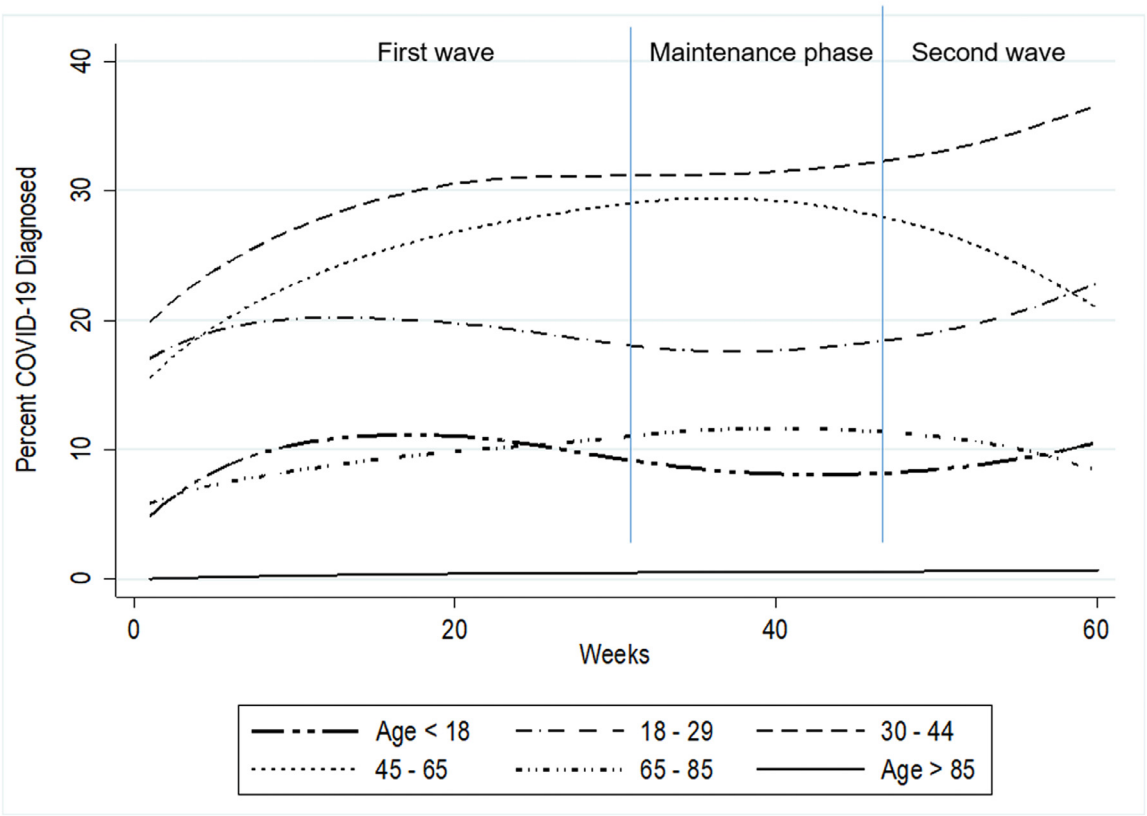

Age	Change in Diagnosis/week (95% CI)	p-value
< 18	-0.04 (-0.08, 0.01)	0.12
18 – 29	-0.01 (-0.08, 0.05)	0.66
30 – 44	0.16 (0.10 – 0.22)	p < 0.001
45 – 64	0.09 (0.02 – 0.17)	0.02
65 – 85	0.06 (0.02 – 0.11)	0.003
> 85	0.01 (0.01 – 0.012)	p < 0.001

Figure 1b. The trajectory of incident COVID cases in Pune city across different age groups from 9 March 2020 to 31 May 2021.

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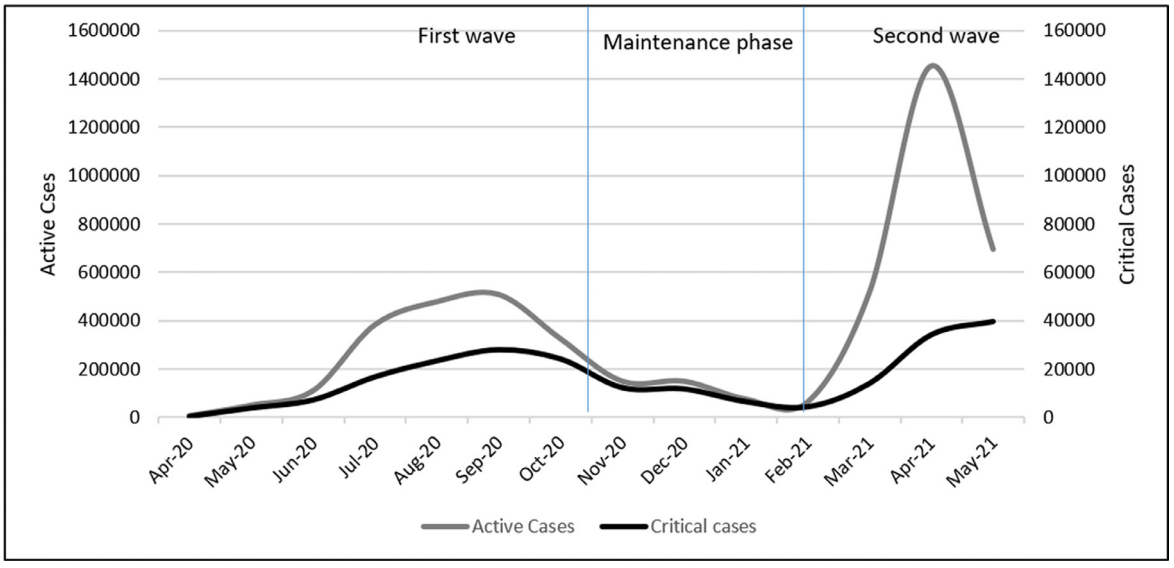


Figure 1c. Monthly active COVID-19 cases and critical care cases in Pune city from 9 March 2020 to 31 May 2021.

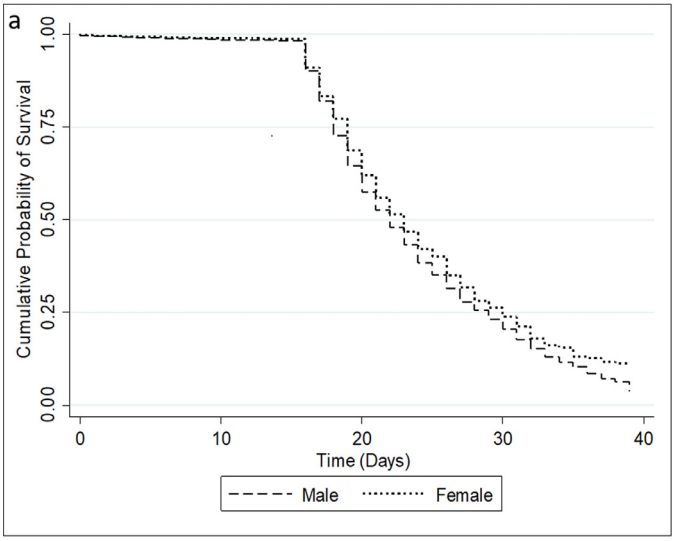


Figure 2a. Median time to death from diagnosis among men and women.

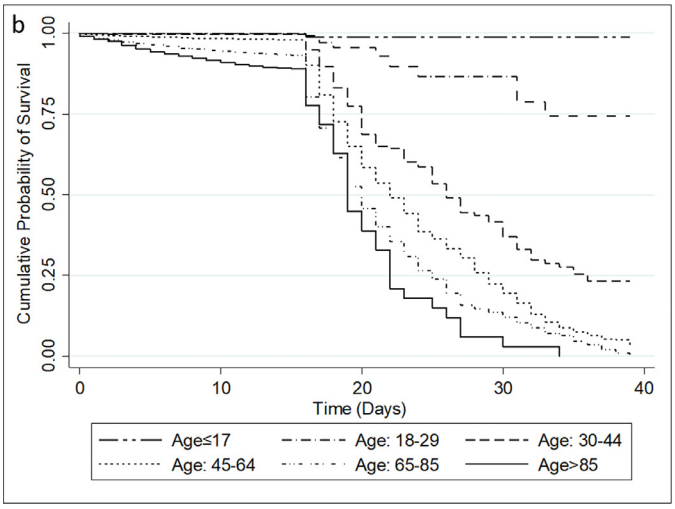


Figure 2b. Kaplan Meier curve showing median time to death from diagnosis among different age categories.

(65%) were men. Of mortalities, 3704 (47%) had one or more comorbidities; 2699 (34%) had hypertension, and 2239 (28%) had diabetes (Supplementary Figure 2). Among those who died, the median time to death from diagnosis was 6 days (IQR, 2–11). As shown in Figure 2a, time to death was slightly different for men vs women (6 (IQR, 2–12) vs 5 (IQR, 2–11) days, $P<0.01$). For age group categories, the median time to death in days was in the following order: 6 (IQR, 3–10) for >85 years; 6 (IQR, 2–11) for 65–85 years; 6 (2–12) for 45–64 years; 6 (1–12) for 30–44 years; 3 (0–9) for 18–29 years; and 3 (0–7) for <17 years ($P<0.01$) (Figure 2b).

Case fatality rate and risk factors

Of the 7920 who died, 4146 (52%) died in the first wave, 590 (8%) in the maintenance phase and 3184 (40%) in the second wave ($P<0.01$). The CFR rapidly declined from 3.91 per 1000 PD (95% CI; 3.56–4.25) to 1.66 per 1000 PD (95% CI: 1.61–1.72) during the first wave. During the same period, clinical management guidelines were introduced recommending the use of intravenous steroids for COVID-19. The CFR further declined to 0.77 per 1000 PD in the second wave. Moreover, the CFR was 3.53 times greater before the new guidelines for intravenous steroid use for severe illness was introduced (aCFRR, 3.53, 95% CI 3.23–3.86). Figure 3a.

Overall CFR per 1000 person-days (PD) was 1.16; it was lowest for the 0–17 and 18–39 age groups at 0.06/1000 PD and highest for ages >85 years at 8.62/1000 PD (Table 2). The CFR decreased over time; 1.80/1000 PD in the first wave, 1.42/1000 PD in the maintenance phase, and 0.77/1000 PD in the second wave. The age group 65–85 years saw the largest decline in CFR over time (Figure 3b). In Poisson regression models, men (adjusted CFR ratio [aCFRR] 1.46; 95% CI 1.40–1.53) aged 65–85 years (aCFRR 90.15; 95% CI: 72.44–112.20) and aged >85 years (aCFRR 155.04; 95% CI 121.49–197.86) had increased risk of mortality (Table 2). Furthermore, the risk for deaths was 1.49 times higher for the first wave (aCFRR 1.49; 95% CI 1.37–1.62) compared with the maintenance phase, while it was almost 35% lower for the second wave (aCFRR 0.65; 95% CI 0.59–0.70) (Table 2). Furthermore, the fatality rate was 47% lower in the second wave than in the first wave (aCFRR 0.43; CI 0.41–0.45). Risk factor analysis for deaths by 3 analysis periods did not change significantly except for the 0–17 years age group (aCFRR 1.7; 95% CI 1.0–2.9) who had a higher likelihood of deaths in the first wave compared with the maintenance phase (Supplementary Table 2).

Discussion

Our report encompasses the full spectrum of Pune city's COVID-19 pandemic to close to the end of the second wave. The trend of COVID-19 case incidence in Pune city followed a pattern similar to India with two exceptions. First, the peak of the second wave in Pune occurred approximately 12 days earlier than the country. Second, there was a slight dip in cases during the first wave corresponding to Pune's regional lockdown (Mave et al., 2021). The first wave of the COVID-19 pandemic lasted 7–8 months and the maintenance phase had low COVID-19 incidence. The second wave had exponential growth of cases and the world's largest peak and absolute number of cases (Dong et al., 2020). The overall case fatality ratio was 1.7% in Pune city, higher than the reported nationwide case fatality ratio of 1.2%. Notably, the CFR declined sharply during the first wave, but it was 1.49 times higher than the phase between the 2 pandemic waves. Furthermore, the CFR of the second wave was 35% lower than the phase between the pandemic waves and 61% lower than the first wave.

The reasons for the decline in CFR as the pandemic progressed are unclear and need further exploration. First, the proportion of COVID-19 cases among middle-aged adults (30–44 years) whose risk of death is relatively lower increased over time, resulting in fewer deaths. Further, the ratio of critical care cases to total active cases during the second wave was lower compared with the first wave. Second, since the first wave ended, the predominant circulating strains in India, a new variant of SARS-CoV-2-B.1.617, are known to be highly transmissible, as demonstrated by the rapid growth of cases during the second wave. Although the World Health Organization has recently categorized this strain as a variant of concern, the severity of the disease associated with this strain is yet to be investigated (Gayathri, 2021; GISAID - hCov19 Variants 2021; Risk assessment for SARS-CoV-2 variant: Delta (VOC-21APR-02, B.1.617.2) 2021). Third, our test positivity analysis indicates that more cases were identified during the second wave with a lower test positivity rate than the first wave during the pandemic. Hence the CFR is likely to be closer to the infection fatality rate in the second wave (Wei et al., 2020), indicating that the increased availability of testing may have led to early diagnosis and access to care, preventing further complications and deaths.

The sharp decline of COVID-19 mortality during the first wave also appears to coincide with the availability of more information and revised national guidelines on clinical management such as optimal use of corticosteroid, antivirals and appropriate early supportive treatment following hospitalization of moderate and severe COVID-19 (Anesi et al., 2021, Dennis et al., 2021 and (Gavriatopoulou et al., 2021). Indeed, be-

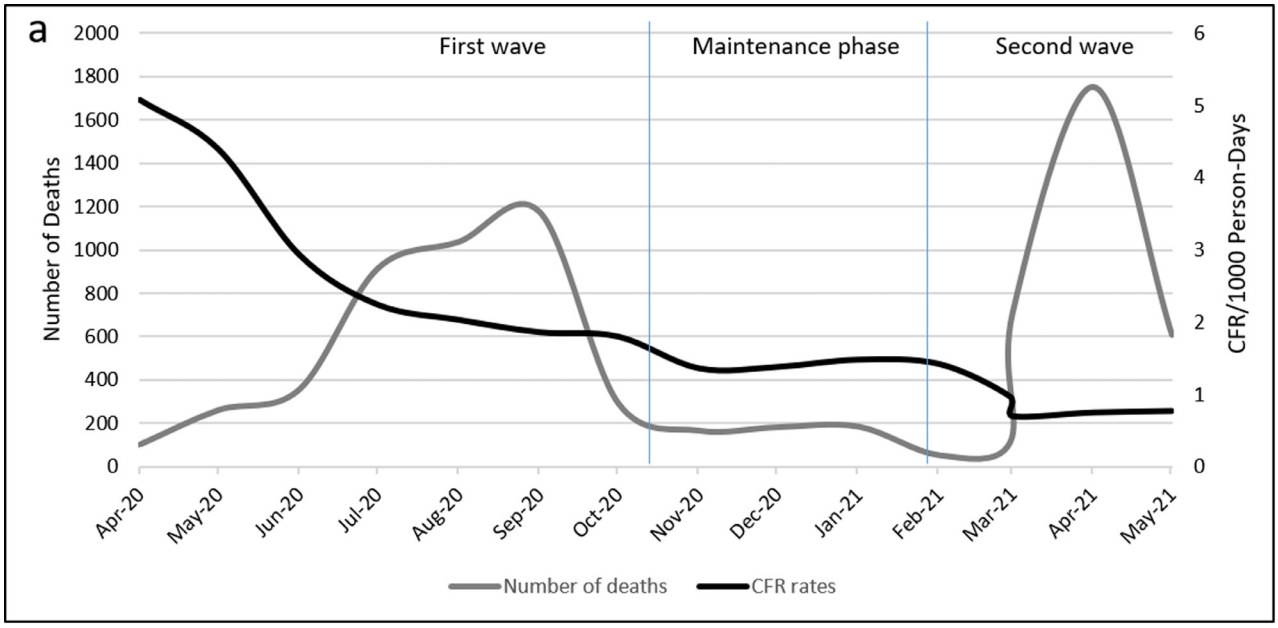


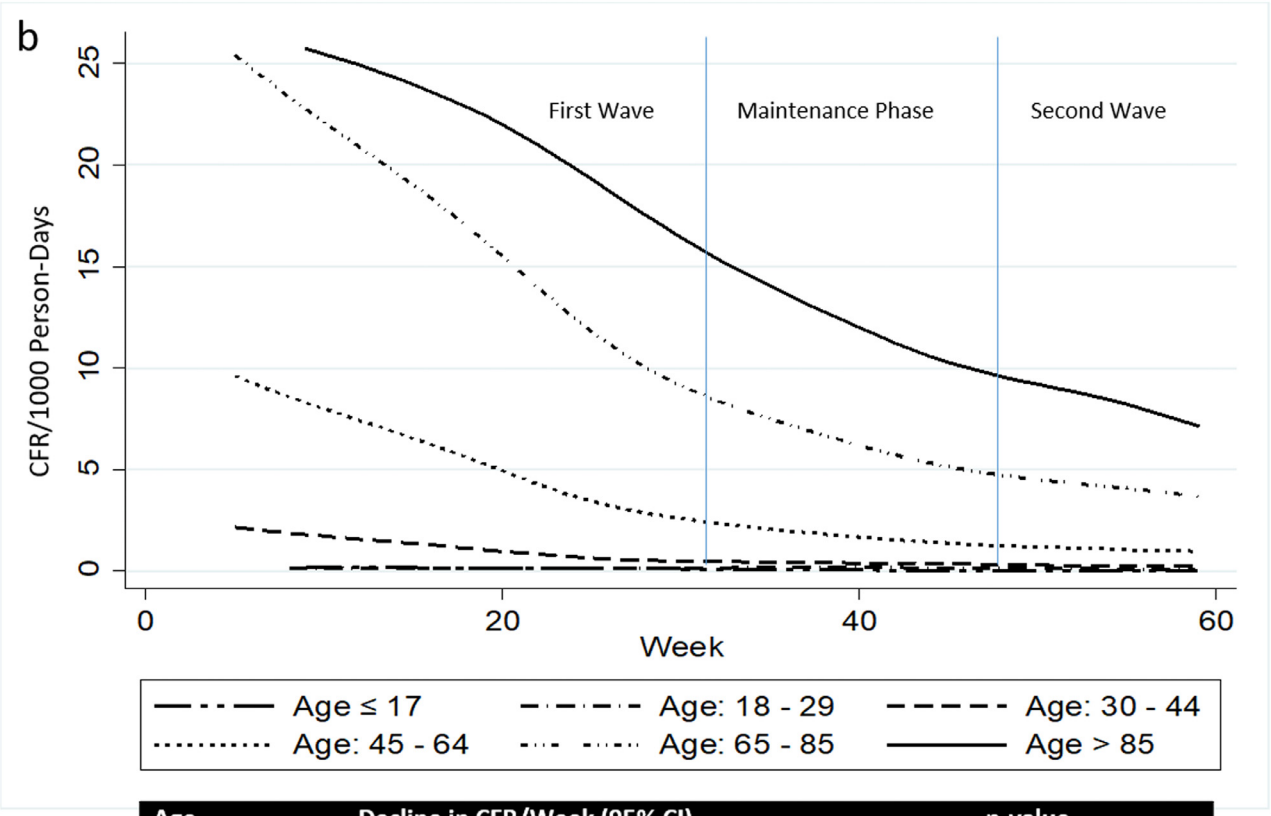
Figure 3a. Monthly case fatality rate per 1000 person-days in Pune from 9 March 2020 to 31 May 2021, and the absolute number of deaths.

Table 2
Factors Associated with COVID-19 Mortality using Poisson Regression Analysis in Pune city, India.

Characteristics	Time to Death Median (IQR	CFR/1000 Person Days (95% CI)	Unadjusted case fatality rate ratio (95% CI)	Adjusted case fatality rate ratio (95% CI)
Overall	6 (2 – 11)	1.16 (1.13 – 1.19)	-	
Age, median (IQR)		-	1.073 (1.072 – 1.074)	-
Age categories				
0 – 17	3 (0 – 7)	0.06 (0.04 – 0.08)	0.95 (0.65 – 1.41)	0.92 (0.62 – 1.35)
18 – 29	3 (0 – 9)	0.06 (0.05 – 0.07)	1	1
30 – 44	6 (1 – 12)	0.32 (0.29 – 0.34)	5.24 (4.17 – 6.58)	5.23 (4.16 – 6.57)
45 – 64	6 (2 – 12)	1.67 (1.61 – 1.73)	27.72 (22.26 – 34.51)	26.96 (21.65 – 33.58)
65 – 85	6 (2 – 11)	5.45 (5.28 – 5.63)	90.38 (72.62 – 112.48)	90.15 (72.44 – 112.20)
>85	6 (3 – 10)	8.62 (7.68 – 9.64)	142.85 (111.94 – 182.29)	155.04 (121.49 – 197.86)
Gender				
Female	5 (2 – 11)	0.93 (0.89 – 0.97)	1	1
Male	6 (2 – 12)	1.33 (1.29 – 1.37)	1.43 (1.36 – 1.50)	1.46 (1.40 – 1.53)
Period				
First wave	6 (2 – 11)	1.80 (1.75 - 1.86)	1.27 (1.16 – 1.38)	1.49 (1.37 – 1.62)
Maintenance	7 (2 – 13)	1.42 (1.31 - 1.54)	1	1
Second wave	6 (2 – 11)	0.77 (0.75 - 0.80)	0.54 (0.50 – 0.59)	0.65 (0.59 – 0.70)

The first wave of the pandemic is between March 09th,2020, and October 31st, 2020; the maintenance phase is between November 01st,2020, and February 15th, 2021. The second wave is between February 16th,2021, and May 31st, 2021, and this analysis was censored for May 31st, 2021, for incident cases and June 07th, 2021, for deaths.

fore the nationwide recommendation of advanced clinical management in early June 2020, the CFR was 3.53 times higher during the first wave, before becoming stable at ~2%. The relatively higher cumulative case fatality ratio observed in Pune city at 1.7% than the countrywide reported ratio of ~1% can be explained by access to better curated and granular data at the Pune city level. Although it was much lower than western counterparts, consistent with prior studies (Cao et al., 2020, Jain et al., 2020), the oldest age groups, particularly those >65 years, had the highest likelihood of death across the pandemic and the largest decline in the CFR over time (Signorelli and Odone, 2020). We observed higher mortality among men, similar to prior studies (Roth et al., 2021), although the time to death was longer for both older age groups and men (Laxminarayan et al., 2020). Moreover, the risk of death was the lowest overall among children (Tsabouri et al., 2021). Notably, children had 1.75 times higher risk of mortality during the first wave than young adults; however, this needs to be interpreted with caution as the proportion of children with COVID-19 was comparatively smaller and comorbid conditions were not captured for them. Even though older adults had the highest risk of death, the proportion of deaths among the incident cases in the 18–65 years age group and men, who are traditionally the wage-earners of the Indian family, were closer to 50% and 66%, respectively. Furthermore, considering the emerging reports of post COVID-19 sequelae and associated morbidity and mortality for this group (Nalbandian et al., 2021), the economic repercussions of the pandemic may remain for the foreseeable future in India (Dhar et al., 2021). Notably, the total disease burden and proportional critical cases were significantly higher during the second wave, requiring hospital beds, oxygenation, ventilator support and healthcare workers to manage the illness. In this context, our report gives an insight into how the Indian health system managed the unprecedented burden placed by the second wave of the COVID-19 pandemic, widely publicized in Indian and global media reports (Steffy T, 2021). The strengths of our analysis include the availability of more complete data enabling comparative analysis of first and second waves with the maintenance phase of the pandemic. While the period demarcation for these waves can be countered as arbitrary, arbitrary delineation of pandemic waves has been done worldwide to assess the progression of the pandemic (Li et al., 2020). To reduce period bias, we used trends in weekly case data and



Age	Decline in CFR/Week (95% CI)	p-value
< 17	-0.004 (-0.01, -0.003)	p < 0.001
17 – 29	-0.001 (-0.003, 0.001)	0.59
30 – 44	-0.04 (-0.06, -0.03)	p < 0.001
45 – 64	-0.20 (-0.25, -0.16)	p < 0.001
65 – 85	-0.51 (-0.60, -0.43)	p < 0.001
> 85	-0.48 (-0.52, -0.44)	p < 0.001

Figure 3b. Case fatality rate per 1000 person-days over time among different age categories.

test positivity to assign the 3 phases for this analysis. The absence of data on comorbidities among COVID-19 survivors limited our ability to assess the relationship between comorbidities and mortality. However, we show that among those who died, over half had one or more comorbidities, suggesting a relationship between comorbidity and mortality (Singh et al., 2020).

Only aggregate data of critical cases were available; detailed data on hospitalization, oxygenation and ventilator support requirements were unavailable. Furthermore, data were unavailable on SARS-CoV-2 variants and their impact on case burden and deaths and whether providers uniformly implemented the MoHFW recommendations in Pune city. The majority of deaths (99%) occurred in the hospital settings in this dataset; thus, COVID-19 deaths in the community may not have been captured, therefore underreporting of COVID-19 deaths for Pune city cannot be ruled out. Furthermore, the association between the introduction of steroids and decreased CFR should be considered exploratory since this depicts only cohort effect with the introduction of a new treatment. The data on disease severity was not collected in the routine surveillance program; therefore, correlation between CFR and disease severity could not be assessed. Despite these limitations, to our knowledge, this is the first real-world epidemiologic analysis of the progression of the pandemic and related mortality in a COVID-19 hotspot city, one of many such affected cities in India.

In conclusion, we demonstrate that as the burden of COVID-19 expanded from the first wave to the second wave, the CFR declined. Our report suggests the role of evolving therapeutics in reducing CFR, but further confirmation is needed. In addition, investigation of the impact of predominant circulating strains on mortality is urgently required. Notably, our report highlights the need for healthcare preparedness, including hospital beds, oxygenation, ventilator support and healthcare workers to manage a pandemic of this scale worldwide. Further, there is an urgent need to investigate new or repurposed therapies and implement mass vaccinations to halt the morbidity and mortality of the devastating COVID-19 pandemic in India and worldwide.

Declaration of Competing Interest

Authors declare no conflicts of interest.

Acknowledgments

We thank the Pune Knowledge Cluster members, Dr. Ajit Kembavi and Dr. Ashwini Keskar, for supporting data acquisition. We acknowledge the generous support and congratulate the PMC commissioner, officials, and staff involved in the successful COVID-19 surveillance program.

Author contributions

VM, JM, NG, PB, SN, AJ, LS conceived the study. SN, JM, AJ performed data management and curation. DJ, PB, VM, NG conducted the

data analysis, and all authors contributed to data interpretation and manuscript writing.

Funding

This analysis was done as part of the Pune Knowledge Cluster (PKC) comprising Pune-based academics, academic institutions, and industry partners. The PKC principal investigators, Dr. LS Shashidhara and Dr. Ajit Kembavi, received funding support from Pune Knowledge Cluster Initiative under the Government of India. JMM was funded by the Science and Engineering Board (SERB) Startup Research Grant SRG/2020/000062. This study was not funded separately. This paper's content is solely the authors' responsibility and does not necessarily represent the official views of the PKC or its funder.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijregi.2021.12.006.

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