Acta Sci. Pol., Administratio Locorum 23(1) 2024, 5–17.
https://czasopisma.uwm.edu.pl/index.php/aspal plISSN 1644-0749 eISSN 2450-0771 DOI: 10.31648/aspal.9397

ORIGINAL PAPER
Received: 18.09.2023 Accepted: 22.10.2023

TERRITORIAL PATTERNS OF COVID-19 IN IRAN

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ABSTRACT

Motives: Spatial analysis has become an essential tool in understanding the underlying factors that contribute to the distribution of viral pandemics, diseases, injuries, and mortality patterns. By visualizing geographical data in spatial maps, researchers can identify local distribution patterns and potential drivers behind these patterns. In health and medical sciences, there has been a growing recognition that spatial analysis and mapping techniques are helpful in addressing various challenges related to the allocation of healthcare resource in both urban and rural areas.
Aim: The objective of this study was to analyze the spatial distribution pattern of the COVID-19 pandemic and the Index of Proximity Distribution (IPD) across 31 provinces of Iran between February 2019 and February 2023. A two-stage sampling method combining convenience and cluster sampling was used to examine COVID-19 distribution patterns in 31 provinces of Iran between 22 February 2020 and 22 February 2023. COVID-19 and IPD data were collected as part of this panel study. Data were analyzed using t-tests, chi-square tests, and analysis of variance (ANOVA) in SPSS version 28 ($\alpha = 0.05$). Subsequently, daily COVID-19 infection data for each province in the analyzed period were processed in ArcGIS software, and the spatial distribution pattern of the pandemic in Iran were visualized by point density analysis. Standard distance and standard deviation ellipse techniques were employed to assess the density or dispersion of infected individuals and to determine the spatial distribution pattern of COVID-19 in Iran. A spatial autocorrelation (Moran's I) analysis was conducted to identify the spatial distribution pattern of COVID-19 in Iran. Additionally, distance-based spatial autocorrelation was used to examine the prevalence of COVID-19 infection across Iranian provinces. In a grouping analysis, 31 Iranian provinces were classified into five groups based on the number of COVID-19 cases, and spatial statistics were used to examine the prevalence of COVID-19 within each group. A hot spot analysis and a standard distance (SD) analysis were conducted to explore spatial correlations in the number of individuals affected by COVID-19 in each province.
Results: Based on the Moran index, a random spatial pattern with a Z-Score of 1.485 was identified in March 2019, whereas a clustered distribution of COVID-19 with a Z-Score of 3.039 was determined in February 2023. The distance-based spatial autocorrelation analysis revealed a positive value of the Moran index (0.136627) at a distance of 383.3 kilometers from Tehran, which points to positive spatial autocorrelation and a higher number of COVID-19 cases in nearby regions. Conversely, the Moran index assumed a negative value of 0.040246 at a distance of 726.6 kilometers from Tehran, which suggests that the number of pandemic cases decreased over distance from Tehran. Moreover, based on the results of the hot spot analysis, Tehran province was identified as a hot cluster with a higher

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prevalence of COVID-19 cases in that region. In contrast, Bushehr province was classified as a cold cluster with a lower prevalence of COVID-19 cases in comparison with the surrounding regions. These findings provide valuable insights into the spatial distribution and clustering of COVID-19 cases in Iran. The shift from a random spatial pattern in 2019 to clustered distribution in 2023 indicates that the pandemic spread rate increased over time. The positive spatial autocorrelation near Tehran highlights the role of proximity and population movement in the transmission of the virus. Furthermore, the identification of hot spots and cold spots in a country can inform targeted interventions and resource allocation to effectively manage and control the pandemic. Overall, this study demonstrates the value of spatial analysis in identifying the spatial distribution patterns and the dynamics of the COVID-19 pandemic in Iran. The integration of spatial analysis techniques with epidemiological data contributes to a better understanding of spatial-temporal patterns, facilitates effective public health responses and resource allocation strategies. These findings contribute to the growing body of knowledge on the spatial epidemiology of COVID-19 and can aid in informing future preparedness and response efforts in Iran and other regions that face similar challenges.

Keywords: epidemiology, spatial analysis, Index of Proximity Distribution (IPD), COVID-19, Iran

INTRODUCTION

The last days of December 2019 witnessed the emergence of a global landmark event as the first confirmed case of an infection with a novel coronavirus was reported in Wuhan, a bustling metropolis nestled in Hubei Province at the heart of Central China. This pivotal moment sparked a series of consequential events that would soon engulf the globe in uncertainty (Cheshmehzangi et al., 2021). The Hubei health authorities sprang into action on 8 January 2020, launching an extensive survey to decipher the nature and extent of this mysterious viral outbreak. The clock ticked relentlessly, and by 20 January 2020, the dire situation could no longer be concealed, and an outbreak was officially declared. It was not just a run-of-the-mill disease; it was COVID-19, the harrowing pandemic that would reshape the course of history. In the blink of an eye, in the early days of March 2020, the viral contagion had transcended boundaries, traversing continents and oceans to lay its claim on a multitude of nations, including Iran (Nojomi et al., 2021). The spread of this pandemic was unlike anything we had ever witnessed; its ramifications were both staggering and unprecedented.

Traditionally, infectious diseases, such as the notorious COVID-19, are known to proliferate through close personal interactions and physical contacts. The transmission hinges on face-to-face communication, a characteristic that makes tracking and comprehending the spread of these diseases a formidable task. Interpersonal interactions that occur at various locations over time on a large scale should be captured to gain insights that can empower effective control measures. Yet in practice, the acquisition of micro-level data at a significant scale remains a challenge. In light of this scarcity, we are left with no choice but to rely on alternative indicators as proxies for interpersonal interactions and contacts. This method becomes all the more critical in our quest to understand and mitigate the spread of infectious diseases (Ma, Li, & Zhang, 2021; Ma, Li, Lan et al., 2021). In certain instances, spatial-based surveys have been undertaken to venture into the field and amass comprehensive data on the pandemic's dynamics. These efforts aim to provide invaluable information that can serve as a lifeline in our battle against infectious diseases, including the formidable adversary that is COVID-19 (Isaza et al., 2023). In this regard, and despite significant advancements in the field of disease management, infectious diseases remain a crucial concern in epidemiology and public health. Epidemiology plays a key role in identifying geographic areas and vulnerable populations that are at a higher risk of disease contraction and mortality due to associated risk factors (Kalbus et al., 2023; Miethke-Morais et al., 2021). Identifying

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these geographical areas and high-risk groups is instrumental in implementing appropriate healthcare and social interventions to mitigate the impact of these risk factors (Dhingra & Vandana, 2011).

Spatial epidemiology serves as a valuable tool in unraveling the causes behind diseases, injuries, and mortality (Boudou et al., 2023; Dawood, 2023; Kazi et al., 2023; Montoya et al., 2023). In the first step of analysis, geographical data are visualized, particularly in geographical maps, to provide insights into the spatial distribution patterns of diseases, injuries, and deaths, and facilitate causal identification (Wu, Shen et al., 2023; Wu, Williams et al., 2023). In recent years, spatial analyses and maps have been increasingly used in health and medical sciences due to their superior visualization capabilities compared to statistical tables (Afzali et al., 2020; Gomez Selvaraj et al., 2020; Huang & Kwan, 2023).

Given the expansion and active provision of health and medical services in various countries, spatial analyses should be incorporated in the healthcare sector to address the challenges related to the allocation of medical resources in urban and rural areas (Lu et al., 2023; Mungmunpuntipantip & Wiwanitkit, 2023; Zhu et al., 2022). Recent developments emphasize that spatial analysis, facilitated by the production of maps, is an essential and valid tool in processing, analyzing, and visualizing spatial information in domains such as health and environmental protection, disease ecology, and community health. Spatial analyses facilitate the determination of disease locations, assessment of healthcare facilities and services, and delineation of societal boundaries; therefore, they constitute fundamental elements of epidemiological and health studies (Arvin et al., 2023; Bratton & Wójcik, 2022; Krauss et al., 2023; Yao et al., 2023). The identification of these geographical areas and high-risk groups enables the selection of appropriate healthcare, medical, and social measures to mitigate the impact of these risk factors (Borges et al., 2022; Juneau et al., 2023).

The advancements in spatial technology have revolutionized data production and modeling, and opened new horizons in data analysis (Gamelas et al., 2023; Ortiz et al., 2022; Ramos et al., 2023; Takefuji, 2023). Consequently, topics such as spatial dependence, spatial links, spatial heterogeneity, spatial scale effect, and spatial clustering have been integrated into spatial process models (Coro, 2021; Shang Wui & Jahanbani Ghahfarokhi, 2022; Shen et al., 2020; Tu et al., 2023). Despite the fact that spatial phenomena may follow irregular distribution patterns, spatial analysis approaches have revealed that these phenomena follow discernible patterns that can be comprehended and recognized. These patterns enable the identification of general laws that transcend the boundaries of space and time (Banerjee et al., 2022; Boareto et al., 2022; Furati et al., 2021; Kolebaje et al., 2023; Ma et al., 2021; Ma et al., 2021; Sidwell & Smee, 2004).

The spatial distribution patterns of COVID-19 in Iran have been analyzed in several studies (including Isaza et al., 2023; Nojomi et al., 2021; Sharifi et al., 2022; Raoofi et al., 2020). Rahnama and Bazargan (2020) relied on ArcGIS software and spatial self-correlation to analyze the data of individuals diagnosed with COVID-19 between 22 February 2020 and 22 March 2020 (21,638 cases) and found that the provinces of Qom, Mazandaran, Gilan, Qazvin, Isfahan, Semnan, Markazi, and Yazd were situated within the HH cluster. This suggests that the number of COVID-19 cases in these provinces exceeded the national average and that 32.26% of Iranian provinces were grouped in the HH cluster. Additionally, an analysis of COVID-19 hot spots revealed that Qom, Golestan, Semnan, Isfahan, Mazandaran, and Alborz provinces were located in hot clusters, while Bushehr, Ilam, and Kermanshah provinces were located in cold clusters (Rahnama & Bazargan, 2020).

The present study aims to investigate spatial relationships in the distribution of COVID-19 cases from a medical perspective by modeling the spatial distribution of COVID-19 epidemiology in Iran.

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MATERIALS AND METHODS

Survey Design and Data Collection

The survey was conducted in Iran between 22 February 2020 and 22 February 2023, to analyze the spatial distribution of COVID-19 cases and the Index of Proximity Distribution (IPD).

Sampling Method

1. A two-stage sampling method involving convenience and cluster sampling was used.
2. Data were collected from 31 provinces in Iran.

Data Recording

Daily data on COVID-19 cases and the IPD were recorded during the study period.

Data Analysis

1. Data were analyzed in SPSS version 28.
2. Data were processed statistically in t-tests, chi-square tests, and analysis of variance (ANOVA) at a significance level of $\alpha=0.05$.

Spatial Data Visualization

The data on individuals infected with COVID-19 in each province was entered into ArcGIS software on a daily basis within the specified time interval.

Spatial Distribution Analysis

1. The daily spatial distribution of COVID-19 cases in Iran was visualized in a point density analysis.
2. Standard distance and standard deviation ellipse were used to assess the density or dispersion of the infected population and to identify the spatial distribution pattern of COVID-19 in Iran.

Spatial Autocorrelation Analysis

The spatial distribution pattern of COVID-19 in Iran was examined in a spatial autocorrelation (Moran's I) analysis.

Prevalence Classification

In a grouping analysis, 31 Iranian provinces were classified into five groups based on the number of COVID-19 cases.

Spatial Statistics

The spatial statistics of these homogeneous groups were examined to assess the prevalence of COVID-19 in different provinces of Iran.

Hot Spot Analysis

The spatial statistics in the hot spot analysis were used to examine spatial correlations in the number of COVID-19 cases across Iranian provinces.

Formulas for Calculating Standard Distance (SD) and Standard Deviational Ellipse (SDE)

1. Standard distance (SD) was calculated using the below formula (Coskun, 2023; Dolorfino et al., 2023):

$$SD = \sqrt{\frac{\sum_{i=1}^{n}(x_i - \bar{X})^2}{n} + \frac{\sum_{i=1}^{n}(y_i - \bar{Y})^2}{n}} \quad (1)$$

where: *x_i* and *y_i* are the coordinates of attribute *i*; $\bar{X}$ and $\bar{Y}$ are the central means of the attributes, and *n* is the total number of attributes.

2. The standard deviational ellipse (SDE) was calculated using the below formula (Gong, 2010; Moore & McGuire, 2019; Wang et al., 2015):

$$SDE_x = \sqrt{\frac{\sum_{i=1}^{n}(x_i - \bar{X})^2}{n}} \quad (2)$$

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where: x_i and y_i are the coordinates of attribute i; $\bar{X}$ and $\bar{Y}$ are the central means of the attributes, and n is the total number of attributes.

RESULTS AND DISCUSSION

On 22 February 2023, cases of COVID-19 infection were reported in Qom, Tehran, Gilan, and Markazi provinces. On that date, a total of 28 cases were confirmed in Iran, and 67.86% of all cases were reported in Qom province. The prevalence of COVID-19 in Iran began to increase on 2 March. Studies have shown that the spatial distribution of COVID-19 rapidly spread from Tehran, Qom, Gilan, Markazi, Mazandaran, and Isfahan provinces to their surrounding regions. The density of COVID-19 cases was highest in the northern, central, and northwestern parts of Iran, whereas eastern and southeastern regions were characterized by the lowest prevalence of the disease. On 22 February 2023, 23.6% of infected individuals in Iran were residents of Tehran province, 9.1% were from Isfahan province, and 7.9% were from Mazandaran province. Tehran and Qom provinces had the highest density of COVID-19 cases in Iran, while the lowest density was observed in the northwestern, southern, and southeastern regions. Research demonstrated that the density of cases decreased further away from the central areas of COVID-19 prevalence and distribution. The highest density of cases was noted in the northern and central regions of Iran.

The spatial distribution of COVID-19 cases in Iran measured with the standard distance method revealed the highest concentration of cases around Tehran province. A total of 602 cities (48.3% of all Iranian cities) were within the SD radius, which pointed to a high density of cases in the neighboring province of Tehran. The SDE analysis revealed that the prevalence of COVID-19 was more inclined towards northwest Iran. The direction of disease spread suggests that the spatial distribution was oriented predominantly towards northern and northwestern provinces. A total of 627 cities (50.3% of all Iranian cities) were within the SDE radius, which points to the spatial distribution of COVID-19 epidemiology.

Based on the research findings, on 22 February 2020, Moran's *I* was determined at 0.042422, with a z-score of 1.48557 and a p-value of 0.136868. This result indicates that the spatial distribution of COVID-19 cases in Iran followed a random pattern, with cases distributed across Qom, Tehran, Gilan, and Central provinces. However, by 21 February 2021, Moran's *I* increased to 0.200685, with a z-score of 3.039310 and a p-value of 0.002371, which points to a clustered spatial distribution pattern of COVID-19 in Iran. This result suggests that a high number of cases were reported in the provinces of Tehran, Isfahan, Mazandaran, Gilan, and Qom.

The z-score analysis revealed hot spots in Qom, Tehran, Golestan, Semnan, Isfahan, Mazandaran, and Alborz provinces, indicating a high concentration of COVID-19 cases in these areas. In these provinces, positive and statistically significant z-scores confirm the presence of a high number of infections. These hot spots accounted for 22.5% of all provinces, and most of these provinces are located in the northern and central regions of Iran. Conversely, Bushehr, Ilam, and Kermanshah provinces were identified as cold spots with negative z-scores and a low number of infections. These cold spots accounted for 9.67% of all provinces, and they are situated mainly in western and southwestern Iran. These results indicate that the provinces surrounding Tehran formed hot spots due to a high number of COVID-19 infections. Z-scores decreased and assumed negative values further away from Tehran, which led to the formation of cold spots with higher spatial autocorrelation between a smaller number of cases.

Iran's provinces were classified into five groups based on the number of COVID-19 cases. Tehran and Qom provinces were characterized by the highest number of infections, and they were assigned to groups 1 and 2, respectively. Group 3 consisted of Mazandaran, Gilan, Alborz, Markazi, and Isfahan provinces. The findings indicate that the spatial distribution of COVID-19 followed an adaptable pattern that was consistent with Torsten

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Hägerstrand's theory which considers the distance factor. The disease spread rapidly from Teheran, the center of COVID-19, to the neighboring provinces and cities, and it eventually reached distant provinces such as Sistan and Baluchestan, and Hormozgan. Cluster 4 was composed of Razavi Khorasan, Semnan, Yazd, Golestan, Fars, Khuzestan, Lorestan, Qazvin, and East Azerbaijan, which accounted for 29% of all Iranian provinces. Cluster 5 consisted of North and South Khorasan, Sistan and Baluchestan, Kerman, Hormozgan, Bushehr, Kohgiluyeh and Boyer-Ahmad, Chaharmahal and Bakhtiari, Ilam, Kermanshah, Hamedan, Kurdistan, Zanjan, Ardabil, and West Azerbaijan, which represented 48.3% of all provinces. The spatial grouping and clustering of Iranian provinces based on the spread of COVID-19 highlighted the significance of spatial-temporal distance in disease distribution from the center (Tehran) to other provinces, following an adaptable spatial pattern.

Based on the research findings, Moran's *I* was determined at 0.136627, and the z-score reached 2.292634 at a distance of 383.8 km from Tehran province, which indicates a significant positive spatial autocorrelation at a 99% confidence level. The presence of a positive autocorrelation points to a high number of COVID-19 cases within a radius of 383 km. A negative spatial autocorrelation was identified at a distance of 762.6 km from Tehran province, where Moran's *I* and the z-score reached -0.040246 and -0.252883, respectively. In other words, beyond this point, the number of COVID-19 cases decreased. Hence, it can be concluded that distance played a crucial role in the spread of COVID-19 in Iran. The disease spread from the center to the periphery, and the spatial distance was reduced as COVID-19 reached successive provinces (Fig. 1).

Figure 2 provides an insightful visualization of the spatial distribution of COVID-19 in Iran, shedding light on the underlying dynamics of the epidemic.

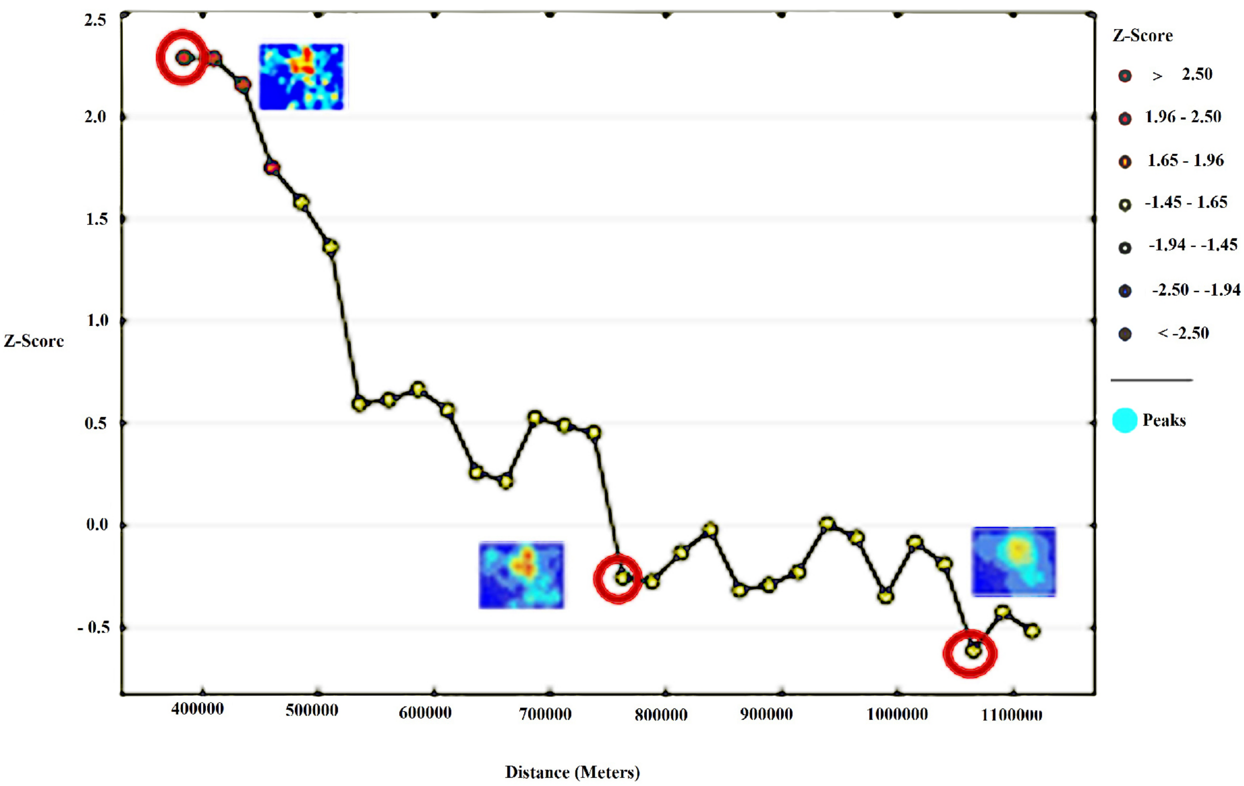

Fig. 1. Spatial autonomy of COVID-19 in Iran

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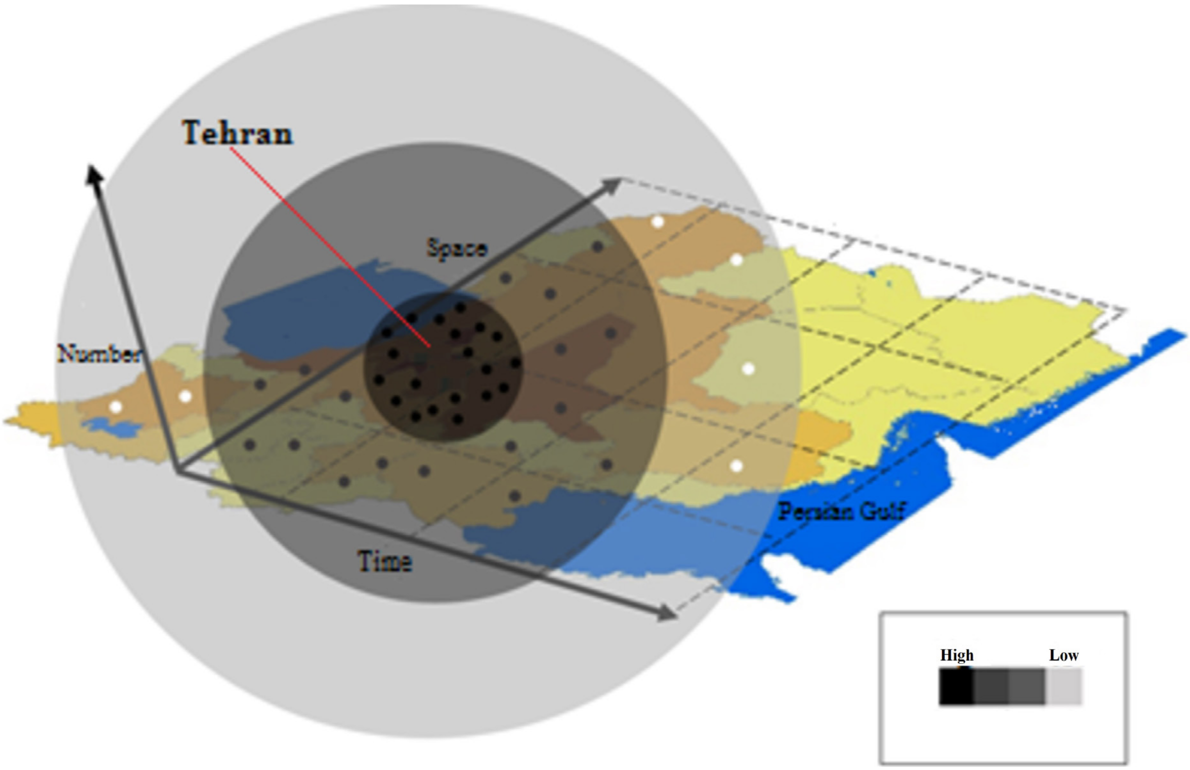

Fig. 2. Spatial pattern of COVID-19 distribution in Iran

Tehran province emerged as the primary focus of disease and the epicenter from which the spatial diffusion and propagation of COVID-19 originated and subsequently affected other provinces.

The concentration of COVID-19 cases was particularly high in the immediate vicinity of Tehran province, which can be attributed to higher population density in these areas. The interplay between spatial features, namely time and distance, exerted a profound influence on the spatial distribution patterns of COVID-19 in Iran.

Time was a factor that played a crucial role in the spatial dynamics of COVID-19. As the epidemic unfolded over the course of the study period, the spatial distribution of cases gradually spread beyond Tehran province, affecting neighboring regions and, eventually, more distant provinces. The temporal aspect of the epidemic's progression underscores the significance of monitoring and analyzing the spatial distribution of COVID-19 in real-time, as the disease navigated through various regions of Iran.

Moreover, distance was also a factor that significantly affected the spatial distribution patterns of COVID-19 in Iran. The spatial distance between provinces influenced the rate and extent of transmission, and infection density was higher in areas situated in closer proximity to Tehran province. The interplay between distance and infection rates highlights the importance of spatial connectivity and inter-regional mobility in the spread of COVID-19.

In summary, Figure 2 provides valuable insights into the spatial distribution of COVID-19 in Iran. Tehran province was the epicenter, and the subsequent spatial diffusion of the disease was influenced by both temporal and distance-related factors. A better understanding of the intricate interplay between these factors is crucial for developing effective surveillance, prevention, and control strategies to mitigate the impact of the epidemic and protect public health across the country.

The spatial distribution of COVID-19 cases in Iran was analyzed in this study, with emphasis on factors

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such as time, distance, and spatial autocorrelation. The results have important implications for scientific discussions:

1. Temporal evolution of COVID-19: The study investigated the temporal evolution of COVID-19 in Iran, and it demonstrated that the number of infections increased after 22 February 2023. This observation highlights the dynamic nature of infectious diseases and the need for continuous monitoring and adaptive public health responses as the situation evolves.
2. Spatial distribution patterns: The analysis revealed that COVID-19 had distinct spatial distribution patterns across Iranian provinces. Infection cases were concentrated in the northern, central, and northwestern parts of Iran, where hot spots were identified. The identification of geographical patterns of disease distribution can facilitate resource allocation and targeted interventions.
3. Use of spatial analysis methods: In the present study, spatial autocorrelations were assessed, and hot and cold spots were identified with the use of statistical methods such as Moran's I, z-score, and the standard deviation ellipse. These methods are essential tools in epidemiology for understanding how disease clusters are formed in space and time.
4. Role of distance in the spread of disease: The analysis underscores the significance of distance in the spread of COVID-19. Infection rates were higher in proximity to Tehran province, and a noticeable decrease in the number of cases was observed beyond a certain distance from Tehran. This finding aligns with the concept that infectious diseases often spread more readily in densely populated areas and through human mobility.
5. Cluster analysis and grouping: Iranian provinces were categorized into clusters based on COVID-19 cases, highlighting the importance of spatial-temporal distance in disease distribution. This approach can inform public health strategies for containment and control, emphasizing the need for regional responses.
6. Epidemiological significance: The results underscore Tehran province as the epicenter of the outbreak and the subsequent spatial diffusion of COVID-19 to other regions. This is a common characteristic of many infectious diseases, where urban centers often serve as focal points for disease spread due to high population density and connectivity.
7. Population density and disease transmission: The article briefly mentions that population density plays a role in the concentration of cases. The interaction between population density and disease transmission is a crucial aspect of epidemiology, as crowded areas can facilitate the rapid spread of infectious diseases.
8. Real-time monitoring: The discussion highlights the importance of real-time monitoring and analysis of the spatial distribution of disease. Timely data and spatial insights are critical for decision-making, especially when dealing with infectious disease outbreaks.

In summary, the research offers insights into the spatial distribution and dynamics of COVID-19 in Iran. It underscores the interplay of time, distance, and population density in disease transmission, and the importance of spatial analyses as methods that guide public health responses. This information is essential for epidemiologists and policymakers in managing and controlling disease outbreaks.

CONCLUSIONS

In conclusion, this study focused on modeling the spatial segregation and distribution of COVID-19 epidemiology in Iran between 22 February 2020 and 22 February 2023. The study revealed that the concentration of COVID-19 cases was highest in the northern and central regions of Iran, and lowest in northwest, south, and southeast regions. An analysis of the standard distance radius of COVID-19 spatial distribution demonstrated that 602 cities (48.3% of Iran's cities) were within this range.

Furthermore, an examination of the standard deviation ellipse representing COVID-19 prevalence in Iran revealed directional movement towards the northern and northwestern provinces. The spatial

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distribution pattern of COVID-19 appeared random on 22 February 2020, but a clustered pattern emerged by 22 February 2023, signifying the spread of COVID-19 across Iran. In a statistical-spatial analysis of hotspots, Tehran, Qom, Golestan, Semnan, Isfahan, Mazandaran, and Alborz provinces (comprising 22.5% of Iran's provinces) were identified as hotspots with a high prevalence of COVID-19 cases. Conversely, Bushehr, Ilam, and Kermanshah provinces (accounting for 9.67% of Iranian provinces) were classified as cold spots with a low number of infections.

Moreover, the spatial grouping analysis of Iran's provinces underscored the significance of the spatial-temporal distance factor in COVID-19 distribution from Tehran to other provinces. This factor plays a pivotal role in the spatial dynamics of the disease by influencing its spread from the epicenter to neighboring regions over time.

Furthermore, the study revealed various scenarios regarding the spatial distribution and dynamics of COVID-19 in Iran, indicating changes over time, the influence of proximity to Tehran, and variations in prevalence between different regions. The findings suggest that pandemics have complex dynamics and require nuanced strategies for control and response.

Different interpretations of the findings or alternative explanations for the observed spatial patterns of COVID-19 in Iran could could be offered:

1. Socioeconomic factors: It is possible that the shift from a random spatial pattern in 2019 to a clustered distribution in 2023 was influenced by socioeconomic factors, rather than an inherent change in the virus's behavior. It could be argued that regions with a higher population density, better healthcare facilities, or better access to testing may naturally cluster more cases.
2. Seasonal variability: The role of seasonal variability in COVID-19 transmission could also be considered. The clustered distribution observed in February 2023 could have been influenced by environmental factors, such as temperature and humidity, which are known to affect the transmission of respiratory viruses.
3. Behavioral changes: Another perspective could focus on changes in human behavior, such as adherence to public health guidelines, mask-wearing, and social distancing, as the primary driver of the observed spatial patterns. Thus, the clustering of cases in 2023 could be attributed to human behavior, rather than inherent changes in the virus.
4. Testing and reporting bias: Some critics may argue that clustering resulted from variations in testing and reporting, rather than the actual distribution of the virus. Regions with more robust testing and reporting mechanisms are more likely to identify and report cases, which could lead to apparent clustering.
5. Genomic variants: An alternative explanation could involve the role of viral genomic variants. The observed clustering could be related to the presence of more transmissible or vaccine-resistant variants in certain regions, rather than changes in population movement or spatial dynamics.
6. Demographic factors: Demographic factors such as the age and health of the population in different regions could be the key drivers of the spatial distribution of COVID-19. Regions with older or more vulnerable populations might naturally cluster more cases.
7. Interventions and travel restrictions: Government interventions, travel restrictions, or border controls in certain regions could lead to the observed clustered distribution. These policies could have artificially contained the virus in some areas, while allowing it to spread in others.
8. Data quality and methodological issues: Critics might question the reliability and accuracy of the data used in the spatial analysis. They could argue that the Moran index, distance-based spatial autocorrelation, and hot spot analysis techniques may have limitations and potential biases that influence the results.
9. Purely temporal factors: A different viewpoint could propose that the shift from random to clustered patterns could have resulted from temporal factors, such as the emergence of new waves of the

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pandemic, vaccination campaigns, or immunity development in the population, rather than spatial dynamics.

In addition, the study has several possible applications and implications:

1. Public health planning and response: The findings can inform public health authorities in Iran and other regions facing similar challenges about the spatial distribution and clustering of COVID-19 cases. This information can guide resource allocation, the deployment of medical facilities, and targeted interventions to manage and control the pandemic more effectively.
2. Epidemiological research: Researchers can use the results to further investigate the factors that contributed to the shift in the spatial distribution of COVID-19. This information can be valuable for epidemiological studies and for understanding the dynamics of the pandemic over time.
3. Monitoring and early warning systems: The shift from random to clustered distribution over time highlights the need for robust monitoring and early warning systems. This data can be used to develop models and forecasting tools to predict the spread of the virus and identify high-risk regions.
4. Travel and movement restrictions: The presence of a positive spatial autocorrelation near Tehran underscores the role of proximity and population movement in virus transmission. The authorities can use this information to implement travel restrictions and guidelines to limit the spread of the virus in highly connected areas.
5. Resource allocation: The identification of hot spots and cold spots contributes to more efficient allocation of resources. Hot spots may require additional medical personnel, testing facilities, and supplies, while cold spots may allow resources to be redirected to areas with greater need.
6. Health communication: Public health officials can use the presented data to develop targeted health communication strategies for different regions. Messaging and awareness campaigns can be tailored to address the specific challenges and trends in different areas.
7. Policy development: Policymakers can use the presented information to craft policies that are more region-specific. Different regions may require different strategies, and policies can be adapted accordingly.
8. Preparedness and response: The findings can inform future preparedness and response efforts not only in Iran, but also in other regions with similar patterns. As a result, regional authorities could predict changes in the pandemic's dynamics and adjust their strategies accordingly.
9. Research funding allocation: This study could influence decisions about where research funding is directed. Areas with hot spots may be prioritized for further research and resource allocation to better understand and combat the virus.
10. International collaboration: The study can facilitate collaboration and knowledge sharing among countries dealing with the pandemic. Similar spatial analysis can be conducted in other regions to compare findings and identify common trends.

Author contributions: All authors have approved the final version of the article. The authors have contributed to this work as follows: A.K.M. developed the research concept and designed the study, A.K.M. collected data, A.K.M. analyzed and interpreted the data, A.K.M. prepared the draft manuscript, A.K.M. revised the article critically for important intellectual content

Funding: This research did not receive external funding.

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