

Impact of COVID-19 Epidemic on the Incidence and Mortality of Tuberculosis by Regions in Taiwan

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Research Article

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Abstract

Tuberculosis (TB) remains a significant health and public issue in many countries. Its incidence and mortality have been decreasing in many countries. The recent COVID-19 could have significant impacts on the transmission and health care for this chronic disease by obligatory facial masking and by affecting healthcare capacities. We asked whether the trend of TB incidence and mortality would be affected by COVID-19 epidemic due to their common air transmission route. We also asked whether the incidence of TB in regions with different COVID-19 incidence would be similar. We obtained the annual new cases of TB and multi-drug resistant TB through Taiwan CDC and estimated the incidence and mortality by the population numbers in 7 administrative regions in Taiwan in 2011–2021. The result showed that incidences of TB and multi-drug resistant TB in recent 10 years show a continuously decreasing trend, even amid the COVID-19 epidemic in 2020-21. In addition, the mortality of TB shows similar decreasing trend in 2020-21. From 2011–2011, the highest incidence of TB was in the southern and eastern Taiwan whereas the lowest incidence of TB was in northern Taiwan. In contrast, the highest incidence of COVID-19 in 2020-21 was in the northern Taiwan while the lowest incidence of COVID-19 in 2020-21 is in the southern and eastern Taiwan. These results indicated that in the low COVID-19 incidence regions of Taiwan, the incidence of TB remained high during COVID-19 pandemic. We concluded that the decreasing trend of incidence and mortality of TB does not change during COVID-19 epidemic in Taiwan. The mask wearing and social distancing could prevent the transmission of COVID-19, however, their effect on the limiting spread of TB may be limited.

Introduction

Tuberculosis (TB) remains a significant public health issue for the world. WHO estimated that 9.9 million individuals suffer from TB in 2020[5]. *Mycobacterium tuberculosis* (MTB) bacterium, a highly aerobic organism, causes TB [1]. Tuberculosis could be divided into active disease or latent disease, based on the presence or absence of clinical symptoms. Typical symptoms of active disease are productive cough with blood-containing sputum, night sweat, low grade fever, and weight loss [2, 3]. Tuberculosis could be transmitted by several routes with the air transmission is the most predominant one. The process by which bacilli are aerosolized is highly correlated with the coughing [4]. The incidence of TB varies from countries to countries. For instance, the highest rates (300 per 100,000 persons or higher) are observed in sub-Saharan Africa, but low rates (less than 25 cases per 100,000 persons) are seen in United States and in Japan [6]. Taiwan is affected by an intermediate TB burden with its incidence rate at 72.5 and 45.7 per 100,000 population in 2005 and 2015, respectively [7][8].

Due to special components in the cell wall of TB bacilli, there are increasing chances of the anti-TB drug resistance [9]. Clinically, it is appropriate to combine different types of antibiotics to treat active TB in order to lower the chance of antibiotics resistances [10]. Nonetheless, drug-resistant TB remains a main issue in the world, which may be attributed to poor drug compliance or using low-quality medication [11]. Multidrug-resistant tuberculosis (MDR-TB) is defined with resistance to the two most effective first-line TB drugs: rifampicin and isoniazid. Extensively drug-resistant TB (XDR-TB) is simultaneously resistant to

three or more of the six classes of second-line drugs [12]. The existence of drug-resistant TB indeed enhances the difficulty in preventing TB transmission. Through the Direct Observe Treatment (DOTs) and MDR-TB project (DOTS-Plus), drug compliance and medical availability have been greatly enhanced. From WHO global data report, there were 480,000 and 201,997 MDR-TB cases in 2013 and 2019, respectively. The total of drug resistant TB cases in 2020 were declined to 157,903. This result is similar with a large reduction (18%) in the total number of newly diagnosed TB cases between 2019 and 2020[13]. In Taiwan, MDR-TB has become a notifiable disease since 2006. The drug resistant rate in 2006 was higher than those reported by the third TB global drug resistance surveillance [15]. Implementation of the Multidrug-resistant Tuberculosis Consortium (TMTC) with DOTS-Plus program successfully reduces the incidence of MDR-TB continuously.

COVID-19, a novel pandemic disease, has claimed millions of lives since end of 2019. Its transmission is highly related to the spreading of its key pathogen, namely SARS-CoV-2 [16]. The main mode by which people are infected with SARS-CoV-2, similar to TB, is exposed to air droplets carrying the pathogen. These various-sized droplets are produced during exhalation, such as quiet breathing, singing, speaking, coughing, sneezing or exercise [17, 18, 19, 20].

Since 2019, all of the governments from different countries have paid much effort to the prevention of COVID-19 transmission by several restrictive and self-prevention policies, such as mask wearing, adaptation or closure of schools and businesses, limitations and restrictions on public and private gatherings, restrictions on domestic movement, international travel restrictions, and so on [21]. In Taiwan, most were imported cases until May, 2021, an outbreak of local cases from northern Taiwan [22]. The strict policies of the country border control were effective to prevent the viral transmission from imported cases. The strategies of limiting gatherings, restricting domestic movement, and facial mask wearing successfully curb this regional outbreak in Taiwan.

Based on previous reviews and researches, MTB could be transmitted by various-sized droplets, from large to fine or aerosol particles [23]. Mask wearing, surgical masks or N95 respirators, plays a crucial role in impeding the entrance of these contaminated droplets. The COVID-19 epidemic in 2020-21 provided an opportunity to address whether the transmission of MTB could be influenced by mandatory mask wearing and social distancing adopted by COVID-19 prevention measures during this specific period of COVID-19 pandemic. Moreover, the health care capacities and resources are largely occupied and consumed respectively during the major COVID-19 epidemic. It would be interesting to see whether the mortality rate of TB, that is related to the health care quality, would be increased or not during this period.

Method

All demographic data of TB and MDR-TB, including new reported cases per year and mortality from 2010 to 2021, were acquired from a public domain from the Taiwan National Infectious Disease Statistics System (NIDSS), Taiwan CDC (<https://nidss.cdc.gov.tw/>) (last updated in February 9, 2022) [24, 25, 26]. Based on the NIDSS statistical measurements, the regions were classified based on geographical

administration to seven groups, which included Taipei, Northern, Central, Southern, Kao-Pin, Eastern, and Outlying Islands, including the Pescadores, Quemoy, Matsu Islands, etc. For reporting to NIDSS, patients' residential regions were used rather than the regions where they were infected.

For estimation of the dynamic incidence of TB and MDR-TB, general population statistics (including the numbers of general population in each region) from 2010 to 2021 were obtained from the Taiwan Statistics Bureau [27] to estimate the national- and region-specific disease incidence. Microsoft Excel 2016 was used for statistical analysis. The association between TB incidence and COVID-19 incidence was analyzed by Spearman's rank correlation [28].

Results

No additional decreases in the incidence of TB and MDR-TB in COVID-19 pandemic (2020–2021)

Since the beginning of 2020, Taiwan has executed a series of public policies to contain the COVID-19 transmission, including mask wearing, social distancing, and contact tracing. Since most TB infection, as well as COVID-19, results from airborne and droplet transmission, we asked whether masking and social distancing policy could reduce not only the covid-19 transmission, but also the TB transmission. We analyzed the recent 10-year TB incidence data from NIDSS, with a particular focus for the year 2020–2021 when COVID-19 became epidemic (Fig. 1). The result showed that the incidence of both TB and MDR-TB did not decrease faster during year 2020–2021, as compared to that in the preceding years from 2010 to 2019. Consistently, the decreasing trend of overall TB mortality was not aggravated during the COVID-19 pandemic.

Incidence of TB and MDR-TB in Eastern and Southern Taiwan is higher than that in other regions in Taiwan

Although we did not see a further decrease of TB incidence amid mandatory mask wearing and social distancing policy by COVID-19, we asked whether there was a correlation or a discrepancy between the COVID-19 and TB incidence in different geological regions upon these prevention measures. By geographic distributions, all confirmed cases from 2010 to 2021 were categorized into seven groups. For TB, irrespectively the years, the highest TB incidence occurred in the “Eastern” region, followed by the “Kao-Ping” region (Fig. 2), irrespectively the years. Moreover, the highest MDR-TB incidence was noted in the “Eastern” region.

Geographical distribution of COVID-19 in Taiwan, from 2020 to 2021

TB and COVID-19 have similar transmission routes by various-sized droplets from respiratory fluids. The strategies of mask wearing and social distancing could have reduced the possibility of these droplets entering uninfected people. We speculated the regional incidence of TB might be associated positively

with the regional incidence of COVID-19. All confirmed cases of COVID-19 were divided into 7 groups. The incidence was then calculated. From 2020 to 2021, in contrast to the highest incidence of TB in Eastern region, the highest incidence of COVID-19 was found in the “Taipei” region, where the capital of Taiwan is located (Fig. 3). The lowest COVID-19 incidence is found in Southern, Kao-Pin, and outlying islands.

Dissociation of the incidence of TB and COVID-19 by regions

Despite the low incidence of COVID-19 in the “Kao-Pin” and the “Eastern” regions, the incidence of TB remained high in these regions. Moreover, in “Taipei” region, where the highest incidence of COVID-19 occurred, did not show an increased incidence of TB. There was a dissociation of TB and COVID-19 incidence by regions although the significance was not significant (Spearman’s rank correlation coefficient = -0.51 if the outlying islands were not counted due to low incidences, Fig. 4). The policies of mask wearing and social distancing could prevent the transmission of COVID-19, however, their effect on the limiting spread of TB was limited.

Discussion

Due to the high TB burden in the beginning of 21 century in Taiwan, Taiwan CDC has advocated the campaign of “Mobilization Plan to Halve Tuberculosis Incidence in Ten Years” since 2006 by several strategies, including Direct Observe Treatment (DOTs)[22]. This campaign appears quite successful as the incidence indeed decreased gradually. Even in the past 10 years, the incidence of TB was continuously decreased by about 10 (per 100,000 persons) every two years from 2010 to 2019. This result was different from WHO global tuberculosis report 2021[5]. In their report, the impact of COVID-19 related disruptions on estimated incidence is limited in 2020 and more noticeable in subsequent year. The rebounding of TB incidence was noted after the end of 2020. The sharp decline of incidence in 2020 was attributed to health care inconvenience and delayed diagnosis in high TB burden countries. The variation of TB notification trends in these countries, between 2019 to 2020, was due to the different times first affected by the COVID-19 pandemic, the disease severity, the capacity and resilience of health systems, and so on. The policies of mask wearing and social distancing might have no apparent or just slightly influence on the disruptions of TB incidence. That might also be a reason for the immediate rebounding in these high TB burden countries in 2021. In Taiwan, there was no sharp decline of incidence between the beginning of 2020 and the end of 2021, compared to that in the preceding years. The policies of prevention COVID-19 transmission were enforced since January, 2020, especially after May, 2021 when the local cases outbroke. From this perspective, the current data indicated that the rebounding of TB incidence may not be present in Taiwan in the future. The availability and accessibility of medicine were not obviously impacted in Taiwan under the COVID-19 pandemic, which was opposite in high TB burden countries.

In the 7-region model of Taiwan, the TB incidence declined gradually in all regions, except the outlying islands. There was no sharply decline of TB incidence neither in high COVID-19 incidence regions (ex:

Taipei) nor in low incidence regions (ex: Kao-Pin). This result implied that the policies of prevention COVID-19 transmission might not be successful in the prevention TB transmission. Another probable reason is long incubation times of TB (about 2 to 12 weeks), which may take more years to see the difference in incidences.

About the mortality of TB in Taiwan, the rate approximately gradually decreased from 2010 to 2020, even in the period of COVID-19 pandemic. This result was much different from the global data. Previous researches revealed that the annual number of TB deaths could rise to the levels seen in 2015 or even 2012[29, 30]. In WHO global tuberculosis report 2020, their analysis implied that the additional number of TB deaths could occur globally for different combinations of a decrease in case detection (compared with levels before the pandemic) and the number of months for which this decrease occurs [31]. The healthcare policy is important regarding the health care of the chronic respiratory disease such as tuberculosis in the COVID-19 pandemic.

Conclusion

Tuberculosis (TB) is one kind of mycobacterial diseases threatening the world for a long period. To decrease incidence and mortality annually is an important issue in public health, especially in high TB burden countries. Since the beginning of 2020, COVID-19 has taken millions of lives away in the world. In the period of COVID-19 pandemic, the TB incidence, in high TB burden countries, sharply declined in 2020 and rebounded immediately in 2021. In Taiwan, the TB incidence declined gradually, even under COVID-19 pandemic. Besides, the global mortality of TB greatly increased due to delay diagnosis and treatment, however, the increased mortality did not occur in Taiwan.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

Data are available from Taiwan Centers for Diseases Control and Department of Household Registration, Ministry of the Interior, Republic of China (Taiwan).

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Conceptualization, Chien-Hui Hong and En-Cheng Lin; data curation and analysis, En-Cheng Lin; drafting the initial manuscript, En-Cheng Lin; writing—review and editing, Chien-Hui Hong; supervision, Chien-Hui Hong. All authors have read and agreed to the published version of the manuscript.

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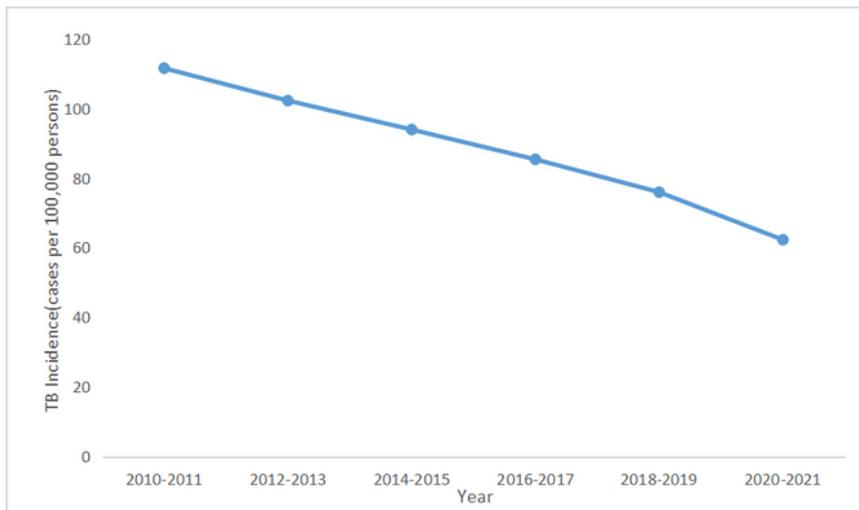
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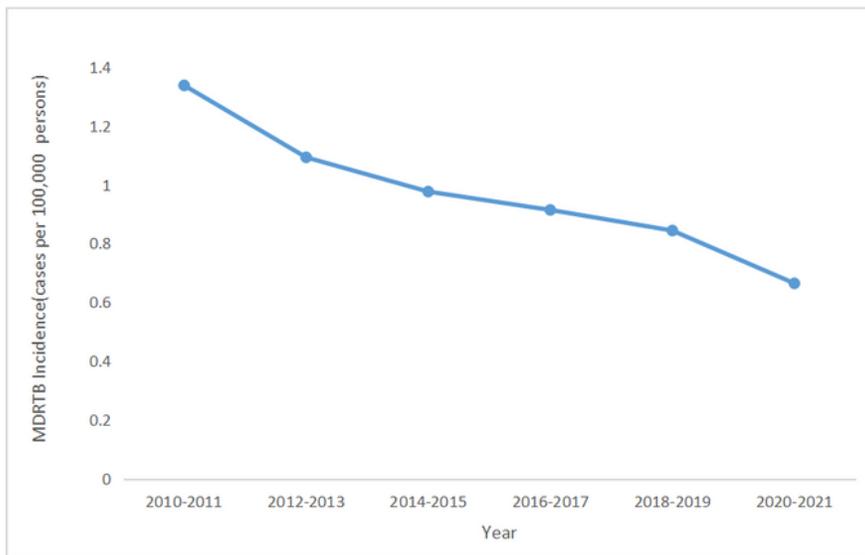
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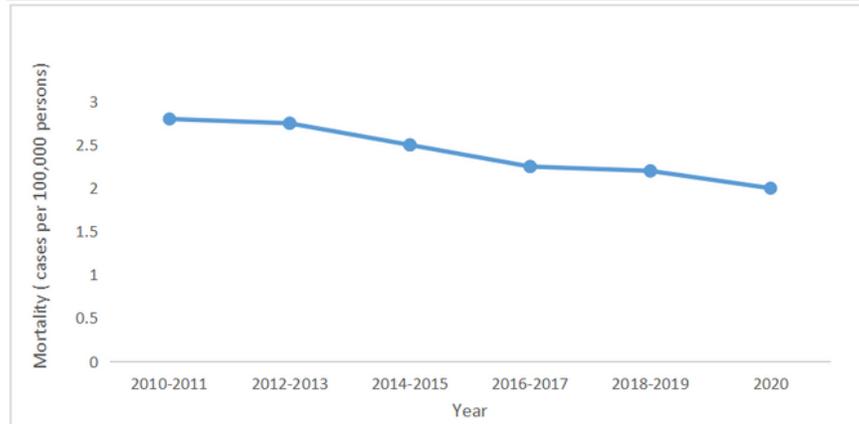
Figures



A



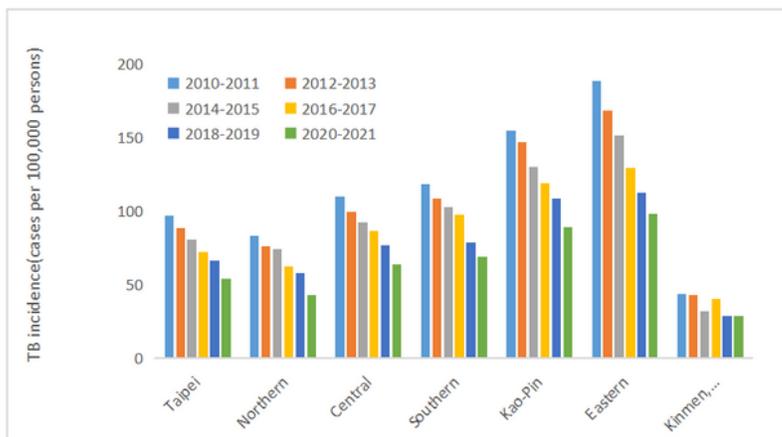
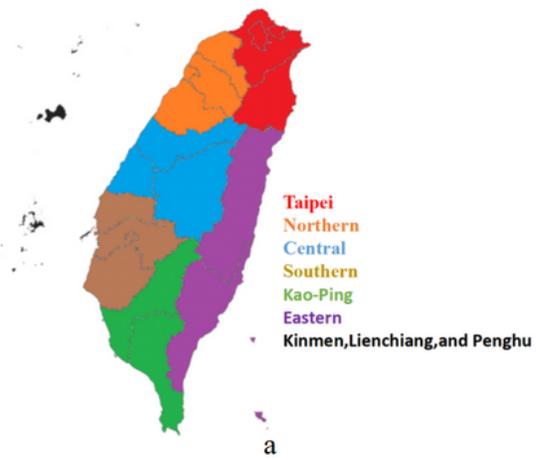
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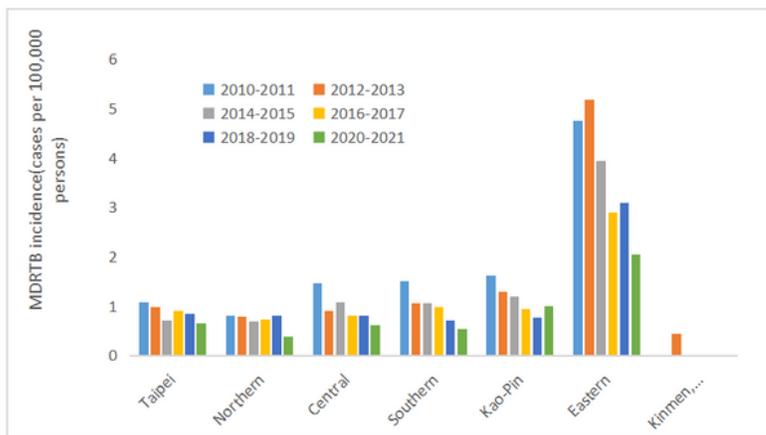
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Figure 1

All data of TB and MDR-TB cases, from 2010 to 2021, were acquired from NIDSS. (A) The incidence of TB has declined gradually. (B) The incidence of MDR-TB also continuously decreased. (C) The mortality of TB decreased in recent 10 years. In 2020, the mortality still decreased, compared to that in the previous years.



b



c

Figure 2

All confirmed cases from 2010 to 2021 were categorized into (A) seven groups, based on the regions where the patients lived. (B) The highest TB incidence was found in the “Eastern” region, followed by the “Kao-Pin” region. (C) The highest MDR-TB incidence was noted in the “Eastern” region.

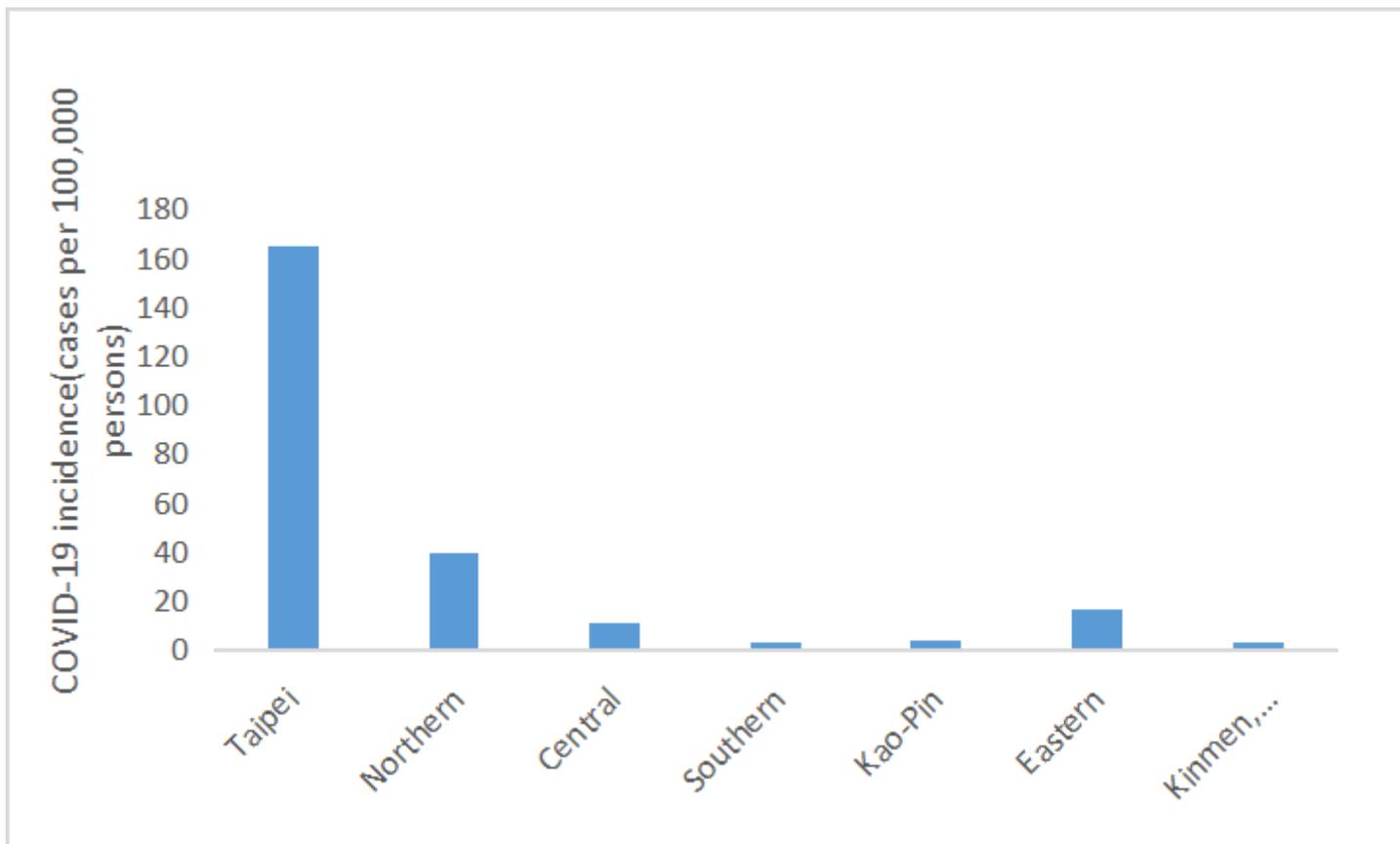


Figure 3

All confirmed cases of COVID-19 were divided into 7 groups and the incidence was calculated. From 2020 to 2021, the highest incidence was noted in the “Taipei” region. In contrast, the “Kao-Pin” and “Kinmen, Lienchiang and Penghu” regions showed low incidence of COVID-19.

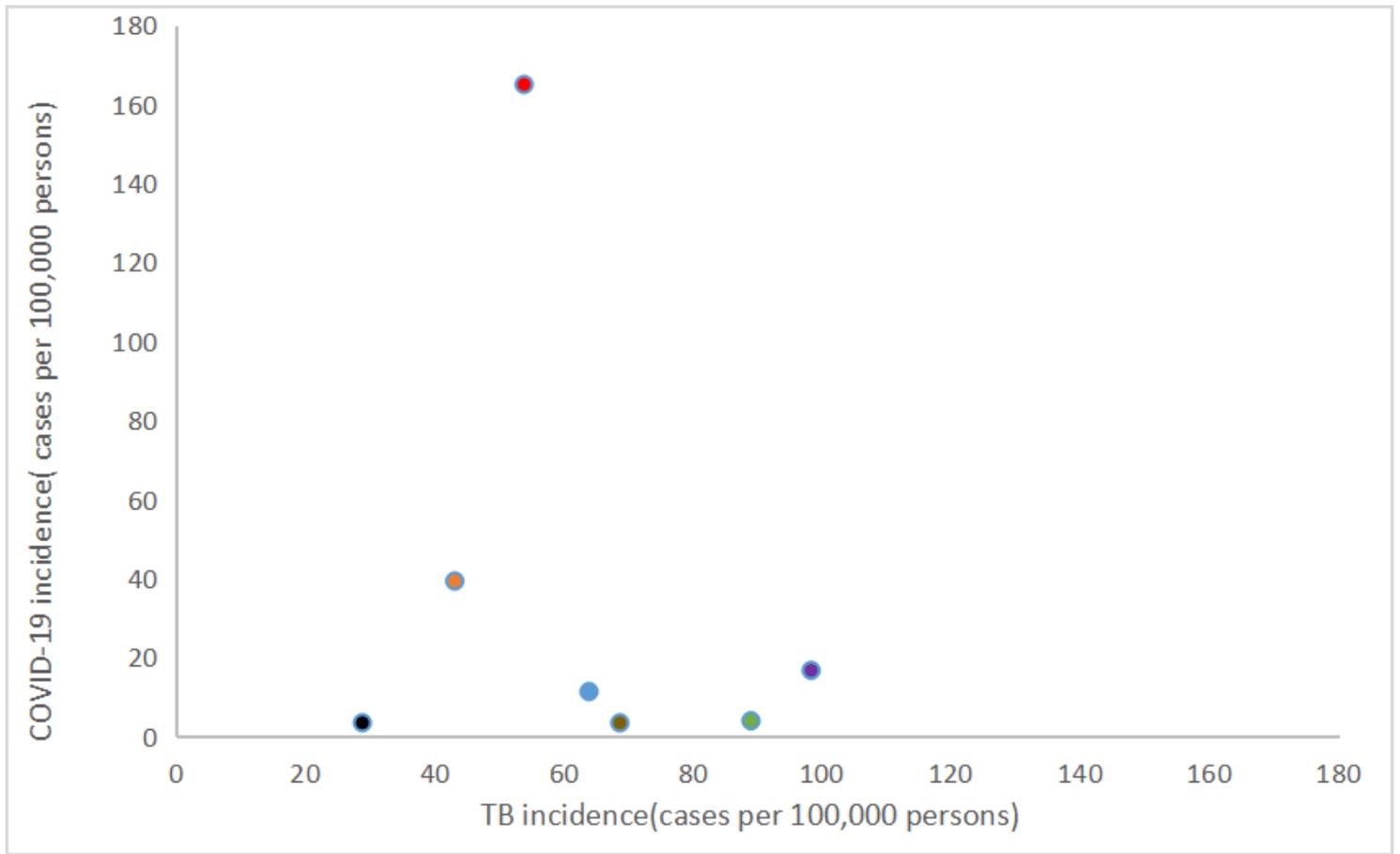


Figure 4

By location, the relation between TB incidence and COVID-19 incidence was analyzed. Spearman's rank correlation coefficient was calculated. The low COVID-19 incidence regions, such as the "Kao-Pin" region, exhibited high TB incidence. The policies for prevention COVID-19 transmission may not be useful in the prevention of TB transmission.