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Spatiotemporal relationship analysis of the 2019-nCoV patients hospitalized in Istanbul: A retrospective database analysis

İstanbul'da hastanelere başvuran 2019-nCov hastalarının yer-zaman ilişkisinin incelemesi: Geçmişe dönük bir veri tabanı incelemesi

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Abstract

Aim: The COVID-19 epidemic has reached every country in the world. Control strategies require effective tracing and isolation activities. Electronic mapping techniques are used in the visualization of spreading characteristics of COVID-19. The Geospatial Information System became an exceedingly popular open web tool to inform professionals and the public. These systems allow public health authorities to monitor the spreading characteristics and plan effective control strategies. The objective of this study was to identify the spatiotemporal mutual relationship of COVID19 patients living in two of the biggest districts of Istanbul (Kadikoy and Uskudar) who were admitted to the hospital.

Methods: A total of 672 adult patients who were diagnosed with possible or confirmed COVID19 infection were included in the analysis. COVID19 diagnosis was confirmed either with positive RT-PCR test or radiographic chest imaging plus the presence of symptoms of the infection. Pearson correlation analysis and Moran's correlation analysis were applied to the data set. Small pieces of regions [100,000 x 100,000] were set for the districts, and each event origin was fitted into the proper region using cartesian coordinate information. Getis-Ord hot spot analysis was performed to pinpoint the infections with higher concentration over time.

Results: Pearson's correlation revealed no significant results, while Moran's analysis showed a significant correlation between distance and admission date [I: 0.64]. We identified at least 10 relevant hot spots in 3 districts.

Conclusion: Determining the spatiotemporal relationship among cases of a central hospital may inform local authorities about dissemination patterns and help improve control measures against epidemics.

Keywords: Spatiotemporal Relationship Analysis, 2019-nCoV, Counties

Öz

Amaç: COVID-19 virüsünü salgını dünyanın neredeyse her yerine yayılmış durumdadır. Kontrol yöntemleri ise etkili takip ve izolasyon yöntemleri gerektirmektedir. Elektronik haritalama teknikleri COVID-19 virüsünün yayılma özelliklerini görselleştirmede kullanılmaktadır. Konum Bazlı Bilgi Sistemi yetkilileri ve halkı bilgilendirmek için çoğunlukla tercih edilmektedir. Bu sistemler halk sağlığı yetkililerine hastalığın yayılma özelliklerini göstererek, daha etkili kontrol planlaması yapılmasını sağlamaktadır. Bu çalışmanın amacı İstanbul'un en büyük iki ilçelerinden ikisinde (Kadıköy ve Üsküdar) yaşayan ve COVID-19 nedeniyle hastaneye kabul edilen hastaların yer-zaman ilişkilerinin belirlenmesidir.

Yöntemler: COVID-19 enfeksiyonu tanısı onaylanmış/olası 672 yetişkin hasta bu çalışmaya dahil edilmiştir. COVID-19 teshisleri; ya pozitif sonuçlanan RT-PCT testleri ile ya da hastalığın belirtilerini görülüyorsa radyolojik göğüs tetkikleri ile doğrulanmıştır. Veriler Pearson korelasyon analizi ve Moran's korelasyon analizi ile değerlendirilmiştir İlçeler için küçük bölge parçaları [100.000 x 100.000] ayarlandı ve her olgunun kaynağı kartezyen yer belirleme kullanılarak kurulan küçük bölge parçalarına oturtuldu. Zaman içerisinde yoğunluğun artması ile enfeksiyonu tam olarak belirlemek için Getis-Ord sıcak nokta analizi kullanılmıştır.

Bulgular: Mesafe ve hastaneye kabul edilme süresi arasında Pearson korelasyonuna göre ilişki bulunmazken, Moran korelasyonun da anlamlı bir ilişki bulmuştur [I:0.64]. 3 bölgede en az 10 sıcak nokta tespit edilmiştir.

Sonuç: İndeks hastane vakaları arasındaki yer-zaman ilişkisinin belirlenmesi, yerel yetkililere hastalığın yayılma örüntüsü hakkında bilgi verebilir ve salgınlara karşı kontrol önlemleri geliştirilmesine yardımcı olabilir.

Anahtar kelimeler: Yer-zamansal ilişki incelemesi, 2019-nCoV, İlçeler

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Ethics Committee Approval: Umraniye Research and Training Hospital Clinical Research Ethics Committee, 4/28/2020, B.10.1.TKH.4.34.H.GP.0.01-133 All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.
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Introduction

Since the beginning of 2020, the world was overshadowed by the rapidly spreading novel severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] named COVID-19. The World Health Organization reported 3679499 confirmed cases of COVID-19, including 254199 deaths globally, as of 6:32pm CEST, 7 May 2020 [1]. On the 11th of March, the first coronavirus infection case was reported in Turkey and there are 135569 confirmed cases and 3689 deaths reported as of the 8th of May, most of which were detected in the city of Istanbul [1].

During the COVID19 epidemic, choosing the best intervention strategy is critical to effectively control the spreading of disease, especially when uncertainties regarding the disease are present. Control measures can be categorized under two main strategies: Suppression or mitigation. Both strategies require effective tracing and isolation activities. Time of contact with suspected or confirmed cases and location are two important variables to better understand infectivity characteristics of the virus and dependency of virus dissemination on human behavior. Although health professionals started using conventional mapping techniques to visualize the relationship between place and health many centuries ago [2], new technological tools capturing spatiotemporal data were used in China to early identify spreading characteristics and plan effective use of resources [3]. Similar mapping techniques are being used in the visualization of spreading characteristics of other viral diseases for decades. Country-level maps are produced to show the distribution of viral diseases over time [4]. Throughout these mapping methods, it was possible to estimate the movement of the pandemics and future patterns of spread. Geospatial and time analysis is a valuable tool in determining the spatial spread and quantifying determinants of contamination. In countries where health and sociodemographic data collection systems are developed, such information has been widely used by governments to identify the spatiotemporal movement of chronic infections [5,6]. This analysis method has been also used to identify hot spots for the infection source in geographies where preventive measures must be planned considering both individual and geographic-area variation [7]. Location and time are two important environmental determinants of health status because they include risk factors of contagious diseases. Integrating and analyzing location-based real-world information and generating predictive modelling using novel information technologies during the pandemic can help health care providers and planners to identify those risk factors and new methods for prevention [8]. Recently, Geospatial Information System dashboards have developed open web tool applications by WHO and other scientific institutions to inform professionals and the public. Furthermore, the dedicated mobile phone-based application was used to collect personal data from public authorities and inform users about their risks in a highly detailed spatial scale [9].

All published studies and dashboards use country or regional data sources for geospatial analysis. However, most of the logistic and health sources planning must be conducted at the district level, as well. Under the social distancing and strict travel restriction circumstances, narrower scaled modelling of spatiotemporal maps may be more useful and realistic to understand dissemination and control it. The Turkish government has implemented severe social distancing measures and travel restrictions immediately after the detection of the first COVID19 case in the country [10]. All COVID19 patient-related real-time data, including actual residential information are collected from hospitals and stored in a central database [Public Health Management System] for surveillance and home-based treatment purposes. It allows public health authorities to monitor all events at thousands of public health facilities simultaneously and centrally.

In this study, we aimed to identify the spatiotemporal mutual relationship of COVID19 diagnosed patients living in two of the biggest districts of Istanbul [Kadikoy and Uskudar] who were admitted to our hospital by using residential address-based information systems and patients’ clinical data.

Materials and methods

Patient data collection and diagnosis

All patients over 18 years of age admitted to 2. Abdulhamid Han Research and Training Hospital [N 41°00'05.4", E 29°01'11.2"] who were diagnosed with possible or confirmed COVID19 infection between 1st of March – 9th of April 2020 are included in the analysis. COVID19 diagnosis was confirmed either with a positive RT-PCR test developed by the Turkish Ministry of Health central GDPH Microbiology Reference Laboratory or radiographic chest imaging plus symptom array of the infection [Fever, acute respiratory symptoms, travel, contact with a COVID19 patient]. All clinical, laboratory and demographic data were retrieved from the hospital local database and Public Health Management System. Geolocation information for each patient is obtained using patients’ residential addresses. Before starting geospatial analysis, the data set is modified to remove incomplete or ineligible data from the data set. All analysis mentioned below are applied to cleansed data set to prevent the results from being affected by inconsistencies in the data set. A total of 672 patients with valid address data and admission dates were included in our analysis. Descriptive analysis of the cases was completed using IBM SPSS Statistics Version 20.0. The study area, Istanbul City, is located between Black Sea and Marmara Sea, [in 41° 0' 54.4932" N latitude and 28° 58' 46.3080" E longitude], with a total area of about 5461km2, with 15,52 million habitants and with metro density of 2987/km^2. Kadikoy and Uskudar districts have total area of about 25.2km^2 and 46.41km^2, respectively, and populations of 482.713 and 531.825, respectively. The Medical Ethics Committee at Umraniye Research and Training Hospital approved the study on the 28th of April 2020. As all patients give consent for data collection and retrospective research at the hospital level, it needed no consent from the participants.

Geospatial analysis and mapping of COVID19 infections

To calculate spatial weight for each event, exact latitude and longitude information was attained using address information in the application form. For every address line in the admission form, a request to get coordinate information is sent to Google Geolocation API via Python script, and exact coordinates are returned. This process was completed using Python 3.7 distribution. A distance matrix containing spherical distance from each patient to all other patients is created. To use application date as a measurement for infection propagation, application date data is converted to scaler values as an offset from the first case $[o_0]$. Interpatient distances and admission dates are the selected to be used in geospatial analysis. The distance information obtained from the distance matrix with 672 columns and 672 rows is the first input to be used in every analysis mentioned below.

Inter-distances between patients were calculated by their geo-coordinates. Geospatial analysis is divided into three parts, starting from determining the dependency of the whole data set to analyzing each patient, respectively.

In the first part, a correlation analysis is applied to data set to reveal the relationship between patients. In this phase, the Pearson correlation coefficient, a widely used correlation coefficient indicating a linear association between independent variables [11], is used to measure linear dependency between infection and location of patients. However, geospatial variables are rarely eligible for linear dependency analysis. Therefore, a correlation coefficient designed to measure geospatial dependency, Moran's I, is used in the second part of the analysis [12]. Geospatial correlation was applied to reveal whether admission dates were correlated with distances between all patients.

After the geospatial correlation for the whole data set is obtained, the origin point of every infection is analyzed in the third part. This part of the analysis aims to find out whether cases center upon any area by using Getis-Ord's hot spot analysis [13]. In this phase, each patient is analyzed in conjunction with every other patient regarding the distance between patients and the admission date. In a highly infectious disease, regions with high concentration of infection are required to be explored and isolated. Thus, finding and isolating these spots play a crucial role in getting ahead of disease spread.

Design study

This study aims to find a mutual relationship between different cases with the positive COVID-19 test results. Address information for each case and application that the institution is selected as input variables to establish a correlation between cases. The study is designed as three phases: Data preparation, correlation analysis and hot spot analysis.

Phase I – Data preparation

Patient data is reduced to 672 separate cases with two features, address information of the patient and application date. In order to calculate a spatial weight for each event, exact latitude and longitude information should be obtained. For every address line in the admission form, a request to get coordinate information is sent to Google Geolocation API via Python script, and exact coordinates are returned.

Inter-distances were calculated using their geo-coordinates. Spherical distances with given latitude and longitude can be calculated with the formula suggested by José de Mendoza y Ríos [14], which was later called the "Haversine Distance."

$$d = 2 \times r \times arcsin\left(\sqrt{sin^2\left(\frac{\Delta_\varphi}{2}\right) \times \cos\varphi_1 \times \cos\varphi_2 \times sin^2\left(\frac{\Delta_\lambda}{2}\right)}\right) \quad [1]$$

$$\Delta_\varphi = \varphi_2 - \varphi_1 \quad [2]$$

$$\Delta_\lambda = \lambda_2 - \lambda_1 \quad [3]$$

d: Spherical distance
r: Radius of the sphere*
***:** $r_{Earth} \approx 6{,}371$

The distance matrix is created with the distance between the residential address of each patient to all other patients' residential addresses. The distance information taken from the distance matrix with 672 columns and 672 rows is the first input to be used in every analysis mentioned below.

The second input is selected as admission date, considering the aim of this study to find out the relationship between infection date and geographic proximity. However, the admission date is not eligible to use in calculations with distance due to the format of the date data. Thus, to use admission date as a measurement for infection propagation, admission date data was converted to scaler values as an offset from the first case $[o_0]$.

Phase II – Correlation analysis

In the second phase, Pearson correlation analysis was applied to the data set. There are two data sets created for Pearson correlation analysis, including raw and modified data. Raw data consist of two columns to compare:

$o_{0_{ij}}$: marginal o_0 from event i to event j
d_{ij} : distance from home of event i to home of event j

The second data set was created to fit spatial data better to Pearson's. Frequency analysis is completed on data to fit each event into a related category on the scale of measurement [15]. The analysis yielded 300 different categories covering all the data of both $o_{0_{ij}}$ and d_{ij}.

Pearson's analysis with the original data set has resulted in correlation coefficient **0** which indicates no correlation at all. Along with that, Pearson's analysis with grouped data set resulted in an r-value of $5.9 \times E - 13$ which is again too small, almost indicating zero correlation.

Following Pearson correlation analysis, Moran's correlation analysis is applied next. In Moran's analysis, each data is positioned in a pre-defined discrete geographical region. Since the cartesian coordinates system is continuous, small pieces of regions [100,000 x 100,000] are set on the Anatolian side of Istanbul, and each event origin is fitted into the proper region using cartesian coordinate information.

Further, adjacency of events should be defined, and an adjacency matrix should be formed. Adjacency between cells can be defined by using either Moore neighborhoods [Queen's case] or Von Neumann neighborhoods [Rook's case] [16]. Queen's case is selected for this study and an adjacency matrix is formed. Adjacency matrix became a basis for the weight matrix $[w_{ij}]$ by assigning the highest spatial weight to the closest two origins and similarly assigning lowest weight to most distant two origin. Using $o_{0_{ij}}$ and w_{ij}, Moran's I is calculated.

$$I = \frac{1}{S^2} \times \frac{\sum_i \sum_j w_{ij} \times \left(o_{0_i} - \overline{o_0}\right) \times \left(o_{0_j} - \overline{o_0}\right)}{W} \quad (1)$$

$$W = \sum_{i=1}^{N} \sum_{j=1}^{N} w_{ij} \quad [2]$$

$$S^2 = \frac{\sum_{i=1}^{N} \left(o_{0_i} - \overline{o_0}\right)^2}{N} \quad [3]$$

Moran's I has a value from -1 to +1 where;

- -1 refers to perfect dispersion [negative correlation]
- 0 refers to perfect randomness [no spatial correlation]
- +1 refers to perfect clustering [positive correlation]

Moran's analysis is applied to the patient data set and resulted in an I value of **0.64**, which indicates a positive correlation.

Phase III – Hot spot analysis

A hot spot refers to a place of more than usual interest, activity, or popularity comparing to other areas. In epidemiology, hot spot indicates a region with high concentration of a disease [17]. Hot spot analysis techniques are derived from dispersion studies aiming to understand the distribution of points in space [18]. The aim of hot spot analysis in any spatial relationship study is to pinpoint the event with a higher concentration of defined measurement among the distribution of all events. Hot spot analysis lets discover location related clusters while making detecting anomalies easier [19].

Getis and Ord offered a hot spot metric, G^* to identify spatial patterns and find the events with a higher concentration of measurement metrics. Getis-Ord's methodology evaluates each data point respecting distances between other data points and proximity of admission dates.

$$G^* = \frac{\sum_j^n w_{ij} x_j - \bar{X} \times \sum_j^n w_{ij}}{S \times \sqrt{\frac{\left[\left(n \times \sum_j^n w_{ij}^2\right) - \left(\sum_j^n w_{ij}\right)^2\right]}{n-1}}} \quad [1]$$

$$\bar{X} = \frac{\sum_j^n x_j}{n} \quad [2]$$

$$S = \sqrt{\frac{\sum_j^n x_j^2}{n} - \left(\bar{\bar{X}}\right)^2} \quad [3]$$

The Getis-Ord. analysis is applied to all 672 origin points in the data set. Distance between the location of the selected patient and the location of the next patient is used as w_{ij} in the formula. As for x_j, offset value of admission $[o_{0_{ij}}]$ is used. After evaluation of all 672 locations using distance and admission information, a total number of 10 events emerged as the hot spots.

Results

The mean age of patients was 51.54 (SD:16.42) years, and 53.9% of patients were male. Among all, 27.5% of patients were treated as an outpatient, 5.2% died, 50.4% were discharged and 16.8% were still hospitalized during the study period. Majority of cases were in Uskudar (30.95%), Kadikoy (10.26%), Umraniye (15.47%), Atasehir (7.29%) districts. A detailed distribution map can be seen in figure 1. Peak date of admissions (57 patients, 8.5%) was on the 9th of April, and most patients were admitted to the hospital between the 1st and 15th of April (Figure 2).

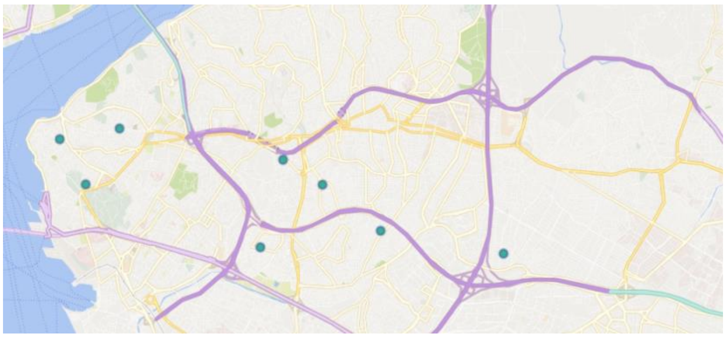

Figure 1: 10 hot spots emerged following hot spot analysis

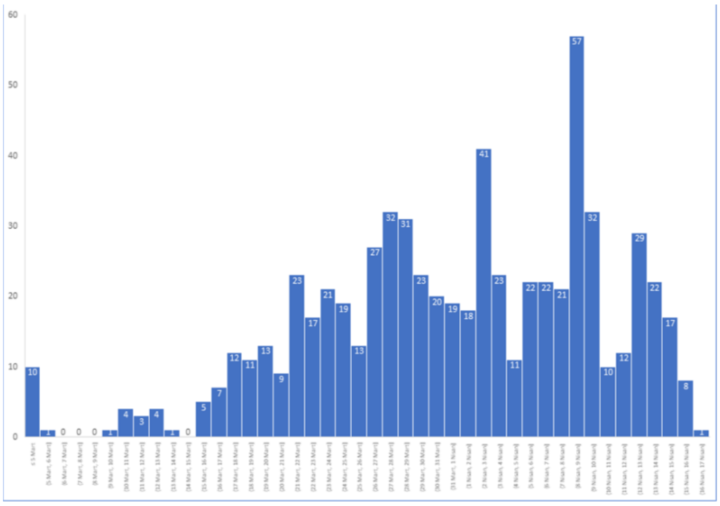

Figure 2: Number of admission per day

Admission dates and distances between patients are given as input with two different approaches, traditional approach, and categorical distance approach [Figure 3]. The traditional approach returned the Pearson's correlation coefficient $r = 0$ which indicates no linear dependency at all. Similarly, the categorical distance approach returned an exceedingly small r value; $5.9 \times E - 13$.

Moran's I, a correlation coefficient specifically designed to measure location-based relationship, is used in the second step of the analysis. Moran's analysis returned a correlation coefficient of 0.64 which significantly implies a correlation between distance and admission date.

In hot spot analysis, while Getis-Ord's G^* increases, hot spots in the data set emerges. Our data set of 672 patients revealed at least 10 relevant hot spots [5 in Kadikoy, 4 in Uskudar and 1 in Atasehir districts], information of which can be found in Figure 3 below.

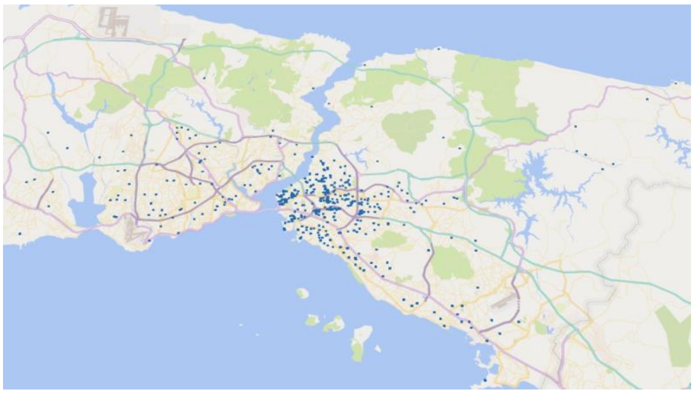

Figure 3: Case density map of the sample group

Discussion

The purpose of this study was to identify the spatiotemporal mutual relationship of COVID19 diagnosed patients living in two counties of Istanbul and we found that there is a significant correlation between distance and admission date. In addition, we found at least 10 relevant hot spots (5 spots in Kadikoy and 5 spots in surrounding districts) that should be considered as the most important location-time points for the dissemination of the disease in our sample. Consecutive and interrelated admissions of those individuals to our central hospital shows that there is a modellable dissemination pattern of the virus within a small but densely populated geography. Detected hot spots require more attention for the initial dissemination and control of the source of disease.

Our hospital was the earliest designated hospital for COVID19 treatment only after the breakout of the pandemic in the North-East part of Istanbul. The number of diagnosed patients over time in this hospital reflects and confirms the similarity with the acute course of the pandemic in the city. To date, COVID19-related geospatial and spatiotemporal analysis are limited and in contrast with previous studies, we investigated spatiotemporal analysis of the infection in a limited geography. Hence the results may be more useful to elucidate early dissemination and control from local management perspective together with country-wise preventive measures. Particularly when general shutdowns and curfews were heavily criticized [20], surveillance measures could be implemented in limited geography based on this local analysis to abate economic and social impacts.

The data used in our analysis have several limitations. First, the data was extracted from a single hospital. As not all patients from these districts were admitted to our hospital, the patient pool could not reflect all dissemination pattern although most of the initial cases were accumulated in our hospital, which was assigned as a COVID19 reference center. Second, population-based testing was not used to identify asymptomatic cases, therefore, spreading of infections through asymptomatic cases could not be included in our correlation analysis. Third, as for geospatial correlation, patient data set covers patients getting treated at the institution coming from different districts of Istanbul. This fact prevents analysis to see the whole picture in two districts included in the analysis. However, 0.64 I value with this missing picture indicates that, if the same analysis can be applied to whole patients' data of these districts, a very strong spatial correlation is to be obtained. Fourth, the effect of cases' daily mobility before admission to the hospital could not be included in the correlation analysis. Finally, hot spot analyses require considerably big data sets to set a profound base to identify location-based dependencies. Considering the data set used in Getis-Ord analysis is relatively small and concentrated on a few districts in Istanbul, it would be expected not to get any meaningful hot spot location at all. However, even with this particular small data set, Getis-Ord's G^* is yielding decent results that imply bigger data sets related to infectious diseases fit the analysis particularly well. Linear correlation yielded that, Pearson's r is not a good indicator of geolocation-based correlation. Even though converting data to a more discrete pattern helps, the correlation coefficient was still too insignificant.

A recently published study showed a distribution pattern of COVID19 in a large-scale spatial [total area of about 185,900 km2] but limited temporal analysis (15 days) in Hubei Province, China [21]. Six types of temporal patterns were defined based on increasing and significant abrupt changes at the county level. However, the spatial data are collected at the city/county level and it is not based on the residential address. They also explained abrupt temporal and spatial changes based on the increases in daily testing capacity and on implementation of mobility control measures from Wuhan. Despite a large number of cases, it only provided temporal changes according to confirmed data from districts, and spatial resolution was limited at the district level. Our study spatial data is based on point location and time. Similarly, we identified a spatial cluster that can be useful for timely control of population flows to prevent a larger outbreak of disease.

Hubei Province study included cases confirmed with nucleic acid only. Hitherto, low sensitivity nucleic acid tests, poor consistency between the positive rate of initial nucleic acid tests, and clinical findings were heavily criticized in China [22]. Our study included both RT-PCR testing positive and CT confirmed cases.

Limitations

There will be future study proposals, but limitations to this study are irrelevant for now.

Conclusion

The results of our study suggest that there is a strong spatiotemporal relationship among the cases of an index hospital, accepting patients from a limited geographic and densely populated area. The early identification of the dissemination pattern and hot spots throughout a similar analysis during the second wave of the pandemic may lead to a more effective control with a less negative impact on economic and social life. This analysis could be further improved using additional data sources and more precise clinical information for the calculations. Expansion of data source set from one hospital to all health care units in the city [increase in the number of patients] and using first symptom appearance date instead of hospital admission date will further improve the precision of the results and could lead more generalizable conclusions.

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