Epidemiological analysis of the Kaohsiung city strategy for dengue fever quarantine and epidemic prevention

Chun-Hong CHEN (980115@nhri.edu.tw)
National Health Research Institutes
Chao Ying Pan
Department of Health ,Kaohsiung city Goverment, Taiwan
Wei-Liang Liu
NMDBC, NHRI
Matthew P. Su
The University of Manchester Faculty of Biology Medicine and Health
Te Pin Chang
NMDBC, NHRI
Hui-Pin Ho
Department of Health, Kaohsiung city Government
Joh-Jong Huang
Bureau of Social Affairs, Tainan city Government
Li Jen Lin
Department of Health, Kaohsiung city Government

Research article

Keywords: Dengue virus, Imported dengue cases, Concealment, Indigenous dengue fever, Airport fever screening, Noncontact infrared thermometers

Posted Date: October 1st, 2019

DOI: https://doi.org/10.21203/rs.2.15494/v1

Version of Record: A version of this preprint was published at BMC Infectious Diseases on May 15th, 2020. See the published version at https://doi.org/10.1186/s12879-020-4942-y.

Abstract

Abstract Background. Dengue is endemic in over 100 countries and is an important public health problem worldwide. Dengue is not considered endemic in Taiwan however, with importation of dengue viruses from neighboring countries via close commercial links and air travel believed to be the cause of local outbreaks. Disease control efforts have therefore focused on preventing the importation of dengue into Taiwan. Here, we investigate the relationships between numbers of imported and indigenous dengue cases to test the validity of this strategy. Methods. Dengue-fever case data from between 2013 and 2018 was obtained from the surveillance systems of the Taiwan Center for Disease Control and Kaohsiung City Health department. Standard epidemiological data, including the monthly numbers of indigenous and imported dengue cases, was calculated. Potential associations between the number of indigenous and imported cases were investigated using correlation analyses. Results. We identified a possible relationship between the period of disease concealment and the number of reported imported dengue cases which resulted in indigenous dengue-fever epidemics within local communities. Further analysis of confirmed dengue cases during previous dengue-fever epidemics in Kaohsiung City found that the risk of indigenous dengue-fever may be related to the likelihood of patients suffering from imported cases of dengue-fever staying within local communities. Conclusion. Given the correlations found between imported and indigenous dengue-fever cases, as well as the relationship between disease concealment period and risk of indigenous dengue-fever, the major priorities for disease control remain prevention of disease importation and efficient identification of dengue cases within high-risk communities.

Background

Dengue is the most prevalent emerging arthropod-borne viral infection (arbovirus) of humans worldwide and is highly endemic in many Western Pacific, Southeast Asia, and South American countries [1,2,3]. Transmitted via bites from infective female *Aedes* mosquitoes, the rapid spread of dengue in the past few decades have been driven in part by climate change and increased rates of global trade and international travel [4,5,6,7]. Approximately 2.5 billion people are now at risk for dengue, with around 100 million clinically manifesting dengue infections estimated to occur worldwide each year [8,9]. Disease symptoms can vary significantly and range from asymptomatic cases to classic dengue fever, as well as more serious complications such as dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS) [10].

The Dengue virus (DENV) itself is an enveloped virus with a single-stranded, positive sense RNA genome, belonging to the genus *Flavivirus* in the family *Flaviviridae*. DENV contains 5'- and 3'- untranslated regions (UTR) and a single open reading frame encoding a single polyprotein that can be cleaved into three structural proteins (capsid [C], premembrane/membrane [prM/M], and envelope [E]) and seven nonstructural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5) [11,12]. There are four genetically and antigenically distinct DENV serotypes, labelled DENV-1, -2, -3, and -4 [13]. Since 2006 southern Taiwan has faced dengue outbreaks of varying magnitudes every year, with relatively large outbreaks occurring in 2014 and 2015; DENV-1 and -2 respectively were identified as the major serotypes in these cases [14].

Dengue transmission in Taiwan is driven by two species of *Aedes* mosquitoes; *Aedes albopictus* and *Aedes aegypti*, with the former being found throughout Taiwan whilst the latter is restricted to the south [15]. Indigenous dengue is not considered endemic in Taiwan, and thus importation of DENV (due to close commercial ties and human migration from neighboring Southeast Asian countries) is thought to be the underlying reason for DENV outbreaks. Preventing the importation of disease has therefore become the major objective for the dengue-fever quarantine and epidemic prevention network in Taiwan.

The emergence of Severe Acute Respiratory Syndrome (SARS) in 2003 highlighted the role of international travel in the rapid spread of infectious diseases and prompted many countries to establish border control strategies and use noncontact infrared thermometers (NCITs) at international airports to reduce the risk of imported infections [16, 17]. Taiwan expanded this noninvasive diagnostic tool to screen for various infections, including dengue, at all major entry borders.

Such strategies to reduce the risk of disease importation are particularly relevant for Kaohsiung, a major city in the south of Taiwan, as it was the main site of the 2014 and 2015 dengue outbreaks [18,19]. Constant surveillance of dengue seroprevalence and use of airport fever screening systems to test suspected dengue fever patients have become central to the city's disease control program.

The relationship between the numbers of indigenous and imported cases remains unclear however [20]. This relationship is in part complicated by asymptomatic disease cases and increased disease latency periods which can result in secondary/ tertiary waves of infection many weeks after the first wave of infections [3]. In theory, the latency period for mosquitoes is between 8 and 12 days whilst the longest latency for humans is between 3 and 8 days [10]. As such, the second wave of infections typically occur after 2 to 3 weeks, and the third wave can occur 4 to 6 weeks after the initial bout of infections. Detailed case reports collected over long time frames are required to unpick the complex interactions between indigenous and imported dengue cases.

Here, we investigated the number of indigenous and imported dengue cases in Kaohsiung city between 2013 and 2018, including the country of importation and status/ occupation of the infected individual. We also mapped out the monthly number of dengue cases confirmed by the Taiwan Center for Disease Control (CDC) surveillance system throughout this period. We then tested for correlations between indigenous and imported cases, testing both the number of cases and the month in which they were reported. We found a significant correlation between the two types of infection after accounting for the disease latency period and delays in case reporting. Our results suggest that importation of dengue is indeed driving dengue outbreaks in Taiwan, indicating that disease prevention strategies should continue to focus on human migration patterns and efficient identification of dengue fever in order to reduce disease incidence.

Methods

Database and Case definitions

We identified all dengue cases reported between January 2013 and September 2018 in the public databases of the Taiwan CDC and Kaohsiung City Health department. Here, we followed definitions of dengue as set by the Taiwan CDC [21]. As such, a confirmed dengue case requires the positive detection of RNA using real-time reverse transcriptase polymerase chain reaction (real-time RT-PCR), and/or serological diagnosis by IgM/IgG ELISA in the Diagnostic Center of the Taiwan CDC [22].

An imported dengue case was defined as a confirmed case in which the patient had traveled to a dengue-endemic country in the two weeks prior to the onset of illness, whereas indigenous cases were defined as cases reported for infected individuals without any travel history. The total number of imported dengue cases included inbound passengers diagnosed as dengue-positive by airport screening methods and those diagnosed by clinics or hospitals following entry into the local community.

Surveillance of dengue

The airport fever screening program was introduced in 2003 to detect travelers infected with SARS, dengue or other diseases. In this study, we analyzed data collected from January 2013 to September 2018 from the International Kaohsiung Airport in Taiwan. All airline passengers, outbound and inbound, were requested to have their body temperature measured by the NCITs. Two thermal NCITs were set up at each entry gate, with each NCIT having an infrared-thermal camera. Travelers with an NCIT detected temperature of higher than 37.5°C were rechecked by quarantine officers with a symptoms survey and assessed using an ear thermometer. Travelers with a temperature above 38°C which had arrived from a dengue-affected area were triaged for additional diagnostics and their specimens were taken for testing with the Dengue NS1 Rapid Test at an airport inspection station. Duplicate specimens were sent to the central laboratory of the Taiwan CDC for simultaneous confirmation by molecular and/or serological diagnosis.

Statistical analysis

All statistical analyses were conducted using the SPSS Statistics software, version 22. Overall mean scores were calculated and compared using paired t-tests. Potential correlations between the numbers of indigenous and imported cases were analyzed by Pearson correlation tests and two-way analysis of variance (ANOVA). $p < 0.05$ was considered to be statistically significant.

Results

1. **Statistical analysis of indigenous and imported cases of dengue-fever in Kaohsiung between 2013 and September 2018**

1-1. Statistics for total imported dengue-fever cases in Kaohsiung city

A total of 239 imported dengue cases (32, 44, 61, 37, 34 and 31 cases for 2013, 2014, 2015, 2016, 2017 and 2018, respectively) were identified in Kaohsiung during 2013–2018 (Table 1), including 80 women (33.5%) and 159 men (66.5%). The majority of cases involved individuals arriving from Southeast Asian countries; 48 from the Philippines (20.0%), 47 from Indonesia (19.6%), 33 from Vietnam (13.8%), 30 from Malaysia (12.6%), 24 from Thailand (10.0%) and 13 from Singapore (5.4%). Moreover, cases were also imported from the Indian subcontinent (India, Bangladesh, Sri Lanka, and Maldives) and the South Pacific region (Tuvalu).

Further analysis of the 239 imported dengue cases found that the 142 of the infected individuals were Taiwanese nationals who had traveled abroad (59.4%). However, foreign workers and tourists entering the country accounted for a further 15.5% and 8.8% respectively (Table 2). Analysis of patient occupation is included in Table 3, with home management, business and studying the most commonly cited occupations (in total accounting for 46.4% of cases). Figure 1 shows fluctuations in the monthly reporting rates of imported dengue cases in Kaohsiung City (Fig. 1).

1-2. Predominant serotypes of annual indigenous dengue-fever cases in Kaohsiung city

Between 2013 and September 2018 there were 35,148 indigenous dengue-fever incidences in Kaohsiung city, with 70 cases in 2013, 14,999 cases in 2014, 19,723 cases in 2015, 342 cases in 2016, 3 cases in 2017, and 11 cases up until the end of September in 2018 respectively. Primary dengue-fever incidences were concentrated in the 24 consecutive months between May 2014 to April 2016 (Fig. 2). During this period, there were 35,062 indigenous dengue-fever cases in Kaohsiung (99.8%). The major epidemic dengue-fever serotype in 2014 was serotype 1, while the major epidemic dengue-fever serotype from 2015 to April 2016 was serotype 2.

1-3. Concealment of cases for more than 3 days

Further analysis of the 239 confirmed imported cases revealed that 37 infected individuals did not stay within local communities after becoming infected with dengue; this includes 5 of the 32 cases which occurred in 2013 (15.6%); 3 of the 44 cases in 2014 (6.8%); 1 of the 61 cases in 2015 (1.7%); 10 of the 37 cases in 2016 (27.0%); 12 of the 34 cases in 2017 (35.3%); and 6 of the 31 cases in 2018 (19.4%) (Table 4).

We also identified a significant number of cases whose concealment period was greater than 3 days (139/239, 58.16%). Of these, we found 24 such cases in 2013 (75.0% of cases that year), 32 in 2014 (72.7%), 39 in 2015 (63.9%), 22 in 2016 (59.5%), 14 in 2017 (41.2%) and 8 in 2018 (19.4%) (Fig. 3).

2. **Statistical analysis of the number indigenous and imported cases of dengue-fever in Kaohsiung city between 2013 and September 2018.**

The 35,148 confirmed diagnosed indigenous dengue-fever cases collected in Kaohsiung between 2013 and September of 2018, along with the 239 imported cases, were sorted by month of identification (n=69). A significant positive correlation (Paired sample correlation coefficient, r = 0.407, p = 0.001) was found between the numbers of imported and indigenous cases reported each month (Table 5).

However, actual clinical surveillance reports were delayed by around 1 to 2 months during local dengue fever epidemics; furthermore, a concealment period of at least 2 days was common. Instead of investigating correlations between reported cases in the same month, we therefore tested for relationships between the number of imported cases in a single month and the number of indigenous cases reported two months later, after also accounting for differences in the concealment period. We found significant positive correlations between the number of imported cases reported and the number of indigenous cases reported two months later when accounting for concealment periods of more than 2 days (Pearson correlation coefficient, r = 0.459, p = 0.0001), more than 3 days (r = 0.394, p = 0.001) and more than 4 days (r = 0.387, p = 0.001) (Table 6).

Discussion

Dengue-fever spreads via “virus-mosquito-man” transmission. Current preventive strategies focus on the mosquito itself, with a particular focus on environmental rectification and maintenance (such as targeting mosquito breeding sites) [23,24]. The large-scale dengue-fever outbreaks that occurred in Kaohsiung between 2014 and 2015, which were likely the result of imported dengue cases, have shown the limitations of this vector-focused approach.

The spread and control of infectious diseases are the first to grasp the opportunities and prevent diseases immediately. Kaohsiung City experienced a severe dengue epidemic outbreak from 2014 to 2015, in part due to a lack of real-time reporting of cases which allowed the virus time to spread in the community. Following this, the Kaohsiung City Government refocused its’ disease prevention efforts on border quarantine to prevent importation of disease, which should thus also reduce the number of indigenous cases resulting from secondary infections. Kaohsiung City Government carries out the following action plans to make better the anti-epidemic capacity of dengue fever in Kaohsiung City. These efforts included establishment of quarantine referral station, foreign workers and fishermen dengue fever quarantine, new residents and foreign students to return home to health care measures and increased epidemic prevention incentives for the local or returning citizens.

During the 2014 and 2015 outbreaks there were 14,999 and 19,723 cases of indigenous dengue-fever respectively. Case reports from early 2016 showed signs of a continuation of the 2015 epidemic, with 340 indigenous cases reported before April. However, there were only 2 cases of native dengue-fever infections throughout the remainder of 2016. Following this, in 2017 and 2018, Kaohsiung city achieved the two lowest number of indigenous cases on record, with 3 and 11 cases respectively [19]. This significant reduction in the number of dengue cases was in part due to a complete reorganization of the dengue quarantine and epidemic preventive network in Kaohsiung in April 2016. A new project focusing on imported cases was initiated in July 2016 to cover both border quarantine and epidemic prevention work. In October of the same year, the only “Quarantine referral station” in the nation was established in Kaohsiung International Airport in order to identify infected travelers. Kaohsiung city’s airport and seaport have thus become the front line of epidemic prevention in the dengue-fever border quarantine network in South Taiwan.

Kaohsiung possesses large native populations of Aedes aegypti and Aedes albopictus, resulting in a high risk of secondary dengue infection after an initial case has been imported from abroad. Although the ongoing collection and testing of thousands of human and mosquito specimens suggests that the dengue virus has not yet localized in Kaohsiung, it is vital that control programs targeting mosquitoes continue in order to reduce the likelihood of future localization and to minimize the risk of secondary outbreaks following the initial wave of infections [25]. Dengue control efforts, whether focused on vector control or on prevention of disease importation, are expensive both in terms of resources and workload. In order to maintain the low number of dengue cases reported in Kaohsiung whilst reducing unnecessary expenditure, constant innovation is required. This includes improved, efficient targeting of high-risk individuals in order to reduce the likelihood of dengue spreading throughout local communities. For example, foreign workers and fishermen from dengue-endemic countries could be NS1 screened for dengue within the first 3 days of entering Taiwan [26]. Those identified as dengue positive, they will be arranged to hospital inpatient care and this will be able to isolate the carrier with the dengue virus from the vector mosquitoes in the community, so as to effectively block the dengue virus from spreading into the community through the foreigners.

Based on the above findings, the lowest record of local confirmed dengue fever cases occurred in Kaohsiung city in the past few years was the result of the using its unique geographical location to strengthen quarantine functions outside the battle zone, optimizing dengue medical network resources, and building dengue quarantine and epidemic prevention networks, and effectively shorten the incubation period of dengue cases. In other words, the dengue protection network has successfully utilized Taiwan's natural advantages for disease control to effectively adopt an effective quarantine strategy. In spite of this, the threat posed by dengue (as well as other communicable diseases) is likely increase in line with increases in international exchange and trade. In order to prevent future dengue outbreaks in Taiwan, local networks must be able to constantly innovative and adopt an international focus if they are to continue to effectively combat dengue.

Conclusions

Dengue fever outbreaks in Kaohsiung are the result of imported cases of the disease; dengue virus is transported to Kaohsiung via infected individuals and then spread within the community. It is vital therefore that strategies including modern quarantine methodologies and high-efficiency health care are utilized in order reduce the likelihood of dengue-fever becoming endemic to Kaohsiung.

Abbreviations

Dengue virus: DENV

Dengue hemorrhagic fever: DHF

Dengue shock syndrome: DSS

Severe Acute Respiratory Syndrome: SARS

Noncontact infrared thermometer: NCIT

Centers for Disease Control: CDC

Declarations

Ethics approval and consent to participate

The need for ethics approval was deemed unnecessary according to “Communicable Disease Control Act” of Taiwan. Data sets were extracted without personal identifiers and organized into literature by this study, institutional research guidelines were adhered, to ensure scientific soundness.

Consent for publication

All authors have read the manuscript and approve the manuscript to be published.

Availability of data and material

The datasets used and/or analyzed during this study are available from the corresponding author on reasonable request. A person who wants to access the raw data should contact with the corresponding author.

Competing interests

All authors declare that they have no competing interests.

Funding.

This study was supported by the NHRI (National Health Research Institutes, Taiwan grant no. NHRI-08A1-MRGP12-035) and the Department of Health, Kaohsiung City Government, Taiwan (08A1-MRAP04-035).

Authors' contributions

CYP, JJH, LJL and CHC contributed to research conception and design. CYP, HPH, LJL and CHC analyzed the data. CYP, WLL, TPC and CHC performed experiments. CYP, WLL, MPS, LJL and CHC wrote the manuscript. All authors read and approved the final manuscript.

Acknowledgements

We thank the Centers for Disease Control (CDC) of Taiwan for their support in performing data collections and the analytical techniques to RT-PCR, dengue virus-specific IgM/IgG capture ELISA detection and DENV serotyping.

References

1. Gubler DJ. The global emergence/resurgence of arboviral diseases as public health problems. Arch Med Res. 2002; 33: 330-42.
2. Patterson J, Sammon M and Garg M. Dengue, Zika and Chikungunya: Emerging Arboviruses in the New World. West J Emerg Med. 2016 ;17: 671-9.
3. Mayer SV, Tesh RB and Vasilakis N. The emergence of arthropod-borne viral diseases: a global prospective on dengue, chikungunya and zika fevers. Acta Trop. 2017; 166: 155-63.
4. Massad E, Amaku M, Bezerra Coutinho FA, Struchiner CJ, Burattini MN, Khan K et al. Estimating the probability of dengue virus introduction and secondary autochthonous cases in Europe. Sci Rep. 2018; 8: 4629. doi: 10.1038/s41598-018-22590-5.
5. Kraemer MU, Kraemer MUG, Sinka ME, Duda KA, Mylne AQN, Shearer FM et al. The global distribution of the arbovirus vectors Aedes aegypti and Ae. albopictus. Elife. 2015; 4: e08347. doi:

10.7554/eLife.08347.

6. Cleton N, Koopmans M, Reimering J, Godeke G and Reusken C. Come fly with me. Review of clinically important arboviruses for global travelers. J Clin Virol. 2012; 55: 191-203.
7. Benitez MA. Climate change could affect mosquito borne diseases in Asia. Lancet 2009; 373: 1070. doi: 10.1016/s0140-6736(09)60634-6.
8. Brady OJ, Gething PW, Bhatt S, Messina JP, Brownstein JS, Hoen AG et al. Refining the global spatial limits of dengue virus transmission by evidence-based consensus. PLoS Negl Trop Dis. 2012; 6: e1760. doi: 10.1371/journal.pntd.0001760.
9. Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL et.al. The global distribution and burden of dengue. Nature. 2013; 496: 504-7.
10. Gubler DJ. Dengue and dengue hemorrhagic fever. Clin Microbiol Rev 1998; 11: 480-96.
11. Calisher CH, Karabatsos N, Dalrymple JM, Shope RE, Porterfield JS, Westaway EG et al. Antigenic relationships between flaviviruses as determined by cross-neutralization tests with polyclonal antisera. J Gen Virol 1989; 70: 37-43.
12. Lindenbach BD and Rice CM. Molecular biology of flaviviruses. Adv Virus Res 2003; 59: 23-61.
13. Gibbons RV and Vaughn DW. Dengue: an escalating problem. BMJ 2002; 324: 1563-6.
14. Chang K, Huang CH, Lee IK, Lu PL, Lin CY, Chen TC, et al. Differences in Mortality and Clinical Manifestations of Dengue Hemorrhagic Fever in Taiwan in Different Years: A Comparison for Cases in 2014 and 2015 Epidemics. The American journal of tropical medicine and hygiene. 2017; 97: 361-8.
15. Chang LH, Hsu EL, Teng HJ and Ho CM. Differential survival of Aedes aegypti and Aedes albopictus (Diptera: Culicidae) larvae exposed to low temperatures in Taiwan. J Med Entomol 2007; 44: 205-10.
16. Chen KT, Twu SJ, Chang HL, Wu YC, Chen CT, Lin TH et al. Taiwan SARS Response Team. SARS in Taiwan: an overview and lessons learned. Int J Infect Dis. 2005; 9: 77-85.
17. Shu PY, Chien LJ, Chang SF, Su CL, Kuo YC, Liao TL, et al. Fever screening at airports and imported dengue. Emerg Infect Dis. 2005; 11: 460-2.
18. Wang SF , Chang K, Loh EW, Wang WH, Tseng SP, Lu PL et al. Consecutive large dengue outbreaks in Taiwan in 2014–2015. Emerging Microbes & Infections 2016; e123; doi:10.1038/emi.2016.124
19. Tsai JJ, Liu CK, Tsai WY, Liu LT, Tyson J, Tsai CY, et al. Seroprevalence of dengue virus in two districts of Kaohsiung City after the largest dengue outbreak in Taiwan since World War II. PLoS Negl Trop Dis. 2018; 12: e0006879. doi.org/10.1371/journal.
20. Yang CF, Chang SF, Hsu TC, Su CL, Wang TC, Lin SH, et al. Molecular characterization and phylogenetic analysis of dengue viruses imported into Taiwan during 2011-2016. PLoS Negl Trop Dis. 2018; 12: e0006773. doi: 10.1371/journal.
21. Kuan MM and Chang FY. Airport sentinel surveillance and entry quarantine for dengue infections following a fever screening program in Taiwan. BMC Infect Dis. 2012; 12: 182. doi: 10.1186/1471-2334-12-182.

22. Huang JH, Liao TL, Chang SF, Su CL, Chien LJ, Kuo YC et al. Laboratory-based dengue surveillance in Taiwan, 2005: a molecular epidemiologic study. Am J Trop Med Hyg 2007; 77: 903-9.
23. Roiz D, Wilson AL, Scott TW, Fonseca DM, Jourdain F, Müller P et al. Integrated Aedes management for the control of Aedes-borne diseases. PLoS Negl Trop Dis. 2018; e0006845. doi: 10.1371/journal.
24. Weeratunga P, Rodrigo C, Fernando SD, Rajapakse S. Control methods for Aedes albopictus and Aedes aegypti. Cochrane Database of Systematic Reviews 2017; Issue 8. Art. No.: CD012759. doi: 10.1002/14651858.CD012759.
25. Chang CJ, Chen CS, Tien CJ and Lu MR. Epidemiological, clinical and climatic characteristics of dengue fever in Kaohsiung City, Taiwan with implication for prevention and control. PLoS One. 2018;13: e0190637. doi: 10.1371/journal.pone.0190637.
26. Perng GC, Ho TC, Shih HI, Lee CH, Huang PW, Chung CH, et al. Seroprevalence of Zika and Dengue Virus Antibodies among Migrant Workers, Taiwan, 2017. Emerg Infect Dis. 2019; 25: 814-16. doi: 10.3201/eid2504.181449.

Tables

Due to technical limitations, the tables have been placed in the Supplementary Files section.

Figures

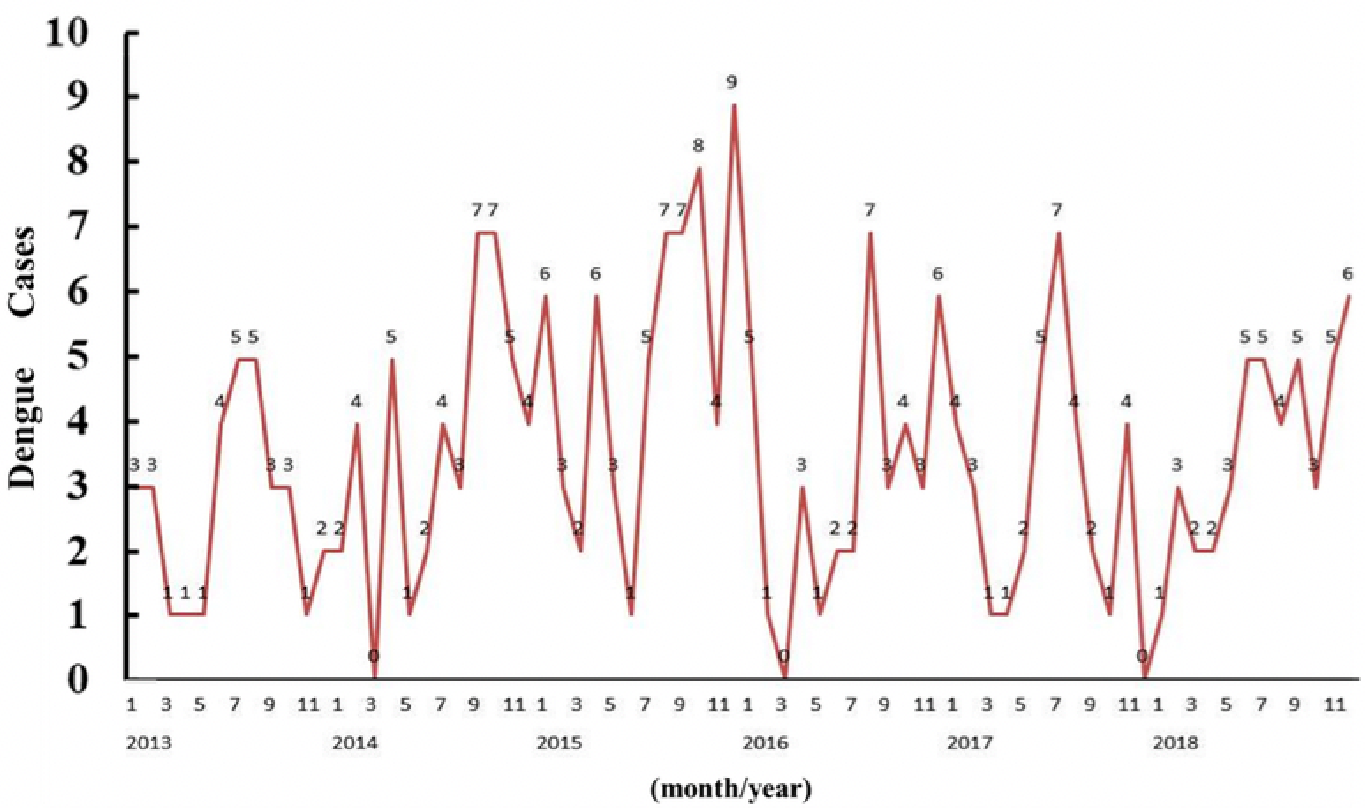

Figure 1

Fluctuations in the number of dengue cases from 2013 to September 2018. The recorded by the Taiwan CDC surveillance system in Kaohsiung City from 2013 to September 2018. Monthly data are shown to reflect imported cases for all years.

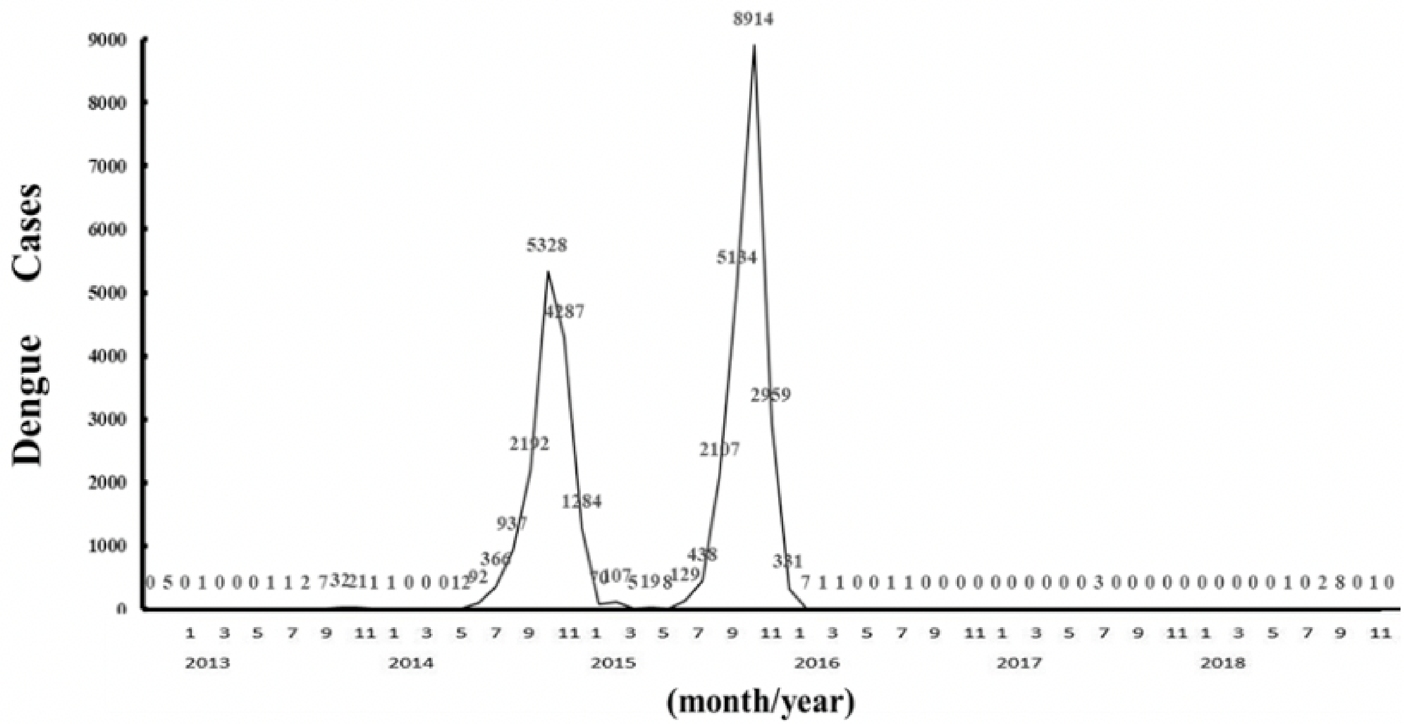

Figure 2

The number of indigenous cases of dengue in Kaohsiung city from 2013 to September 2018.

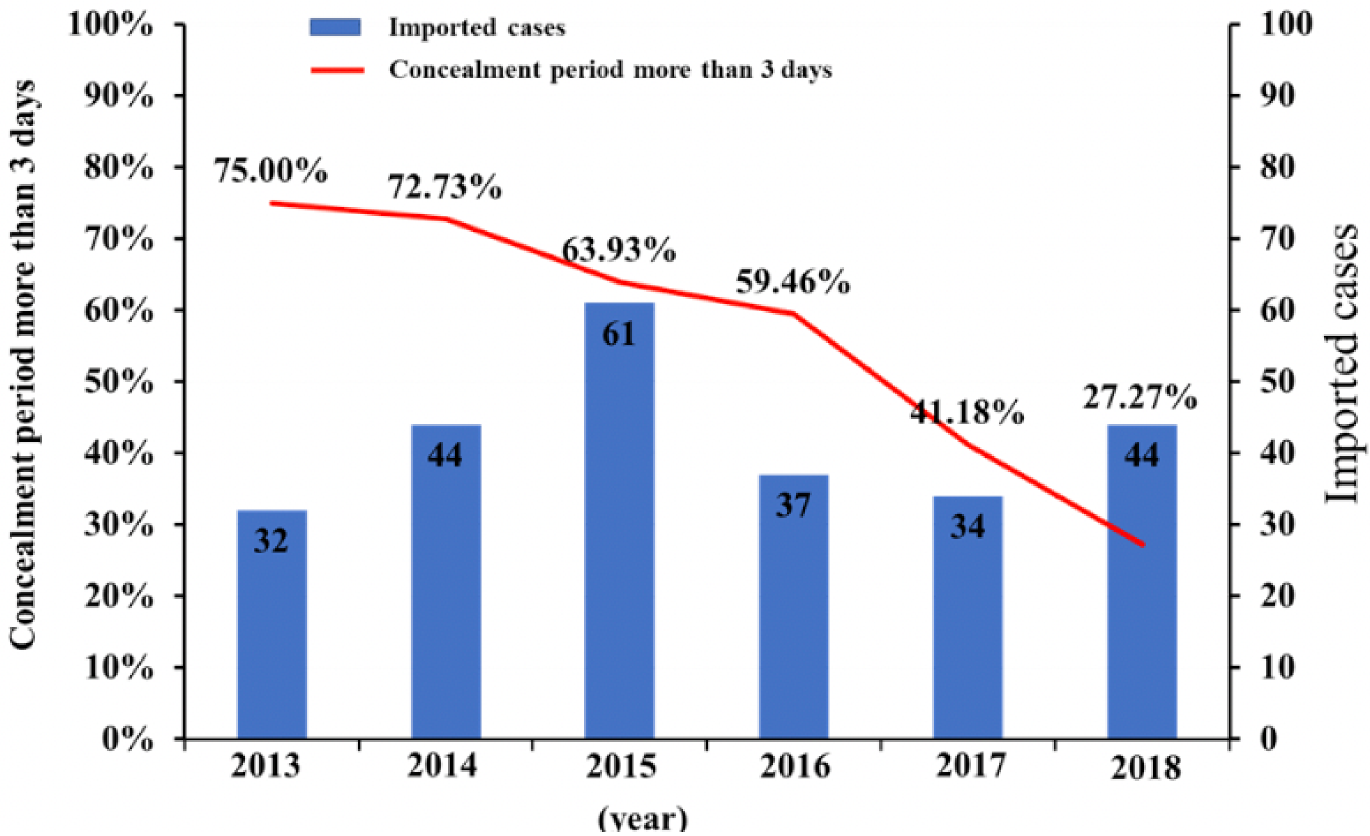

Figure 3

Analysis and correlations between the imported dengue cases and concealment period. The number of imported dengue cases and the percentage of cases with a concealment period of more than 3 days in Kaohsiung city from 2013 to September 2018.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table3.docx
- Table4.docx
- Table5.docx
- Table6.docx
- Table1.docx
- Table2.docx