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Identification of Local Clusters of Hand Foot and Mouth Disease Based on Local Geary C Statistic

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ABSTRACT:

Background: Hand, foot, and mouth disease (HFMD) is a common childhood illness caused by enteroviruses. Increasingly, the disease has a substantial burden throughout Vietnam. To better understand of the epidemiology of HFMD, this study aims to investigate the use of local Geary's C statistic in the identification of local clusters of HFMD in Ho Chi Minh city, Vietnam.

Methods: Histogram was first used to study the distribution of HFMD cases the incidence of HFMD. Local Geary C statistics was then applied to identify the spatial clusters of HFMD cases and HFMD incidence including high-high, low-low, negative and other positive clusters. Finally, HFMD cases and infection rates collected in Ho Chi Minh were used to explore the spatial clusters of HFMD.

Results: It was found that, in the case of using HFMD cases, two high-high clusters in District 12 and Binh Tan in the city center, one low-low cluster in District 5 in the east of the city center and two negative clusters in Binh Thanh and District 7 in the west of the city were successfully detected. On the other hand, in the case of using HFMD infection rates, a total of three high-high clusters, one low-low cluster, one negative and one other positive clusters were successfully detected, in which, the three high-high clusters were found in the districts of Binh Tan (289 cases/100,000 inhabitants), Binh Chanh (283 cases/100,000 inhabitants) and Tan Phu (281 cases/100,000 inhabitants) in the east of the city.

Conclusions: findings in this study confirm the usefulness of local Geary's C statistic in the identification of spatial clusters of HFMD.

KEYWORDS: Hand, foot, and mouth disease, Spatial distribution, Local clusters, Local Gearry's C statistic.

1. INTRODUCTION

Hand, foot and mouth disease (HFMD) is a common infectious disease caused by a group of enteroviruses, most frequently Coxsackie A 16 (CAV16) and Enterovirus 71 (EV71) (1,2). HFMD is a viral illness commonly seen in young children under 5 years of age, characterized by typical manifestations such as oral herpes and rashes on the hands and feet (3). Typical clinical manifestations of HFMD in children include fever, skin eruptions on hands and feet, and vesicles in the mouth. However, cases involving the central nervous system and/or pulmonary edema have also been reported (4). HFMD outbreaks caused by Enterovirus A71 (EV-A71), CVA16, CVA6 and Echoviruses (Echo) were reported frequently around the world (5). HFMD is caused by Human enteroviruses (EVs) that are members of the Enterovirus genus of the Picornaviridae family (2). EVs were initially classified into Poliovirus (PV), Echo, CV-A and B, and emerging EVs. Since 1999, EVs have been divided into four categories of Enterovirus A, B, C, and D, in the light of their molecular, biological, and genetic characteristics (3). There are no vaccines neither specific treatment for this disease. It is therefore, understanding the spread of HFMD can make greate contribution to the fight of HFMD.

Alsop et al. introduced the term HFMD when they described an outbreak that occurred in the summer of 1959 in Birmingham (6). The disease then gradually spread around the world (7). In 2009, an outbreak in the mainland China involved 1,155,525 cases, 13,810 severe cases and 353 deaths. Outbreaks have been reported in other countries in the Western Pacific Region, including Australia, Brunei Darussalam, Japan, Malaysia, Mongolia, the Republic of Korea, Singapore, and Vietnam (8). In Vietnam, the first case of HFMD was reported in 2003 (7) and within the following years the disease was reported in all major cities and provinces in the country. The number of reported cases and deaths of HFMD were 5719 and 23 in 2007; 10,958 and 25 in 2008; and 10632 and 23 in 2009, respectively (7). National surveillance data obtained by the Ministry of Health showed that there has been an increasing trend in recent years which peaked in 2011 when Vietnam recorded 113,121 cases of HFMD and 170 deaths (9). Since 2011, the Ministry of Health classified HFMD as a severe infectious disease with out break potential (class B communicable disease) and the disease has been reported weekly by the national communicable disease surveillance system which collects reports from all the hospitals (7).

A lots of attemps has been put into the use of spatial statistics to investigate spatial patterns of such an infectious disease as HFMD. For instance, spatio-temporal distribution and hotspots of HFMD were successfully carried out in in northern Thailand (10). Spatial clustering and changing trend of hand-foot-mouth disease were identified during 2008-2011 in China (11). GIS has been also used to map HFMD reported cases for the whole of Sarawak (12). In 2014, a study was conducted for a temporal and spatial mapping of HFMD in Sarawak (13). Also in Sarawak, in 2016, Inverse Distance Weighted was used to interpolate the reported HFMD cases for the whole of Sarawak to identify the high-risk pattern of HFDM (14). Most recently, a spatial and temporal analysis has been successfully used to study prototypes virus of hand, foot and mouth disease infections and severe cases in Gansu, China (15). It can be seen that spatial statistics in general and local spatial statistics in particular have been widely applied in studies of infectious disease. It is therefore, in this study, to better undestand of the epidemiology and the spread of HFMD, we aim to investigate the use of local Geary's C statistic in the identification of local clusters of HFMD in Ho Chi Minh city, Vietnam. More specifically, histogram was first used to study the distribution of HFMD cases the incidence of HFMD. Local Geary C statistics was then applied to identify the spatial clusters of HFMD cases and HFMD incidence including high-high, low-low, negative and other positive clusters.HFMD cases and infection rates collected in Ho Chi Minh were used to explore the spatial clusters of HFMD. Finally, findings in this study will be discussed.

2. STUDY AREA, DATA USED AND METHODS

2.1. Study area and data used

In 2011, a large outbreak of hand, foot and mouth disease (HFMD) in Vietnam resulted in 113,121 children seeking medical attention, of whom170 died (8). A study of revealed that little is known about epidemiology of HFMD in the Vietnamese population. In 2005, a sentinel surveillance system at a pediatric hospital diagnosed 764 children with HFMD in Ho Chi Minh City (16). Among them, 96% were five years of age or younger. All cases had specimens taken for virological investigation. Human EV was isolated from 411 (54%) patients. Of those, 173 (42%) were identified as EV71 and 214 (52%) as CAV16. Of the patients with EV71 infection, 51 (29%) had severe neurological complications and three were fatal. In 2006–2007, sentinel surveillance at the same hospital reported 305 cases diagnosed with a neurological disease, of which 36 cases (11%) and three deaths were associated with EV71 (8). A outbreak of HFMD occurred in Ho Chi Minh city in 2023, certain districts in the city have witnessed a high incidence rate of HFMD infections per 100,000 inhabitants such as Binh Tan, Binh Chanh, Tan Phu, District 6, and District 8 (17). According to Ho Chi Minh City's health sector, the HFMD epidemic has increased rapidly and may last another 3-4 months since August, 2023. In particular, the time students returning to school will coincide with the second peak of the HFMD epidemic. In the most recent week (week 27th), the city recorded 1,614 HFMD cases, showing an alarming increase of almost 2.5 times compared to the average of 716 cases reported four weeks earlier (17). In this study, a datasets of HFMD cases and HFMD incidence were collected in Ho Chi Minh City in the first 8 months of 2023 was employed to investigate the use of local Geary's C statistic in the identification of local clusters of HFMD in Ho Chi Minh city.

2.2. Methods

This study used local Geary's C statistic to identify local clusters of HFMD in Ho Chi Minh city, Vietnam. Geary's C is also known as Geary's contiguity ratio or simply Geary's ratio (18). This statistic was developed by Roy C. Geary (19). The Geary's C statistic is a measure of spatial autocorrelation that attempts to determine if observations of the same variable are spatially autocorrelated globally (rather than at the neighborhood level). Spatial autocorrelation is more complex than autocorrelation because the correlation is multi-dimensional and bi-directional. The Geary's C statistic is defined as:

$$C = \frac{n-1}{2S_0}\frac{\sum_{i=1}^{n}\sum_{j=1}^{n} W_{ij}\left(x_i - x_j\right)^2}{\sum_{i=1}^{n}(x_i - \bar{x})^2} \qquad (1)$$

where: x_i and x_j are the HFMD for districts i and j; n is the total number of districts in the whole study area; and W_{ij} is a $(n \times n)$ spatial weight matrix; the term S_0 corresponds to the sum of all the weights; $\bar{x}$ is the mean of the HFMD and be given by the following equation:

$$\bar{x} = \sum_{i=1}^{n}\frac{x_i}{n}. \qquad (2)$$

The Geary C statistic can equivalently be expressed as a ratio of two sums of squares, i.e., the squared difference between observations at i and j in the numerator, and the sum of squared deviations from the mean in the denominator:

$$C = \frac{\sum_{i=1}^{n}\sum_{j=1}^{n} W_{ij}\left(x_i - x_j\right)^2 2S_0}{\sum_{i=1}^{n}(x_i - \bar{x})^2\,(n-1)} \qquad (3)$$

Clearly, the denominator is an unbiased estimator for the variance. The numerator on the other hand is a rescaled sum of weighted squared differences. The factor 2 is included to center the expected value of the statistic under the null hypothesis of no spatial autocorrelation to the value of 1 (not zero). Statistics smaller than one, indicating a small difference between an observation and its neighbors, suggest positive spatial autocorrelation. Statistics larger than one suggest negative spatial autocorrelation (large differences between an observation and its neighbors). The value of Geary's C lies between 0 and some unspecified value greater than 1. Values significantly lower than 1 demonstrate increasing positive spatial autocorrelation, whilst values significantly higher than 1 illustrate increasing negative spatial autocorrelation. Geary's C is inversely related to Moran's I, but it is not identical. While Moran's I and Geary's C are both measures of global spatial autocorrelation, they are slightly different. Geary's C uses the sum of squared distances whereas Moran's I uses standardized spatial covariance. By using squared distances Geary's C is less sensitive to linear associations and may pickup autocorrelation where Moran's I may not (20).

A local version of Geary's c was outlined in Anselin (1995) as:

$$C_i = \sum_{j=1}^{n} W_{ij}(x_i - x_j)^2 \quad (4)$$

Since the squared deviations cancel out the mean, it is irrelevant whether the variable is expressed on the original scale, or in standardized form, although in a multivariate setting, the latter is the preferred practice. Also, a number of variants of this statistic can be defined, depending on which of the scaling constants are included. For example, an alternative form, also given in (21) and further investigated in a study of Sokal (22) includes a consistent estimate for the variance as a scaling factor:

$$C_i = \frac{1}{m_2}\sum_{j=1}^{n} W_{ij}(x_i - x_j)^2 \quad (5)$$

where:

$$m_2 = \sum_{i=1}^{n} \frac{W_{ij}(x_i - \bar{x})^2}{n^3} \quad (6)$$

The analytical moments for the Local Geary ci were given in Sokal (21), using the expression in Equation 5. More specifically, the expected value for the Local Geary under a randomization approach is shown to be:

$$E[C_i] = \frac{2nW_i}{(n-1)} \quad (7)$$

where W_i is the sum of the weights in row i.

With expressions for the expected value and the variance in hand an asymptotic approximation can be developed, as shown in (21). However, these same authors also cautioned that asymptotic inference based on these moments tends to fail. Instead, the approach taken in practice is to use conditional permutation, as outlined in (21). This consists of creating a reference distribution for each individual location by randomly permuting the remaining values (i.e., all observations except the value at location i) and recomputing the statistic each time. Inference can then be based on a pseudo p-value of a one-sided test computed from the number of replicated statistics that are more extreme (either larger or smaller) than the observed local statistic. As is well known, the resulting pseudo p-values should be interpreted with caution, since they suffer from multiple comparisons, the potential biasing effect of global autocorrelation, and other such complicating factors (22).

3. RESULTS AND DISCUSSIONS

3.1. Analysis of distribution of HFMD

The distribution of HFMD cases and the incidence of HFMD are shown in the histograms in Figure 1. It can be seen that, from left to right, the histogram in Figure 1 (left) shows a decreasing trend in the number of HFMD cases. There were 6 districts having the number of infections ranging from 113 to 463 cases, 5 districts having the number of infections ranging from 760 to 1083 cases. Only 3 districts had more than 2,000 cases. The histogram in Figure 1 (right) shows the frequency distribution of HFMD infections per 100,000 inhabitants. Data from the histogram in Figure 2 (right) shows that there were 5 districts having high HFMD infection rates ranging from 211 cases/100,000 inhabitants to 230 cases/100,000 inhabitants, 4 districts with high infection rates ranging from 270 cases/100,000 inhabitants to 289 cases/100,000 inhabitants.

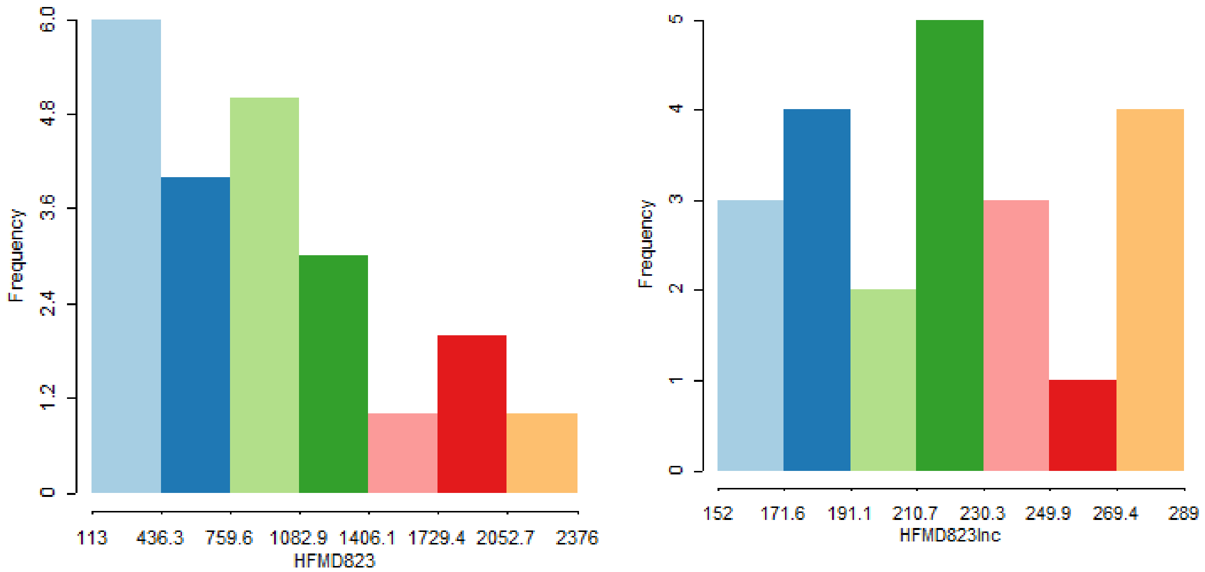

Figure 1. Histograms of HFMD cases (left) and HFMD incidence (right).

The standard deviation map of HFMD and HFMD incidece were shown in Figure 2, respectively. Data from Figure 2 (right) demonstrate that the distribution of HFMD cases per 100,000 inhabitants for each district. It can be seen that, in the first 8 months of 2023, five districts having the high HFMD infection rates included Binh Tan (289 cases/100,000 inhabitants), Binh Chanh (283 cases/100,000 inhabitants), Tan Phu (281 cases/100,000 inhabitants), Nha Be (272 cases/100,000 inhabitants) and District 12 (264 cases/100,000 inhabitants). Meanwhile, five districts having low HFMD infection rates included Can Gio (152 cases/100,000 inhabitants), Cu Chi (158 cases/100,000 inhabitants), Phu Nhuan (163 cases/100,000 inhabitants), District 3 and 4 with 181 cases/100,000 inhabitants. Data from the standard deviation map in Figure 2 (right) illustrate that districts having high HFMD infection rates were mainly concentrated in the central and western and southwest areas of Ho Chi Minh city. Districts having low HFMD infection rates were mainly distributed in the north, east and south areas of the city. Meanwhile, districts having medium HFMD infection rates were mainly distributed in the administrative center of the city. Data from the standard deviation map in Figure 2 (left) shows that a very large number of HFMD cases was mainly concentrated in the west and east of the city. Districts having a large number of HFMD infected cases included Thu Duc (2,376 cases), Binh Tan (2,030 cases), Binh Chanh (1,924 cases), Go Vap (1,465 cases) and District 12 (1,373 cases). Meanwhile, districts having very low and low numbers of HFMD infections were discovered in districts in the south of the city such as Can Gio (113 cases), Phu Nhuan (297 cases), Nha Be (600 cases) and District 7 (762 cases) and districts in the north of the city such as Cu Chi (636 cases), respectively.

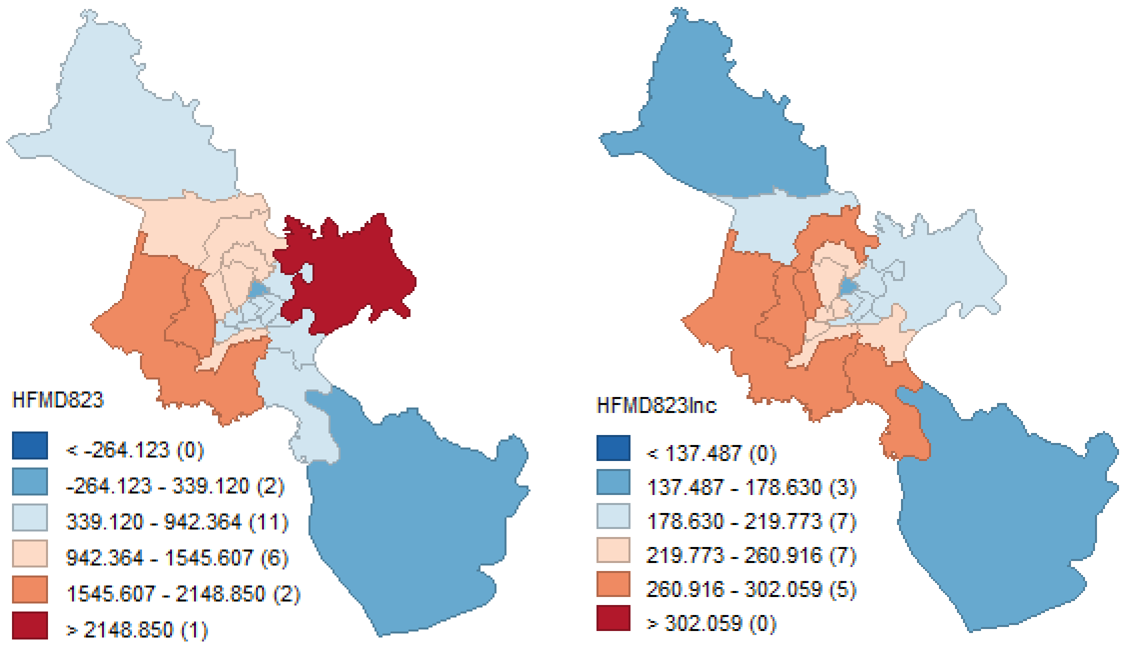

Figure 2. Standard deviation map of HFMD cases (left) and HFMD incidence (right).

3.2. Analysis of HFMD clusters

The results on HFMD cluster using HFMD cases and the incidence of HFMD are shown in Figure 3, respectively. Data from the local Geary cluster map shown in Figure 3 (left) illustrate that, in the case of using data on the number of HFMD cases, a total of two high-high clusters, one low-low cluster and two negative clusters were successfully detected. The remaining 17 districts were statistical significant at the level of 0.05. Two high-high clusters were found near the city center in District 12 (1,375 cases) and Binh Tan (2,030 cases). The only low-low cluster was discovered in District 5 (356 cases) in the east of the city center. Two negative clusters were discovered in Binh Thanh (897 cases) and District 7 (762 cases) in the west of the city. No other positive clusters were detected in this case. Thu Duc (2,376 cases), Binh Tan (2,030 cases), Binh Chanh (1,924 cases), Go Vap (1,465 cases) and District 12 (1,373 cases) were districts having a large number of HFMD cases but no high-high cluster of HFMD cases were detected. No spatial clusters were identified in these districts because their surrounding districts all had smaller numbers of HFMD cases. In addition, Can Gio (113 cases), Phu Nhuan (297 cases), Nha Be (600 cases) and District 7 (762 cases) were also foud with no low-low clusters because there were adjacent districts having a large number of HFMD cases. Data from Figure 3 (left) also demonstrates that 17 districts were statistical significant at the level of 0.05.

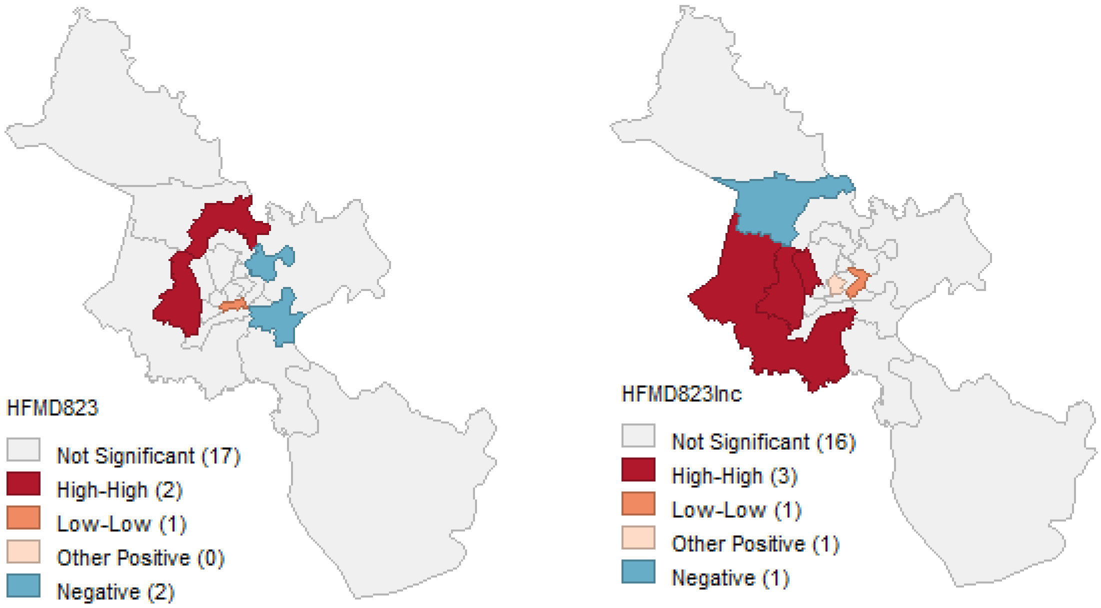

Figure 3. Local Geary cluster map of HFMD cases (left) and HFMD incidence (right).

It can be clearly seen from the local Geary cluster map shown in Figure 3 (right) that, in the case of using data on HFMD infection rates, there were a total of three high-high clusters, one low-low cluster, one negative and one other positive clusters were successfully detected. Te remaining 16 districts were idenfied with statistical unsignificance at the level of 0.05. Among these clusters, three high-high clusters were found in the districts of Binh Tan (289 cases/100,000 inhabitants), Binh Chanh (283 cases/100,000 inhabitants) and Tan Phu (281 cases/100,000 inhabitants) in the east of the city. The only low-low cluster was discovered in District 1 (209 cases/100,000 inhabitants) in the city center. Another positive cluster was also discovered in District 10 (221 cases/100,000 inhabitants) in the city center. A negative cluster was successfully detected in Hoc Mon (206 cases/100,000 inhabitants), a northern district of the city. Similar to those obtained in the case of using data on HFMD cases, Nha Be (272 cases/100,000 inhabitants) and District 12 (264 cases/100,000 inhabitants) were districts having a large number of HFMD cases but no high-high clusters were detected in these districts because their surrounding districts had smaller HFMD infection rates. Data from Figure 3 (right) also shows that a total of 16 districts were found with statistical significance at the level of 0.05.

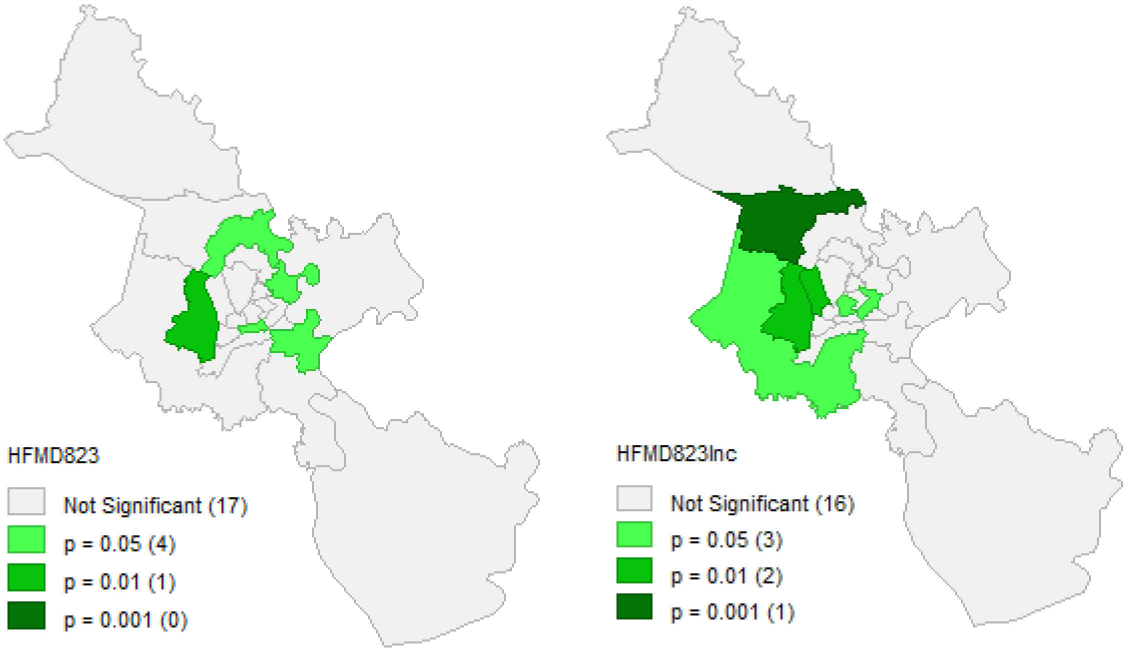

Figure 4. Local Geary significance map of HFMD cases (left) and HFMD incidence (right).

Local Geary significance maps in Figure 4 illustrates the spatial distribution of statistical significance for each district obtained from local Geary C statistic in the Ho Chi Minh City. Statistical levels were expressed using 4 scales including statistical unsignificance (p-value > 0.05) and statistical significance at levels of 0.05, 0.01 and 0.001, respectively. Data in Local Geary significance in Figure 4 (left) show that, in the case of using the data on HFMD cases, no district was found with statistical significance at the level of 0.001. Only Binh Tan was detected with a high level of significance at the level of 0.01. Three districts were statistical significant at the level of 0.05 including District 12, Binh Thanh and District 7. The remaining 17 districts were not statistical significant at the level of 0.05. In the case of using data on HFMD infection rates, data from Local Geary significance in Figure 4 (right) shows that only Hoc Mon was statistical significant at the level of 0.001. Wheareas, two districts, Binh Tan and Tan Phu, were statistical significant at the level of 0.01. Three districts were detected with statistical significance at the level of 0.05 including Binh Chanh, District 1 and District 10. The remaining 16 districts were found with statistical unsignificance at the level of 0.05.

4. CONCLUSIONS

The objective of this study is to apply local Geary's C statistic on the identification of local clusters of HFMD in Ho Chi Minh city, Vietnam. In this research, histogram was first used to study the distribution of HFMD cases the incidence of HFMD. Local Geary C statistics was then applied to identify the spatial clusters of HFMD cases and HFMD incidence including high-high, low-low, negative and other positive clusters. The study results showed that, in the case of using HFMD cases, two high-high clusters in District 12 and Binh Tan in the city center, one low-low cluster in District 5 in the east of the city center and two negative clusters in Binh Thanh and District 7 in the west of the city were successfully detected. On the other hand, in the case of using HFMD infection rates, a total of three high-high clusters, one low-low cluster, one negative and one other positive clusters were successfully detected, in which, the three high-high clusters were found in the districts of Binh Tan, Binh Chanh and Tan Phu in the east of the city. It can be concluded that findings in this study confirm the usefulness of local Geary's C statistic in the identification of spatial clusters of HFMD. Findings in this study also play an important role in the fight against hand, foot, and mouth disease.

Declaration by Authors
Ethical Approval: Approved
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