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Epidemiological characteristics of the three waves of COVID-19 epidemic in Taiwan during April 2022 to March 2023

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KEYWORDS
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Background: Taiwan experienced a relatively low incidence of COVID-19 before 2022. However, from April 2022 to March 2023, the country was struck by a nationwide outbreak that occurred in three waves. Despite the considerable magnitude of the epidemic, the epidemiological characteristics of this outbreak have yet to be clearly understood.
Methods: This was a nationwide, population-based, retrospective cohort study. We recruited patients who had been confirmed as domestically-acquired COVID-19 patients from April 17, 2022, to March 19, 2023. The three epidemic waves were analyzed in terms of numbers of cases, cumulative incidence, numbers of COVID-19-related deaths, mortality, gender, age, residence, SARS-CoV-2 variant sub-lineages, and reinfection status.
Results: The numbers of COVID-19 patients (cumulative incidence per million population) were 4,819,625 (207,165.3) in the first wave, 3,587,558 (154,206.5) in the second wave, and 1,746,698 (75,079.5) in the third wave, showing a progressive decline. The numbers of COVID-19-related deaths and mortalities also decreased throughout the three waves. The coverage of vaccination was observed to increase over time.
Conclusion: During the three waves of COVID-19 epidemic, the numbers of cases and deaths gradually declined, while the vaccine coverage increased. It may be appropriate to consider easing restrictions and returning to normality. However, continued monitoring of the epidemiological situation and tracking the emergence of new variants are crucial to prevent the possibility of another epidemic.
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Abbreviations: COVID-19, Severe Pneumonia with Novel Pathogens; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; Taiwan CDC, Taiwan Centers for Disease Control; CECC, Central Epidemic Command Center; NIDRS, National Infectious Disease Reporting System.

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Introduction

Since the emergence of Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the global pandemic has resulted in more than 760 million reported cases and 6.9 million deaths.[1]

At the end of 2019, Taiwan was alerted to an atypical pneumonia outbreak with unknown pathogen in Wuhan, China, and responded promptly. On January 15, 2020, the government declared "Severe Pneumonia with Novel Pathogens" (COVID-19) as a "Category Five" notifiable communicable disease.[2] All patients confirmed with COVID-19 infection must be reported to Taiwan Centers for Disease Control (Taiwan CDC) within 24 hours. On January 20, Taiwan activated the Central Epidemic Command Center (CECC) to coordinate the national pandemic response efforts.[3]

During January 2020 to April 2021, through a combination of strict border quarantine, test and isolation, as well as non-pharmaceutical interventions, there were only 90 confirmed cases of domestically-acquired COVID-19 out of 208,351 individuals got tested.[4,5] However, beginning in May 2021, it was the first community outbreak occurred in the Taipei region, caused by the Alpha variant, the daily number of cases increased rapidly, exceeding 100 within a week.[6] To strengthen control measures for this outbreak, the CECC raised the COVID-19 warning to Level 3 nationwide on May 19.[7] With the aid of public compliance, active case finding, and contact tracing, the outbreak was successfully contained within three months without lockdowns.[6,8] The warning level was subsequently downgraded to Level 2 on July 26, 2022.[9] Thereafter, although sporadic clusters or events were linked to the Delta variant, they did not lead to large-scale outbreaks.[10]

In late 2021, a newly emerged variant of SARS-CoV-2, known as Omicron, was disseminated globally and was found to possess increased transmissibility.[11] It was introduced into Taiwan and led to a rapidly and extensively outbreak throughout the country in April 2022. The epidemic progressed through three waves, each dominated by different sub-lineages of the Omicron variant. Till early 2023, the epidemic was gradually decline and reached a state of stability.

Prior to 2022, Taiwan had experienced a relatively limited incidence of COVID-19. However, from April 2022 to March 2023, the country was struck by a nationwide outbreak that occurred in three distinct waves. Despite the scale and scope of this epidemic, the underlying epidemiological characteristics remained unclear. Gaining a better understanding of the patterns and trajectory of this outbreak could be beneficial in preparing for future epidemics.

Methods

Study design and case definition

This was a nationwide, population-based, retrospective cohort study. A COVID-19 patient was defined as a person with laboratory confirmation of SARS-CoV-2 infection by reverse transcription polymerase chain reaction (RT-PCR) or with positive rapid antigen test confirmed by a medical doctor (implemented after May 26, 2022).[12] We recruited COVID-19 patients confirmed from April 17, 2022 to March 19, 2023, and excluded imported cases. In this study, death patients referred specifically to patients whose cause of death was attributed to COVID-19. COVID-19-related death was determined when the death certificate listed COVID-19 as an immediate cause or underlying cause of death. Additionally, any deaths in which COVID-19 was reported as a contributing factor on the death certificate were further reviewed by an expert committee.[13,14] All patients were followed up till April 14, 2023.

Three waves of epidemic

To mitigate the weekend effect, we aggregated the data into weekly intervals to present the epidemic trends. The initiation of each epidemic wave was determined by the week with the number of new cases exceeded 10,000 patients or the subsequent week when the number of new cases reached its lowest point. We divided the domestic epidemic into three waves: the first wave was from April 17, 2022 to August 12, 2022 (Week 16-Week 32); the second wave was from August 13, 2022 to December 10, 2022 (Week 33-Week 49); the third wave was from December 11, 2022 to March 19, 2023 (2022 Week 50—2023 Week 11). After March 20, 2023, CECC declared the notification criterium for COVID-19 was adjusted for only patients with associated complications.[15]

COVID-19 reinfection

The definition of COVID-19 reinfection was according to CECC announcement.[16,17] On July 1, 2022, the CECC declared a definition of reinfection as a COIVD-19 patient experienced another positive RT-PCR/rapid antigen test along with worsen symptoms within 3 months of their initial infection and confirmed by a medical profession; or a patient with another positive RT-PCR/rapid antigen test more than three months.[16] On October 3, 2022, it was revised that the time interval of two positive results was shorten to 14 days, and no need to evaluate the symptoms by a medical profession.[17] Proportion of reinfection was calculated as the number of reinfection patients divided by the number of confirm patients per week. Notably, the statistical count of COVID-19 cases was based on the number of infections. If one patient was confirmed infection for twice or more, he/she would be counted as two or more cases in the database.

Data sources

All patients confirmed with COVID-19 infection must be reported to Taiwan CDC via the National Infectious Disease Reporting System (NIDRS).[18] We retrieved the epidemiological data of COVID-19 confirmed cases from NIDRS database, including: notification report number, identity number (ID), birthday, age, gender, residence, confirm date, and date of death. Residence was categorized into six

regions, and the corresponding counties were shown in Supplementary Figure 1.[19]

Among confirmed cases, clinical specimens from patients who got positive results for RT-PCR testing were selected and sent to the National Reference Laboratory of Taiwan CDC for virus genome sequencing analysis to determine the lineage of SARS-CoV-2 variant strain.[20] The selection priority was given to certain categories of patients, such as imported cases, cluster cases, breakthrough infections, reinfections, and patients with unknown sources of infection.[20] We accessed the resulting database to explore the trends of variant strains.

The COVID-19 vaccination database was established by the National Immunization Information System (NIIS). All vaccination against COVID-19 of individuals was recorded in the database. To determine the vaccination coverage over the entire population, the number of individuals who received the vaccine, regardless of their citizenship status or infection status, was divided by the population size of Taiwanese citizens. However, the population count did not include non-citizens, meaning that the coverage percentage could potentially exceed 100%. We retrieved the weekly reports of COVID-19 vaccination statistics published by Taiwan CDC.[21]

Statistical analyses

The data analysis was mainly descriptive. Continuous variables were presented as medians and interquartile ranges (IQRs). Categorical variables were reported as counts, percentages and incidences. Incidence was calculated as the number of patients per week divided by the population size at the end of 2022, per million population.[22] Cumulative incidence was calculated as the number of patients during a specific period of time (wave) divided by the population size. Data cleaning, tabulation and figure plotting were conducted using R (version 4.2.2). The geographical illustration of incidence by county was analyzed using QGIS (version 3.10.12) software.

Ethical approval

This study was approved by the Institutional Review Board of Taiwan CDC (IRB No.112103), with a waiver of informed consent.

Results

There were 10,202,525 patients confirmed with COVID-19 infection during April 17, 2022 to March 19, 2023 in Taiwan. After excluding for 48,644 imported cases, we recruited 10,153,881 domestically-acquired COVID-19 patients in this study.

Throughout the three waves of COVID-19 epidemic, there was 43.6% of the population confirmed to have been infected with COVID-19 (Table 1). In the first wave, there were 4,819,625 patients, corresponding to a cumulative incidence rate of 207,165.3 cases per million population during a time interval of 118 days. This wave reached its peak after 6 weeks, with an average of 309,006 cases per week during the escalation period. The second wave contained 3,587,558 patients with the cumulative incidence of 154,206.5 cases per million population during a time interval of 120 days. It took 8 weeks to reach its peak, with average 246,362 cases per week. The third wave included 1,746,698 patients with the cumulative incidence of 75,079.5 cases per million population during a time interval of 98 days. It took 4 weeks to reach its peak, with average 145,164 cases per week (Table 1 and Fig. 1A). It was observed that the total number of cases, cumulative incidence rates, and average weekly cases during the growth periods all exhibited a gradual decline across the three waves. Notably, within the third wave, an additional peak was observed following the Chinese New Year holiday at the end of January 2023 (Fig. 1A). This spike was likely due to factors such as increased family gatherings or temporary closures of outpatient services during the holiday. By the end of the follow-up, there were 18,295 patients with COVID-19-related death and the mortality was 786.4 per million population. Across the three waves of epidemic, the numbers of COVID-19-related deaths (mortality per million population) were 8,978 (385.9), 5,235 (225.0), and 4,082 (175.5), respectively. It was observed that the numbers of deaths and mortalities during the three waves had declined (Fig. 1B).

In terms of geographic distribution, Taipei and the Northern regions had the highest cumulative incidence rates across three waves. Although the cumulative incidence in the Eastern region was relatively high during the first wave, it subsequently decreased to levels below the nationwide average in the following periods. Each region or county was observed to experience a decline in cumulative incidence across the three waves (Table 1 and Fig. 2).

Of the three waves examined, female patients outnumbered male patients (Table 1). However, the incidence rate of COVID-19 varied across age groups and fluctuated across waves. In the first wave, the highest incidence was observed among toddlers and children (aged 0—4 and 5—11). During the second wave, it shifted to children and teenagers (aged 5—11 and 12—17), while in the third wave, it was observed among teenagers and young adults (aged 12—17 and 18—49) (Table 1 and Fig. 3A). Notably, while the incidence in elderly patients was consistently lower than other populations, they are a high-risk group for developing sever symptoms or experiencing mortality.[23,24] It is crucial for the elderly population to receive full vaccination and adhere to recommended precautions.

During the April 2022 to March 2023 epidemic, domestic cases that were sequenced and analyzed were all found to be of the Omicron variant and its sub-lineages. In the first wave, the Omicron BA.2 dominated, accounting for 93.9% of cases. In the second wave, the Omicron BA.5 was predominant, representing 74.4% of cases. In the third wave, the Omicron BA.2.75 accounted for the majority of cases at 52.7%, followed by BA.5 at 29.4% and BQ.1 at 11.3%, and other variants such as BF.7 and XBB each accounted for less than 3% (Fig. 3B).

The definition of reinfection was announced on July 1, 2022 (Week 26).[16] Due to the limited scope of the epidemic prior to 2022, the number of patients experiencing reinfection in the first wave was 2,881 (0.1%). In the second wave, there was an increased number of reinfections,

Table 1 Epidemiological characteristics of the three waves of COVID-19 epidemic.

	First wave April 17, 2022—Aug 12, 2022			Second wave Aug 13, 2022—Dec 10, 2022			Third wave Dec 11, 2022—Mar 19, 2023			Total April 17, 2022—Mar 19, 2023		
	Cases	%	Cumulative incidence (per million population)	Cases	%	Cumulative incidence (per million population)	Cases	%	Cumulative incidence (per million population)	Cases	%	Cumulative incidence (per million population)
N	4,819,625		207,165.3	3,587,558		154,206.5	1,746,698		75,079.5	10,153,881		436,451.2
Gender												
Male	2,280,934	47.3	198,357.0	1,649,403	46.0	143,437.1	793,215	45.4	68,980.4	4,723,552	46.5	410,774.5
Female	2,537,794	52.7	215,697.9	1,937,550	54.0	164,680.6	952,970	54.6	80,997.0	5,428,314	53.5	461,375.4
Unknown	897	0.02	NA	605	0.02	NA	513	0.03	NA	2015	0.02	NA
Age group (years)												
Median (IQR)	37 (29)			37 (31)			38 (29)			37 (29)		
0—4	236,813	4.9	291,737.6	132,200	3.7	162,861.4	64,681	3.7	79,682.6	433,694	4.3	534,281.6
5—11	404,590	8.4	278,552.3	298,012	8.3	205,175.4	117,542	6.7	80,925.4	820,144	8.1	564,653.1
12—17	237,479	4.9	203,327.0	283,110	7.9	242,395.8	103,240	5.9	88,393.0	623,829	6.1	534,115.7
18—49	2,581,831	53.6	246,390.9	1,877,136	52.3	179,140.0	938,933	53.8	89,604.8	5,397,900	53.2	515,135.7
50—64	818,330	17.0	155,337.6	587,553	16.4	111,530.9	296,797	17.0	56,338.8	1,702,680	16.8	323,207.2
65—74	344,270	7.1	132,134.9	260,618	7.3	100,028.2	138,432	7.9	53,131.8	743,320	7.3	285,294.9
75 +	196,312	4.1	132,612.0	148,929	4.2	100,604.0	87,073	5.0	58,819.2	432,314	4.3	292,035.2
Residence												
Taipei region	1,697,505	35.2	228,095.0	1,231,568	34.3	165,486.7	585,586	33.5	78,685.6	3,514,659	34.6	472,267.2
Northern region	861,819	17.9	223,874.0	658,905	18.4	171,163.2	344,008	19.7	89,362.7	1,864,732	18.4	484,399.8
Central region	878,136	18.2	193,452.2	698,424	19.5	153,861.8	321,137	18.4	70,746.0	1,897,697	18.7	418,060.0
Southern region	545,768	11.3	166,994.9	432,689	12.1	132,394.8	216,293	12.4	66,181.7	1,194,750	11.8	365,571.4
Kaohsiung-Pingtung region	715,158	14.8	196,793.0	488,380	13.6	134,389.5	250,588	14.3	68,955.3	1,454,126	14.3	400,137.8
Eastern region	121,239	2.5	228,131.7	77,592	2.2	146,002.5	29,086	1.7	54,730.2	227,917	2.2	428,864.4
Reinfection												
Infected two times	2,879	0.1	123.8	82,704	2.3	3,554.9	158,762	9.1	6,824.2	244,345	2.4	10,502.8
Infected more than two times	2	0.00	0.1	469	0.01	20.2	3,018	0.2	129.7	3,489	0.03	150.0

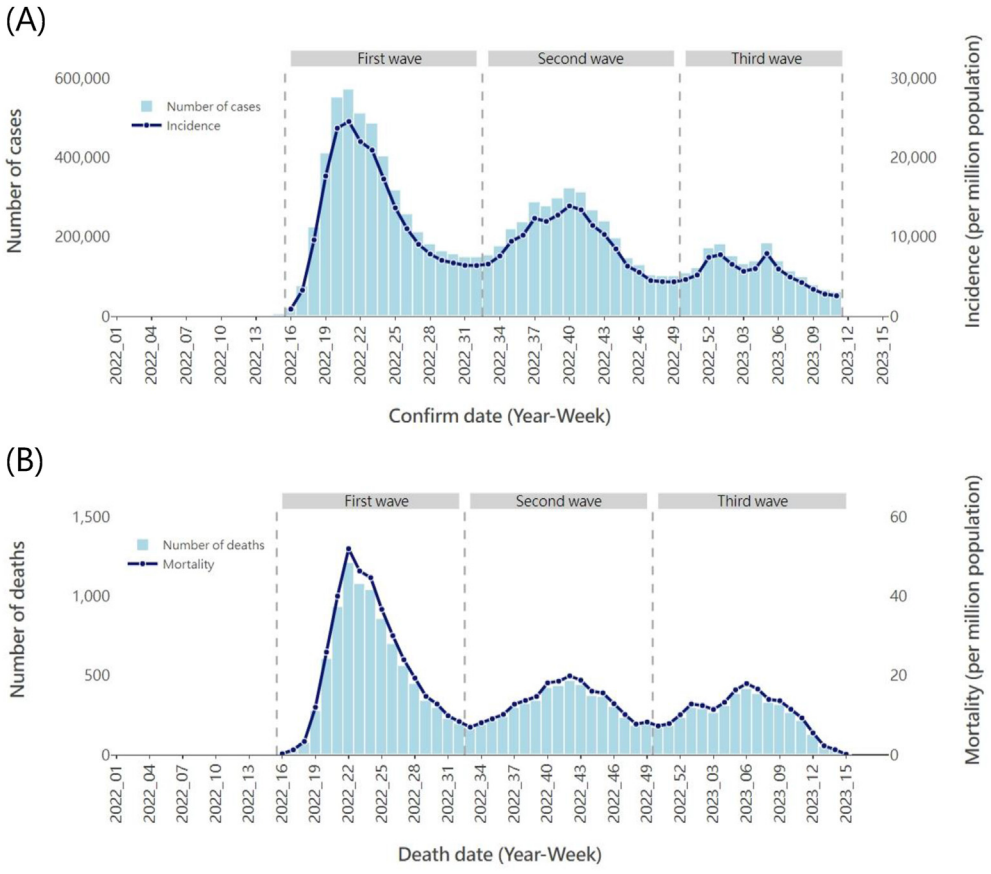

Figure 1 (A) Number of COVID-19 patients by confirm date; (B) Number of COVID-19-related deaths by death date.

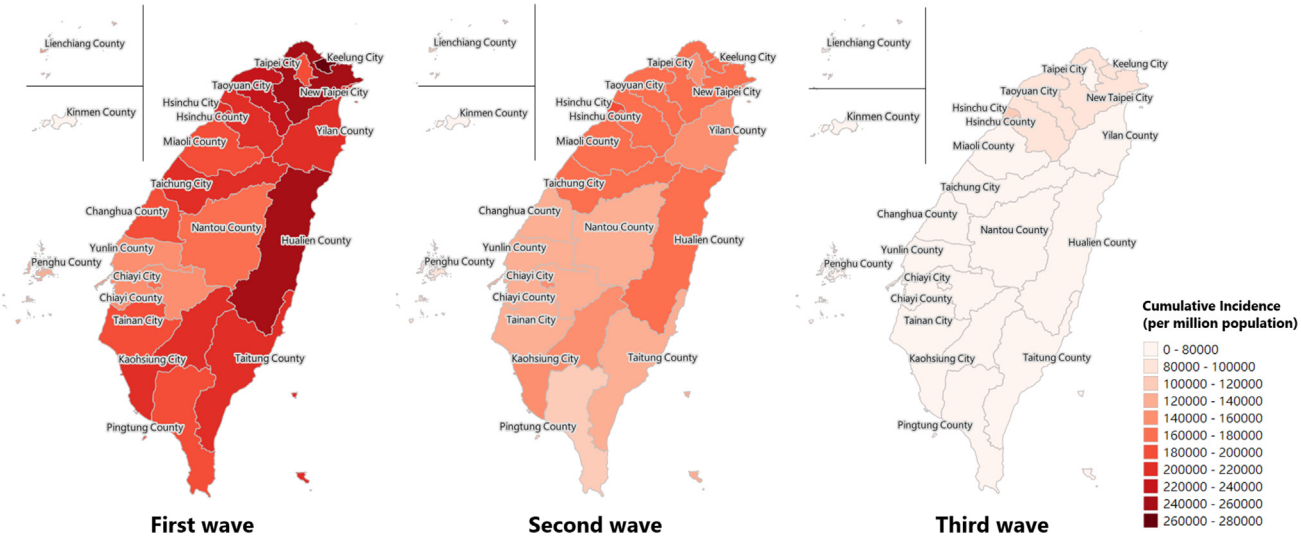

Figure 2 COVID-19 cumulative incidence rate of county during the three waves of COVID-19 epidemic.

which amounted to 83,173 (2.3%). Subsequently, the cases surged to 161,780 (9.3%) during the third wave. Among all of the reinfection patients, 1.4% of them contracted the virus more than twice (Table 1 and Fig. 3C).

The vaccination coverage was a nationwide statistic that represented the proportion of individuals who have received the COVID-19 vaccine, regardless of whether they were confirmed COVID-19 cases. Given the diversity of vaccination regimens, brands, target populations, and immunization schedules, we demonstrated a general timeline of vaccination campaign for each group and collected vaccination coverage data at the onset of each wave. For toddlers (aged 6 months to 4 years), the vaccine campaign was initiated on July 21, 2022, (Week 29) following a

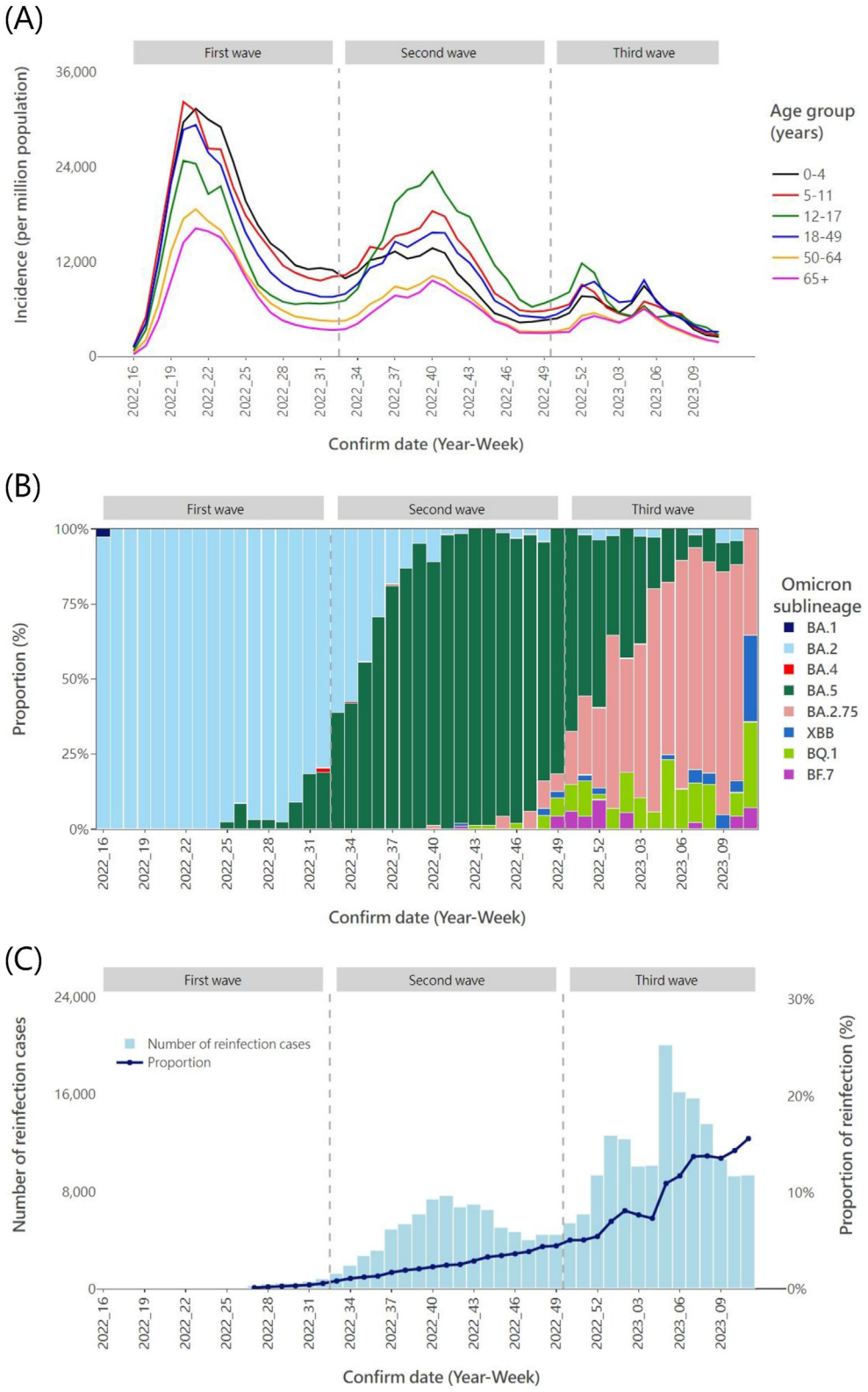

Figure 3 (A) COVID-19 incidence rate stratified by age group; (B) Proportion trend of SARS-CoV-2 variants; (C) Number and proportion trend of COVID-19 reinfection patients. (A) Due to the similar incidence rates among aged 65 to 75 and aged above 75 groups (Table 1), these two groups were combined into a single category labeled "65+" in Fig. 3A.

Table 2 Coverage of vaccination against COVID-19 among population, stratified by age group.

Age group	First wave (Apr 17 - Aug 12, 2022) Vaccination statistics as of Apr 18, 2022			Second wave (Aug 13 - Dec 10, 2022) Vaccination statistics as of Aug 15, 2022			Third wave (Dec 11, 2022—March 19, 2023)Vaccination statistics as of Dec 5, 2022[a]		
	First dose	Second dose	Booster	First dose	Second dose	Booster	First dose	Second dose	Booster
6m-4y	—	—	—	17.2%	—	—	45.2%	20.5%	—
5-11	—	—	—	76.8%	46.6%	—	85.1%	63.3%	0.4%
12-17	88.9%	80.8%	0.2%	94.7%	84.4%	58.0%	95.0%	87.9%	64.4%
18-49	100.3%	94.2%	63.5%	102.8%	98.9%	84.0%	102.9%	99.3%	86.7%
50-64	88.5%	84.3%	65.5%	91.4%	88.3%	78.4%	91.6%	88.7%	80.6%
65+	84.5%	79.9%	66.4%	87.5%	84.0%	74.9%	88.4%	85.1%	77.8%
75+	78.2%	72.1%	57.6%	82.0%	77.1%	66.5%	83.5%	78.8%	70.4%

*Blank fields indicate that the COVID-19 vaccine was not yet available for that particular group or that there was insufficient time between doses (see the last paragraph of Results for details).

[a] The vaccination statistics was modified after Dec 5, 2022, with not including non-citizens. Therefore, the data regarding the third wave was obtained on December 5, 2022.

recommendation that primary series with an interval of at least 4—8 weeks by the Advisory Committee on Immunization Practices (ACIP) at the Ministry of Health and Welfare, Taipei, Taiwan.[25] Coverage of the first dose among them increased during the second wave and that of second dose raised in the third wave. For children (aged 5—11), the vaccine campaign started on May 25, 2022 (Week 21) following a recommendation that two-dose primary series and boosters with an interval of 5 months.[25] For teenagers (aged 12—17) and individuals above aged 18, the campaign for booster dose began on May 25, 2022 (Week 21) and January 7, 2022 (Week 1), respectively. It was observed that vaccination coverage was increasing in each group across three waves of the epidemic, with the highest coverage for each vaccine dose exhibiting among individuals aged 18—49 years. Among the elderly (aged 65+ and aged 75+), the booster coverage reached 70% in the third wave (Table 2).

Discussion

This was a nationwide cohort study describing the epidemic characteristics and trends across three waves of COVID-19 epidemic during April 2022 to March 2023 in Taiwan. It was observed that the numbers of COVID-19 cases and deaths were progressively decline, while the vaccination coverage was increasing.

The incidence of COVID-19 varied among different age groups, geographic regions and waves. This variation may be attributed to multiple and complicated factors, including transmissibility of the virus, vaccine coverage, social interactions, occupations, underlying health conditions, living environments, prevention and control policies, and other unknown factors.[26—29] Due to the presence of several unmeasured variables in this observational study, we were unable to establish the association between these factors and incidence rates. Nonetheless, we could observe certain trends and patterns in the epidemic situation. Generally, we found that counties/regions with high population density tend to have a higher cumulative incidence of COVID-19. For toddlers (aged 0—4) and children (aged 5—11) the incidence rates were the highest in the first wave, possibly be due to a lack of vaccine protection at that period. However, as vaccine coverage increased, the incidence decreased in subsequent waves.

The situation of patients obtaining self-testing or reporting their positive results was unclear in this study. Especially in the third wave, as the epidemic was declining and control measures were being relaxed with putting more emphasis on self-health management, patients with mild or asymptomatic cases may not have sought testing as frequently. Nevertheless, the accessibility for patients with severe symptoms to seek medical care and the criteria of evaluating COVID-19-related mortality remained unchanged.

The number and proportion of patients experiencing reinfection had increased during the second wave and especially in the third wave. Cases of patients being infected for more than twice were not rare either. It's noteworthy that most of these reinfection patients were infected SARS-CoV-2 Omicron twice but with different sublineages within several months. The risk factors and severity of them require further investigation.

The prevention and control policies implemented to combat against COVID-19 were constantly being modified to respond to the evolving epidemiological situation in Taiwan. As the epidemic gradually decreased, the government sought to strike a balance between preserving public health and promoting economic development, while simultaneously trying to return to normality.[30] Regarding the face mask mandate, it remained unchanged from level 3 alert in 2021 to July 2022 (amid the first wave), requiring individuals to wear masks at all times when going out, whether indoors or outdoors.[31] As the epidemic decreased, the regulations were gradually relaxed, beginning with outdoor activities (December 2022, amid the second wave) and later extending to indoor activities as well as in schools (February and March 2023, amid the third wave).[32—34] As for isolation and quarantine measures, the duration of the period was progressively shortened, with a greater emphasis on self-health management.[35] Prior to the COVID-19 outbreak in 2022, confirmed patients were required to be isolated and received medical care in hospitals.[36]

However, as the number of patients surged in May 2022, the policy was revised to allow adults with no or mild symptoms to self-isolate at home for 7 days, followed by another 7 days for self-health management (amidst the first wave).[37] Subsequently, in November 2022, the isolation period was reduced to 5 days, with the length of the self-health management period based on the results of at-home rapid tests (amid the second wave).[38] After March 20, 2023, COVID-19 was adjusted to be notifiable only for patients with associated complications, patients with no or mild symptom were no need to report or be isolated.[15] On the other hand, the provision of antiretroviral therapies and vaccination campaigns against COVID-19, both were government-funded, continued and even expanded. Confirmed COVID-19 patients with risk factors for developing severe conditions were eligible for free antiretroviral treatments.[39] In March 2023, the CECC launched "2023 National COVID-19 Vaccination Campaign" with its main theme being "Vaccine Plus One. Easing Restriction Safely" to enhance individual protection against COVID-19.[40]

There were some limitations in this study: First, the number and proportion of people who had positive results on at-home rapid antigen tests but not seeking medical confirmation were hard to be estimated. It needs further studies applying mathematical modeling analysis or seroprevalence surveys to explore this issue. Second, the sample of patients who had positive PCR specimens was not selected randomly for genome sequencing analysis. Instead, priority was given to certain categories of patients, such as imported cases, cluster cases, breakthrough infections, reinfections, and patients with unknown sources of infection.[20] Therefore, the representativeness of the entire population was uncertain. However, this approach allowed us to monitor the transmission of new variants within the community. Third, for this study, we did not have the accessibility to obtain data on the hospitalization rates and vaccination statuses of individual patients. As a result, we focused our analysis on describing the epidemiological characteristics of COVID-19 across three waves of the epidemic. While this constraint may have limited the scope of our findings, we considered that our descriptive analysis provided valuable insights into the overall patterns and trends of the disease. Nonetheless, future research with more comprehensive data could help to provide a more detailed understanding of the impact of COVID-19, including the effectiveness of vaccination efforts and the severity of the disease.

Throughout the three waves of the COVID-19 epidemic in Taiwan, there was a progressive decrease in numbers of patients and deaths, coinciding with an increase in the number of people receiving vaccinations. It may be appropriate to consider easing restrictions and measures as well as returning to normality. However, it is crucial to continue monitoring the epidemiological situation and tracking the emergence of new variants to prevent the possibility of another epidemic.

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Declaration of competing interest

The authors have no conflicts of interest relevant to this article

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jfma.2023.05.027.

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