Journal of Infection and Public Health 15 (2022) 726–733

Contents lists available at ScienceDirect

Journal of Infection and Public Health

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

Original article

COVID-19 outbreak trends in South Africa: A comparison of Omicron (B.1.1.529), Delta (B.1.617.2), and Beta (B.1.351) variants outbreak periods

Syed Mahfuz Al Hasan[a,*], Jennifer Saulam[b,c], Fumiaki Mikami[b], Kanae Kanda[d], Hideto Yokoi[b], Tomohiro Hirao[d]

[a] Clinical Research Support Center, Kagawa University Hospital, Kagawa, Japan
[b] Department of Medical Informatics, Kagawa University Hospital, Kagawa, Japan
[c] Department of Food Processing and Nutrition, Karnataka State Akkamahadevi Women's University, Vijayapura, Karnataka, India
[d] Department of Public Health, Faculty of Medicine, Kagawa University, Kagawa, Japan

ARTICLE INFO

Article history:
Received 8 January 2022
Received in revised form 27 April 2022
Accepted 19 May 2022

Keywords:
Omicron (B.1.1.529)
Delta (B.1.617.2)
Beta (B.1.351)
Joinpoint regression analysis
South Africa
COVID-19

ABSTRACT

Objectives: We provided COVID-19 outbreak trends in South Africa during the Omicron (B.1.1.529), Delta (B.1.617.2), and Beta (B.1.351) variants outbreak periods from November 2020 to March 2022.
Methods: We used the time series summary data of the COVID-19 outbreak for South Africa available in the COVID-19 data repository created by the Center for System and Science and Engineering at Johns Hopkins University and the Our World in Data database by the University of Oxford from January 2020 to March 2022. We used the joinpoint regression model with a data-driven Bayesian information criterion method for analyzing the outbreak trends. In addition, we used density ellipses and partition modeling on the outbreak data.
Results: During the Omicron outbreak period, COVID-19 cases in South Africa significantly jumped by 4.7 times from December 01 to December 08, 2021. The average daily growth rate of incidence peaked at 23,000 cases/day until December 16, 2021, which was 18.6 % higher than the peak growth during the Delta outbreak period. South Africa experienced peak growth in COVID-19 cases with 18,611 cases/day (January 04 to January 14, 2021) during the Beta outbreak period and with 19,395 cases/day (July 01 to July 11, 2021) during the Delta outbreak period. Density ellipsoid showed a significant correlation between daily cases and daily death count during the Beta and Delta outbreak period which was not prominent in the Omicron outbreak period. Comparatively higher daily death tolls were reported in days with a recovery rate of less than 89.1 % and 91.9 % in the Beta and Delta outbreak period respectively. The backlog counts may be one of the reasons for the significant increase in daily death tolls during the Omicron period.
Conclusions: During the Omicron period, COVID-19 cases peaked growth was 18.6 % higher than the peak growth during the Delta outbreak period. Despite that fact, growth in death trends in the Omicron outbreak period was found low which might be due to the low mortality rate and case fatality proportion. The emergence of the Omicron variant once again reminds us that- “no one is safe until everyone is safe”.

Introduction

The discovery of a new variant of concern of the severe acute respiratory syndrome coronavirus 2, SARS-CoV-2, (causative virus of the coronavirus disease, COVID-19) in South Africa has triggered a global scramble [1]. World Health Organization designated the new variant as a variant of concern and named it Omicron (B.1.1.529) on the 26th of November 2021 [2]. Omicron has numerous mutations similar to changes seen in previous variants of concern and some novel mutations which are associated with the potential to enhance transmissibility, confer resistance to therapeutics, or partially escape infection-acquired immunity and/or vaccine-administered immunity [3–7]. In the current situation, there are too many confounding factors that need to be compared in patients infected with

* Corresponding author.
E-mail addresses: mahfuz.kmu.2017@gmail.com (S.M. Al Hasan), jennifersaulam27@gmail.com (J. Saulam), mikami.fumiaki@kagawa-u.ac.jp (F. Mikami), kanda.kanae@kagawa-u.ac.jp (K. Kanda), yokoi.hideto.md@kagawa-u.ac.jp (H. Yokoi), hirao.tomohiro@kagawa-u.ac.jp (T. Hirao).

https://doi.org/10.1016/j.jiph.2022.05.011

the Omicron variant in South Africa with patients infected by other variants [8].

To date, little data and information is available on the Omicron variant to answer the uncertainties, and studies must be quickly carried out to better define the threat that this variant represents [8]. Obtaining and analyzing information about what has happened until now and what might happen in the future is essential for understanding and controlling the SARS-CoV-2 variants of concern outbreaks at the global level. Researchers in South Africa and around the world are conducting studies to better understand many aspects of Omicron [3]. Based on the real-time data, in this study, we attempted to provide the trends and significant changes in the COVID-19 outbreak in South Africa during the Omicron (B.1.1.529), Delta (B.1.617.2), and Beta (B.1.351) outbreak periods from November 2020 to March 2022. Moreover, through the ellipse and partition models, we tried to demonstrate comparatively how the daily cases, recovery rate, and percent positivity in South Africa were correlated to daily death tolls during the Omicron (B.1.1.529), Delta (B.1.617.2), and Beta (B.1.351) outbreak periods.

Methods

Sources of data and compilation

Data for this time-trend study were primarily retrieved and compiled from two global databases for providing public aggregated global information on the COVID-19 pandemic. In the first part, we used the time series summary data from January 2020 to March 2022 available in the COVID-19 data repository by the Johns Hopkins University Center for System and Science and Engineering which is also supported by ESRI living Atlas Team and Johns Hopkins University Applied Physic Lab [9]. From this database, COVID-19 total cases, total recoveries, and total deaths data for South Africa were sorted out from the master database file from November 2020 to March 2022 as three separate comma-separated values (.csv) files and combined as one excel file. We then calculated the daily COVID-19 cases, daily deaths, daily recoveries, daily recovery rate, and case fatality proportion from the total cases, total recoveries, and total deaths data. For additional data, we used the Our World in Data COVID-19 vaccination dataset [10] by the University of Oxford. This COVID-19 vaccination dataset covers the full period from the first vaccination published data (December 13, 2020) and has been updated regularly ever since. From this database, we filtered out the total tests, people vaccinated, people fully vaccinated, and population dataset for South Africa from February 2020 to March 2022 and compiled it into an excel file. The operational definition of people vaccinated is the number of people who had received at least one dose of the vaccination protocol whereas people fully vaccinated denotes those who completed the initial vaccination protocol. We calculated the daily tests, percent positivity, and percent of the total population partially and fully vaccinated in South Africa from the related variables in the dataset. Percent positivity was calculated from the proportion of people who tested positive for SARS-CoV-2 on a given day and the total number of tests conducted on that specific given day [11].

Study variables from both the excel files were combined into one excel file that matched the date and further filtered out from November 2020 to March 2022. We matched our calculated daily cases and deaths figures, especially during the Omicron outbreak period, with the figures provided in the official COVID-19 Online Resource and News Portal of the National Department of Health of the Republic of South Africa [12]. For missing data and repeated values on two consecutive days in the compiled dataset, we imputed the values also from the official COVID-19 Online Resource and News Portal of the National Department of Health of the Republic of South Africa. This compiled data set then was converted to the comma-separated values (.csv) file for trend analysis. In addition, since January 06, 2022, the Department of Health of the Republic of South Africa had recorded and reported the COVID-19 death backlog as an ongoing audit exercise conducted in each province across the country to address a backlog of COVID-19 mortality [12]. This audit exercise increased the daily death tolls on some specific days when the backlog death counts were added. We have provided the information on the backlog death counts together with the original death counts on the specific dates in a Supplementary table (Table S1).

Segregation of Beta, Delta, and Omicron outbreak period

Beta (B.1.351) outbreak period was considered from the prior month when the Beta variant of SARS-CoV-2 had discovered by scientists in South Africa on December 18, 2020, to March 2021. During this period, South Africa experienced the second wave of its COVID-19 pandemic. The tentative duration of the second wave (November, 2020–March, 2021) was determined from the line graph of the daily cases in South Africa. In the line graph, where the visible surge in new cases followed by a decline was considered a wave. Delta (B.1.617.2) outbreak period was considered from the prior month when the earliest documented sample with the Delta variant of SARS-CoV-2 was identified in South Africa (May 08, 2021) to the prior month of the earliest documented sample with the Omicron variant of SARS-CoV-2 reported (November 2021). The Delta outbreak probably resulted in the third pandemic wave in South Africa [2]. The tentative duration of the third wave (April 2021 to October 2021) was determined from the line graph of the daily cases when the visible surge in new cases was followed by a decline. Omicron (B.1.1.529) outbreak period was considered from the month when the earliest documented sample with the Omicron variant of SARS-CoV-2 was reported in South Africa (November 09, 2021) to the last reported date of this analysis (December 30, 2021). This is an ongoing wave during our analysis. The tentative duration of the fourth wave (November 2021 to continue) was determined from the line graph of the daily cases when the visible surge was followed by a decline.

Trends analysis, density ellipse, and partition models

To analyze the temporal trends and to identify significant changes in trends in the coronavirus disease (COVID-19) outbreak in South Africa from November 01, 2020, to March 31, 2022 (a total of 516 days), we performed a joinpoint regression analysis [13]. We have analyzed the trends segregated on each month from November 2020 to March 2022. We used Windows-based statistical software, the Joinpoint Regression Program (version 4.9.0.0, National Institute of Health, Bethesda, MD, United States) for performing the joinpoint regression by using the joinpoint models. With this analysis, it was possible to identify days when a significant change in the linear slope of the trend is detected over the study period. The best-fitting points, called ‘joinpoints’, are chosen when the rate changes significantly. The analysis starts with the minimum number of joinpoints and tests whether one or more joinpoints (in this study up to 3) are significant and must be added to the model. To describe linear trends by period, the estimated regression coefficients (β) are then computed for each of those trends [13–15]. The multiple joinpoints were used to reflect and provide a background for the changing epidemic patterns. In addition, we used density ellipses analysis to assess the correlation between daily deaths and daily cases of the outbreak data segregated on Omicron, Delta, and Beta outbreak periods. We selected and represented the 50 %, 90 %, and 99 % probability plots for the density ellipses around the data point. We used the partition model using the decision tree method to identify the possible important factors that split the continuous outcome (daily deaths) during the Omicron, Delta, and Beta outbreak periods with a cutting value of the factor variables. The daily cases, recovery rate, and percent positivity values during the Omicron, Delta, and Beta outbreak periods were divided into two groups based on the variability of the daily death and created a tree of partition on the factor variables' responses. In the Omicron period, we used the backlog-reported days as an additional factor to predict the variability in the daily deaths. We used JMP (Version 16.1, SAS Institute Inc., Cary, NC, United States) software package for these analyses.

Results

As of March 31, 2022, about 6.2 % of the South African have had COVID-19 and 97.0 % of them have recovered. About 39.7 % of the population has tested for SARS-Cov-2 and 34.9 % of the total population received at least one dose of vaccine, and 29.8 % were fully vaccinated. So far, South Africa has experienced four waves (surge in new cases followed by decline) of the COVID-19 pandemic. During the outbreak period, case fatality proportion ranged from 2.66 to 3.41 in the Beta (B.1.315) outbreak period and 2.91–3.44 in the Delta (B.1.617.2) outbreak period whereas; in the Omicron (B.1.1.529) outbreak period it ranged from 2.62 to 3.06. The recovery rate ranged from 78.1 % to 95.3 % in the Beta outbreak period, 87.3–96.3 % in the Delta outbreak period, and 90.8–96.9 % in the Omicron outbreak period.

Beta (B.1.315) outbreak period

In South Africa, since November 2020, COVID-19 cases increased gradually at significant rates until mid-January 2021 (Table 1). The incidence growth rate reached almost 3000 cases/day during the last week of November, which increased by 2.6 times since December 08, 2020. By the last week of December 2020, the rate increased significantly by 105 % and the total number of COVID-19 cases crossed 1.0 million on December 27, 2020. During the first and second weeks of January 2021, South Africa experienced the peak growth in COVID-19 cases in the second wave of the pandemic by 18,611 cases/day and since then, cases increased at a comparatively reduced rate. Until the end of the second wave, COVID-19 cases reached almost 1.55 million in South Africa. Death tolls due to COVID-19 climbed at a noticeable rate since December 2020. For every ten days in December 2020, death rates increased by about 1.6–1.7 times until December 28, 2020 (Table 2). During the second wave of the pandemic in South Africa, the death rate peaked in January 2021 at a dire 534 deaths/day (Table 2) with a 55.1 % increase from December 2020. Since early-February 2021, death tolls slowed down to 138 deaths/day (from February 18 to February 28, 2021) and to 51 deaths/day (from March 26 to March 31, 2021).

Delta (B.1.617.2) outbreak period

Since April 07, 2021, COVID-19 cases started to increase again at a concerning rate in South Africa, and during the last week of May 2021 incidence increased to 4261 cases/day (Table 1). With continuous increasing trends, South Africa experienced the third peak growth in their COVID-19 cases by 19,395 cases/day from July 01 to July 11, 2021 and reached 2.2 million COVID-19 cases. Since July 11, 2021, COVID-19 cases started to increase at a reduced rate except for a period from August 11 to August 28, 2021. The growth rate of incidence reduced to 1718 cases/day during the fourth and fifth weeks of September and further reduced to 411 cases/day during the last week of October 2021 (Table 1) and total COVID-19 cases reached to 2.92 million. During the third wave, the death rate peaked from July 19 to July 31, 2021 at 400 deaths/day, and the total death toll reached 72,013 deaths since then, death tolls showed a continuous downward trend. During the fourth and fifth weeks of September 2021, the death rate was 130 deaths/day which reduced markedly to 42 deaths/day since October 09, 2021, and as of the end of October 2021, a total of 89,177 deaths were recorded.

Omicron (B.1.617.2) outbreak period

During the first three weeks of November 2021, the growth rate of incidence was 320 cases/day (Table 1). Suddenly on November 23, 2021, there was an overwhelming increase in the number of daily COVID-19 cases (18,586 cases) in South Africa that raised concern, and the total number of cases reached 2.95 million. Since November 24, 2021, incidence increased by 2746 cases/day and then jumped by 4.7 times from December 01, 2021 and exceeded 3.0 million COVID-19 cases on December 03, 2021. From December 08, 2021, the growth rate of incidence peaked at an average of 23,000 cases/day until December 17, 2021, which was the highest peak growth in the COVID-19 pandemic in South Africa. Since then, the growth rate of incidence slowed down to 1321 cases/day during the last three weeks of March 2022, and the total cases reached 3.72 million. Unlike the case trend, the death trend did not show any noticeable changes and continued to maintain the third wave's decreasing trend till mid-December 2021. During the last few days of December 2021, the death rate jumped to 98 deaths/day. During January and February 2022, death trends showed lots of fluctuations as high as 344 deaths/day and as low as 75 deaths/day. These fluctuations in trends were mainly due to the ongoing audit exercise conducted by the Department of Health of the Republic of South Africa since January 06, 2022. COVID-19-related deaths reached 100,032 in South Africa as of March 31, 2022.

Partition models to assess the variability in daily deaths

During the Beta and Delta outbreak period, the ellipsoid collapsed diagonally (Fig. 1) which indicates a high correlation between daily cases and deaths whereas the ellipsoid was more circular during the Omicron outbreak period. Days with a recovery rate of less than 89.1 % had comparatively higher daily death tolls compared to the days with a recovery rate of 89.1 % and more (478 vs. 127 deaths) during the Beta outbreak period (Table 3). In the Delta outbreak period, days with a recovery rate of less than 91.9 % had 312 deaths on an average compared to days with a recovery rate of 91.2 % and more. During the Beta outbreak period, deaths were reported significantly higher when the number of daily cases was over 5297 cases mark (about 414 vs. 125 deaths). Death was counted markedly high when the daily cases were over 5574 cases in the Delta outbreak period (about 291 vs. 76 deaths). During the Omicron period, days with backlog counts had higher daily death tolls as opposed to the days with no backlog counts (173 vs. 57 deaths).

Discussion

Our analysis showed that during the Omicron outbreak period, COVID-19 cases in South Africa peaked within one month of the first infectious specimen collected on November 09, 2021. When we

Table 1
Trends in COVID-19 cases in South Africa from November, 2020 to March, 2022 [1].

	Trend 1		Trend 2		Trend 3		Trend 4	
	Period	β[2]	Period	β[2]	Period	β[2]	Period	β[2]
Beta Outbreak Period[3]								
Second wave of the Pandemic[4]								
November 2020	Nov 01–Nov 09	1551.01*	Nov 09–Nov 17	2006.43*	Nov 17–Nov 24	2565.01*	Nov 24–Nov 30	2987.88*
December 2020	Dec 01–Dec 08	4118.89*	Dec 08–Dec 18	7751.10*	Dec 18–Dec 29	11410.35*	Dec 29–Dec 31	15863.84*
January 2021	Jan 01–Jan 04	13323.94*	Jan 04–Jan 14	18610.35*	Jan 14–Jan 23	11650.92*	Jan 23–Jan 31	6315.56*
February 2021	Feb 01–Feb 05	3721.83*	Feb 05–Feb 13	2376.59*	Feb 13–Feb 20	1763.93*	Feb 20–Feb 28	1421.23*
March 2021	Mar 01–Mar 20	1179.37*	Mar 20–Mar 31	1084.95*				
Delta Outbreak Period[5]								
Third wave of the Pandemic[6]								
April 2021	Apr 01–Apr 07	601.77*	Apr 07–Apr 30	1191.16*				
May 2021	May 01–May 11	1692.70*	May 11–May 25	2958.19*	May 25–May 31	4260.88*		
June 2021	Jun 01–Jun 08	5073.88*	Jun 08–Jun 15	8043.83*	Jun 15–Jun 22	11964.78*	Jun 22–Jun 30	16062.59*
July 2021	Jul 01–Jul 11	19394.66*	Jul 11–Jul 17	14634.14*	Jul 17–Jul 31	11671.97*		
August 2021	Aug 01–Aug 08	11630.72*	Aug 08–Aug 11	7952.32*	Aug 11–Aug 28	11893.12*	Aug 28–Aug 31	6108.73*
September 2021	Sep 01–Sep 04	8710.66*	Sep 04–Sep 11	5779.27*	Sep 11–Sep 19	3725.33*	Sep 19–Sep 30	1717.24*
October 2021	Oct 01–Oct 09	881.47*	Oct 09–Oct 12	484.77	Oct 12–Oct 25	939.02*	Oct 25–Oct 31	410.56*
Omicron Outbreak Period[7]								
Fourth wave of the Pandemic[8]								
November 2021	Nov 01–Nov 21	319.58*	Nov 21–Nov 24	7387.93*	Nov 24–Nov 30	2745.02*		
December 2021	Dec 01–Dec 08	12946.85*	Dec 08–Dec 17	22999.61*	Dec 17–Dec 25	16088.39*	Dec 25–Dec 31	8362.44*
January 2022	Jan 01–Jan 03	3231.07	Jan 03–Jan 07	9910.07*	Jan 07–Jan 15	5211.54*	Jan 15–Jan 31	3144.03*
February 2022	Feb 01–Feb 18	2600.98*	Feb 18–Feb 28	2070.54*				
March 2022	Mar 01–Mar 12	1550.55*	Mar 12–Mar 31	1320.08*				

[1] Trends analysis identified joinpoints, which are points where line segments of the COVID-19 cases trends are joined. Each joinpoint denotes a statistically significant ($P = 0.05$) change in the trends of the COVID-19 total cases in South Africa from November 2020 to March 2022.
[2] β is the estimated regression coefficient for a specific trend; β was calculated from the data-driven Bayesian Information Criterion (BIC) method for the joinpoint model.
[3] Beta outbreak period was considered from the prior month when the Beta variant of SARS-CoV-2 had discovered by scientists in South Africa on December 18, 2020, to March 2021.
[4] The tentative duration of the second wave (November 2020–March 2021) was determined from the line graph of the daily cases in South Africa and in the line graph, the visible surge in new cases followed by a decline was considered.
[5] Delta outbreak period was considered from the prior month when the earliest documented sample with Delta variant of SARS-CoV-2 was identified in South Africa (May 08, 2021) to the prior month of the earliest documented sample with Omicron variant of SARS-CoV-2 reported in (November 2021).
[6] The tentative duration of the third wave (April 2021–October 2021) was determined from the line graph of the daily cases in South Africa and in the line graph, the visible surge in new cases followed by a decline was considered.
[7] Omicron outbreak period was considered from the month when the earliest documented sample with the Omicron variant of SARS-CoV-2 was reported in South Africa (November 09, 2021) to the last reported date of this analysis (March 31, 2022).
[8] This is an ongoing wave during our analysis. The tentative duration of the fourth wave (November 2021 to continue) was determined from the line graph of the daily cases in South Africa and in the line graph, the visible surges in new cases expected to be followed by a decline was considered.
* Denotes that the estimated regression coefficient (β) was significantly different from 0 for a specific trend ($P < 0.05$) in the COVID-19 cases trends in South Africa.

compared the peak growth of incidence (average cases/day) during the Omicron outbreak period with the Beta and delta outbreak period, we found that peak growth in COVID-19 cases during the Omicron outbreak period was 1.2 times higher than the peak growth during Delta outbreak period. Initially, during the Omicron outbreak period, much of this growth in cases occurred in the Gauteng province, home to Johannesburg [4]. In late-November 2021, South Africa's National Institute for Communicable Diseases in Johannesburg determined the epidemic's growth in Gauteng that each infection seeded above two new cases which were below one in September 2021 [4]. A retrospective analysis of the routine epidemiological data of South Africa suggested that in comparison with Beta and Delta variants, the Omicron variant of SARS-CoV-2 might have been associated with an increased risk of reinfection after a prior infection [16]. Moreover, this Omicron variant seems able to infect or re-infect three to six times as many people as the Delta variant of Sars-CoV-2 [17]. This might have caused the sudden shift in the COVID-19 cases in South Africa during the first half of December 2021. We found that the growth in COVID-19 cases in South Africa crested on an average of 23,000 cases/day between December 08 and December 17, 2021 during the Omicron outbreak period. There is a chance that the crest may be chopped off by testing capacity and more underreporting compared to previous waves [18]. Since December 17, 2021, growth in COVID-19 cases slowed down in South Africa. Compared to other variants outbreak period, in the omicron outbreak period cases peaked at a much faster period which indicates its probable high transmissibility in South Africa. Another possible aspect of the high transmissibility in South Africa is their low level of vaccine coverage. During the onset of Omicron, on November 23, 2021, the vaccination level of South Africa was just 27.9 % [10]. Therefore, with this, the spread/diffusion of Omicron may be high due to low vaccination levels in South Africa during the onset of Omicron.

Currently, there is insufficient data to evaluate with confidence the severity of disease caused by the Omicron variants of SARS-CoV-2 in comparison with other prevalent variants. However, Omicron seems less severe in South Africa compared to Beta and Delta variants of SARS-CoV-2 [19] based on the death rate, hospitalization rate, proportion of patients requiring intensive care, and oxygen therapy data reported in studies. During the Omicron outbreak period, although South Africa had the highest growth in COVID-19 cases compared to other variants' outbreak period, death trends were found significantly lower during this period. During the Beta outbreak period of the pandemic in South Africa, death tolls peaked in January 2021 at a dire 534 death/day. During the Delta outbreak period, the death rate peaked between July 19 and July 31, 2021 at 400 deaths/day. During the Omicron outbreak period, data from the Gauteng province, South Africa, indicate an increase in hospital

Table 2
Trends in deaths due to the COVID-19 in South Africa from November, 2020 to March, 2022 [1].

	Trend 1		Trend 2		Trend 3		Trend 4	
	Period	β[2]	Period	β[2]	Period	β[2]	Period	β[2]
Beta Outbreak Period[3]								
Second wave of the Pandemic[4]								
November 2020	Nov 01–Nov 15	60.12*	Nov 15–Nov 27	93.90*	Nov 27–Nov 30	50.32*		
December 2020	Dec 01–Dec 09	114.54*	Dec 09–Dec 20	194.43*	Dec 20–Dec 28	306.90*	Dec 28–Dec 31	451.63*
January 2021	Jan 01–Jan 31	532.46*						
February 2021	Feb 01 –Feb 03	467.29*	Feb 03–Feb 12	249.86*	Feb 12–Feb 18	177.19*	Feb 18–Feb 28	137.87*
March 2021	Mar 01–Mar 26	98.25*	Mar 26–Mar 31	50.29*				
Delta Outbreak Period[5]								
Third wave of the Pandemic[6]								
April 2021	Apr 01–Apr 06	24.42*	Apr 06–Apr 24	60.11*	Apr 24–Apr 30	41.58*		
May 2021	May 01–May 09	46.38*	May 09–May 17	69.02*	May 17–May 31	86.16*		
June 2021	Jun 01–Jun 07	71.85*	Jun 07–Jun 20	127.25*	Jun 20–Jun 28	171.67*	Jun 28–Jun 30	263.98*
July 2021	Jul 01–Jul 19	358.11*	Jul 19–Jul 31	399.03*				
August 2021	Aug 01–Aug 18	352.56*	Aug 18–Aug 31	303.84*				
September 2021	Sep 01–Sep 17	203.65*	Sep 17–Sep 30	129.61*				
October 2021	Oct 01–Oct 04	36.53*	Oct 04–Oct 09	94.69	Oct 09–Oct 31	41.88*		
Omicron Outbreak Period[7]								
Fourth wave of the Pandemic[8]								
November 2021	Nov 01–Nov 17	27.87*	Nov 17–Nov 22	12.30*	Nov 22–Nov 25	55.42*	Nov 25–Nov 30	17.84*
December 2021	Dec 01–Dec 18	25.10*	Dec 18–Dec 24	73.55*	Dec 24–Dec 28	29.84*	Dec 28–Dec 31	96.50*
January 2022	Jan 01–Jan 04	74.26*	Jan 04–Jan 07	274.88*	Jan 07–Jan 16	124.06*	Jan 16–Jan 31	118.16*
February 2022	Feb 01–Feb 06	124.97*	Feb 06–Feb 16	164.79*	Feb 16–Feb 19	343.27*	Feb 19–Feb 28	83.10*
March 2022	Mar 01–Mar 11	27.70*	Mar 11–Mar 15	5.42	Mar 15–Mar 18	42.36*	Mar 18–Mar 31	12.24*

[1] Trends analysis identified joinpoints, which are points where the line segment of the COVID-19-related deaths trends are joined. Each joinpoint denotes a statistically significant (P = 0.05) change in the trends of COVID-19-related deaths in South Africa from November 2020 to March 2022.
[2] β is the estimated regression coefficient for a specific trend; β was calculated from the data-driven Bayesian Information Criterion (BIC) method for the joinpoint model.
[3] Beta outbreak period was considered from the prior month when the Beta variant of SARS-CoV-2 had discovered by scientists in South Africa on December 18, 2020, to March 2021.
[4] The tentative duration of the second wave (November 2020–March 2021) was determined from the line graph of the daily cases in South Africa and in the line graph, the visible surges in new cases followed by a decline was considered.
[5] Delta outbreak period was considered from the prior month when the earliest documented sample with Delta variant of SARS-CoV-2 was identified in South Africa (May 08, 2021) to the prior month of the earliest documented sample with Omicron variant of SARS-CoV-2 reported in (November 2021).
[6] The tentative duration of the third wave (April 2021–October 2021) was determined from the line graph of the daily cases in South Africa and in the line graph, the visible surge in new cases followed by a decline was considered.
[7] Omicron outbreak period was considered from the month when the earliest documented sample with the Omicron variant of SARS-CoV-2 was reported in South Africa (November 09, 2021) to the last reported date of this analysis (March 31, 2022).
[8] This is an ongoing wave during our analysis. The tentative duration of the fourth wave (November 2021 to continue) was determined from the line graph of the daily cases in South Africa and in the line graph, the visible surge in new cases expected to be followed by a decline was considered.
[*] Denotes that the estimated regression coefficient (β) was significantly different from 0 for a specific trend ($P < 0.05$) in the COVID-19 related deaths in South Africa.

admissions of COVID-19 cases, from 153 cases in week 45–2201 cases in week 48, and in deaths, from 18 deaths in week 45–83 deaths in week 49 [20]. This increase was associated with the increasing prevalence of the Omicron variant among the reported COVID-19 cases [7]. According to an analysis of 211, 000 COVID-19-positive cases during the Omicron outbreak, adults were experiencing a 29 % lower admission risk, adjusted for vaccination status, relative to South Africa's first wave of infection [21]. In a recent preprint, authors found that people diagnosed with Omicron in South Africa between October and November 2021 were 80 % less likely to be admitted to hospital than those diagnosed with another variant in the same period [22]. The proportion of patients requiring oxygen therapy (17.6 % vs. 74.0 %) and admission to intensive care (18.5 % vs. 29.9 %) reduced significantly during the Omicron outbreak period compared to the Delta period [23]. Moreover, the median length of stay in the hospital decreased to 3 days in the Omicron outbreak period as opposed to 7–8 days during the other outbreak periods. There was a marked decrease in the death rate during the Omicron outbreak period (2.7 %) as compared to Delta (29.1) and the first wave of COVID-19 (19.7 %) in South Africa [23]. Before omicron hit South Africa, the population as a whole had built up a considerable amount of immunity against SARS-CoV-2. Maybe, a large proportion of people who were once at higher risk of severe disease during the earlier time of the pandemic, are now probably at lower risk [19,24].

The positive story of reduced severity of Omicron in South Africa may not be generalized to other countries. As what is unclear is whether the picture will be similar in countries where there were high levels of vaccination but low levels of previous infection [25]. However, panic and havoc started in the rest of the world in the late-November 2021. The number of countries reporting Omicron variant cases continued to increase globally. On December 01, 2021, a total of 352 confirmed cases were reported by 27 countries and 70 confirmed cases were reported by 13 European Union and European Economic Area (EU/EEA) countries [26] which jumped to a total of 4691 confirmed cases in the EU/EEA countries as of December 19, 2021 [27]. The majority of confirmed cases had a history of travel to southern African countries, with some having taken connecting flights at other destinations between Africa and Europe. Several European countries had reported subsequent household or community transmission [26]. An analytical report from the Imperial College of London COVID-19 response team estimated that Omicron had a 5.4 times greater risk of reinfection compared to the Delta variant in England [28]. This implies that past infection can provide only 19 % protection against reinfection by Omicron [29]. The Omicron variant of SARS-CoV-2 displays a significant growth advantage

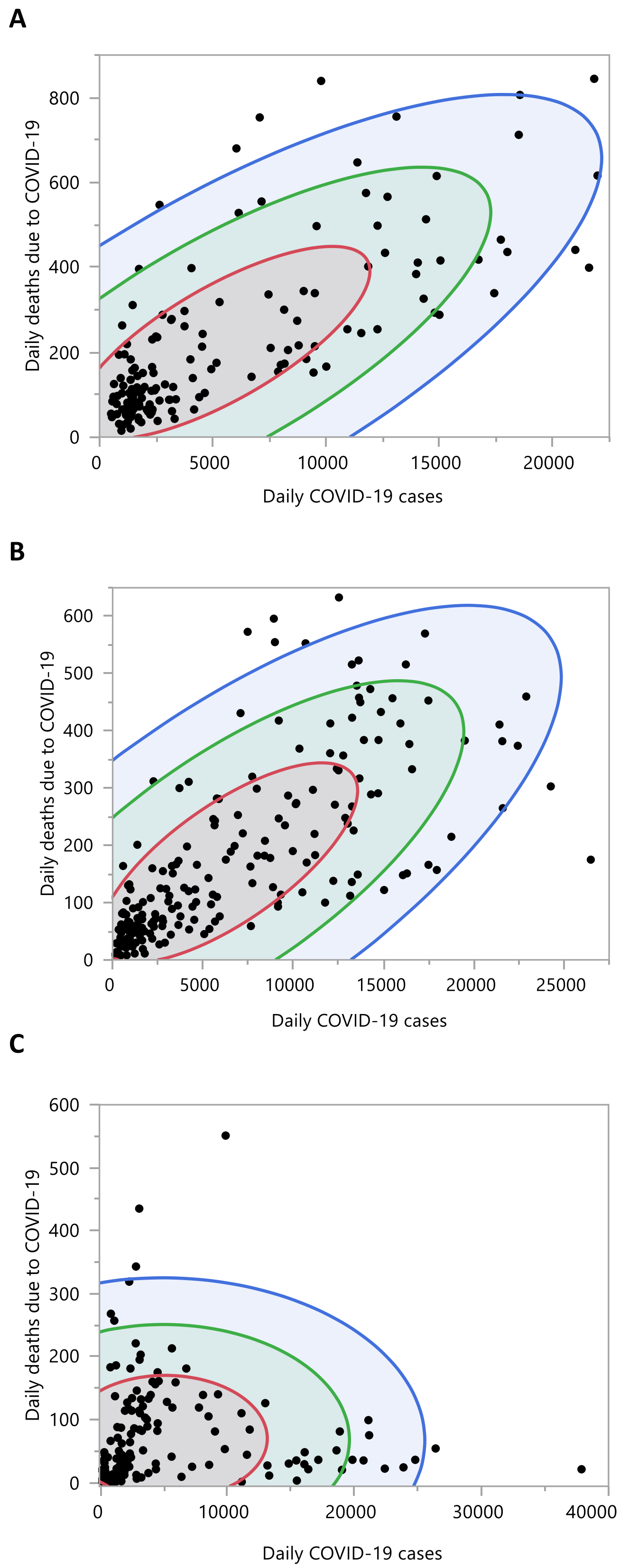

Fig. 1. Density ellipses to assess the correlation between daily deaths and daily cases segregated on A. Beta (B.1.351), B. Delta (B.1.617.2), and C. Omicron (B.1.1.529) outbreak periods. Red line with red contour represents the 50 %, green line with the green contour represents the 90 %, and blue line with blue contour represents the 99 % probability plots around the data points.

over the Delta variant. Data from South Africa and UK showed Omicron's rapid growth over the Delta variant [7].

Nonetheless, our study has several major limitations. One of the major analytical lackings we had was that we did not adopt and consider the methods to control for reporting and case-to-death distribution delays. We did not have any prior information about this in South Africa. The variations in the reporting and testing system capacity within a country in different periods made the identification of the true time more complicated. In this current analysis, we had not considered this delayed response. Another limitation is the interpretation of the results lacks the integration of post-infection and post-vaccine immunity as well as intrinsic virulence differences between variants. These limitations are due to the lack of sufficient data regarding these parameters and are out of our scope of analysis. Even though through the joinpoint regression analysis, we could detect the turning points of the outbreak but the causal relationship of this turning point with factors cannot be established and our results require further confirmation with individual-level data. Moreover, there is a possible overlap among the three outbreaks which cannot be detected through the joinpoint analysis. Our finding should not be generalized to other countries as COVID-19 severity and mortality vary enormously depending on the country, the prevalence of vaccination, the population's characteristics including age, socio-economic level or co-morbidities, medical management guidelines, or the number of simultaneous cases leading to the saturation of the health system [30]. In our analysis, we have not considered these vital issues while doing the trend analysis. We are unable to incorporate possible confounding factors in our trend analysis model due to the unavailability of incorporating options. Large-scale case-control studies, controlled for as many of these factors as possible, are essential to seriously investigate clinical severity [8]. In addition, we were highly deficient in explaining the possible drivers that might have acted to change the trends during this outbreak. Many factors together with their interplay might have affected the changes in the trends. For this research, we have extracted the data from the COVID-19 data repository by the Johns Hopkins University Center for System and Science and Engineering and matched it with the information provided on the official website of the National Department of Health of the Republic of South Africa. In the data compilation stage, we found a mismatch in the daily case report on November 23, 2021. The official COVID-19 statistics statement from the National Department of Health of the Republic of South Africa reported 868 new cases on November 23, 2021, but the actual value should be 18,586 new cases based on our calculation. This mismatch in the Government report we could not solve, and we did our trend analysis by considering the value based on our calculation.

Despite these limitations, this is the first-ever study in the scientific literature that provided the trends and significant changes in the COVID-19 outbreak in South Africa during the Omicron, Delta, and Beta outbreak period. We reported the recent ongoing trends of the outbreak caused by the Omicron variant of SARS-CoV-2 in South Africa and compared it with the Delta and Beta variants. In summary, during the Omicron outbreak period, COVID-19 cases in South Africa increased from October 24, 2021, which significantly jumped by 4.7 times since December 01, 2021. From December 08 to December 17, 2021, the Omicron variant induced growth rate of incidence peaked which was till now the highest in the COVID-19 pandemic in South Africa Comparatively higher daily death tolls were reported in the days with a recovery rate of less than 89.1 % and 91.9 % in the Beta and Delta outbreak period respectively. The emergence of the Omicron variant once again reminds us that- "no one is safe until everyone is safe". Moreover, it's an unavoidable actuality and an

Table 3
Partition models parameter using decision tree method on the daily cases and daily deaths data segregated on the Beta, Delta and Omicron outbreak periods in South Africa [a].

	N	Death/day[b]	LogWorth[c]	R^2[b]	AICs[d]
Beta Outbreak Period[e]					
Recovery rate ≥ 89.11 %	103	126.6 ± 90.4	5.924	0.533	1907.7
Recovery rate < 89.11 %	48	427.6 ± 194.1	2.128		
Case/day < 5297	100	124.7 ± 90.0	3.531	0.507	1915.9
Case/day ≥ 5297	51	413.7 ± 197.3	1.765		
Percent positivity[f] < 17.23 %	119	162.6 ± 138.5	2.868	0.359	1955.3
Percent positivity[f] ≥ 17.23 %	32	444.3 ± 205.1	0.919		
Delta Outbreak Period[g]					
Recovery rate ≥ 91.92 %	133	83.1 ± 63.9	10.126	0.565	2573.5
Recovery rate < 91.92 %	81	312.1 ± 136.6	0.211		
Case/day < 5574	120	75.3 ± 57.4	10.189	0.521	2594.1
Case/day ≥ 5574	94	290.3 ± 140.9	2.185		
Percent positivity[f] < 16.20 %	133	118.2 ± 122.9	0.899	0.200	2703.8
Percent positivity[f] ≥ 16.20 %	81	254.5 ± 147.6	0.919		
Omicron Outbreak Period[h]					
Recovery rate ≥ 96.31 %	59	31.4 ± 38.9	0.903	0.152	1744.9
Recovery rate < 96.31 %	92	97.8 ± 93.7	1.913		
Case/day < 2111	66	38.2 ± 55.3	0.651	0.127	1749.2
Case/day ≥ 2111	85	98.1 ± 92.1	3.012		
Percent positivity[f] < 15.94 %	63	26.9 ± 27.2	0.411	0.209	1734.4
Percent positivity[f] ≥ 15.94 %	88	104.0 ± 94.7	5.304		
Backlog count[i] = No	131	56.5 ± 67.5	––[j]	0.223	1731.7
Backlog count[i] = Yes	20	172.4 ± 107.6	––[j]		

[a] Using the analysis platform, we conducted only one split over the dataset. We used decision tree method of the partition model to make a single pass through our dataset to produce a single portioned tree.
[b] COVID-19 related deaths per day were reported as mean ± SD values on the partitioned daily cases groups.
[c] LogWorth values reported after one split; node splitting is based on the LogWorth statistic; values gives an idea about further splitting on an arm will be done on which variable basis.
[d] AICs denote the corrected Akaike's Information Criteria.
[e] Beta outbreak period was considered from the prior month when the Beta variant of SARS-CoV-2 had discovered by scientists in South Africa on December 18, 2020, to March 2021.
[f] Percent positivity denotes the percentage of people tested positive for SARS-CoV-2 on a given day.
[g] Delta outbreak period was considered from the prior month when the earliest documented sample with Delta variant of SARS-CoV-2 was identified in South Africa (May 08, 2021) to the prior month of the earliest documented sample with Omicron variant of SARS-CoV-2 reported in (November 2021).
[h] Omicron outbreak period was considered from the month when the earliest documented sample with Omicron variant was reported in South Africa (November 09, 2021) to the last reported date of this analysis (March 31, 2022).
[i] Since January 06, 2022, the Department of Health of the Republic of South Africa had been recorded and reported COVID-19 death backlog as an ongoing audit exercise across the country to address a backlog of COVID-19 mortality.
[j] Values are not available for this parameter.

almost iron-clad law: the pandemic will not come to an end while vaccine justice and equity are pushed to the margins [31].

Declaration of Competing Interest

The authors declare no conflict of interest.

Acknowledgments

We are very grateful to all the healthcare professionals all over the world for their enormous sacrifice and fight for the lives of patients who are giving us protection against SARS-CoV-2 irrespective of variants. We would like to express our immense gratitude to the Johns Hopkins University Center for System and Science and Engineering which is also supported by ESRI living Atlas Team and Johns Hopkins University Applied Physic Lab. We also like to express our immense gratitude to the University of Oxford team for their Our World in Data COVID-19 vaccination dataset. Without their brilliant compilation of these huge data sources, this study would not have been possible. We are very grateful to all who are behind this innovation and compilation. We extend our thanks to the contributors of this compilation- Hongru Du, A Katz, Tamara Goyea, Yuhang Zhang, Energeticodefish, cancername, and Arthur Zhang. We express our immense gratitude to Ms Joann Kozai for her kind help to edit our revised manuscript.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jiph.2022.05.011.

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