Journal of Remote Sensing and GIS Applications in Environmental Sciences
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Exploring the Spatial Relationship between Agrochemicals Exposure and Covid-19 Infection and Mortality

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Article Info

Article type:
Research Article

Article history:
Received: 4 April 2025
Revised: 14 November 2025
Accepted: 27 December 2025
Published: 4 January 2026

Keywords:
Agrochemicals,
Coronavirus,
Spatial relationship,
Geographically Weighted Regression.

ABSTRACT

Objective: Various environmental factors have resulted in disparities in the number of infections of COVID-19 and its mortality in different areas. People with underlying diseases have a higher infection and mortality rate than the general population. The use of agricultural pesticides and fertilizers is one of the major contributors to the spread of underlying diseases. Therefore, they may indirectly contribute to increased COVID-19-related infection and mortality. Accordingly, exploring the spatial relationship between the use of pesticides and fertilizers, and the infection to COVID-19, death due to infection, and mortality to infection ratio are the main objectives of this paper.

Methods: In this regard, the Geographically Weighted Regression model was used to explore the relationships in the rural district of the East Azerbaijan province in Iran.

Results: The findings revealed a significant spatial relationship between the use of herbicides, potassium, phosphate, and insecticides and an increase in COVID-19-related infection, particularly mortality. Areas of high total use and hotspots of herbicide and potassium were significantly positively correlated with an increase in COVID-19 mortality. High usage of phosphate and insecticides, as well as their hotspots, were associated with high COVID-19 infection and death in most indices. Their coefficients, however, were lower than those of herbicides and potassium. There is no evidence of a relationship between increasing COVID-19 infection and mortality and high total fungicide and nitrate use and hotspots.

Conclusion: The findings of this study revealed a positive spatial relationship between the use of agrochemicals and an increase in COVID-19 infection and mortality.

Cite this article: Ahmadi, H., Beyraghi Khatibi, N., Argany, M. & Ghanbar, A. (2026). Exploring the Spatial Relationship between Agrochemicals Exposure and Covid-19 Infection and Mortality. *Journal of Remote Sensing and GIS Applications in Environmental Sciences*, 6 (18), 18-35. http//doi.org/10.22034/rsgi.2025.66478.1131

Publisher: University of Tabriz.
DOI: http//doi.org/10.22034/rsgi.2025.66478.1131

Journal of Remote Sensing and GIS Applications
in Environmental Sciences
rsgi.tabrizu.ac.ir

Introduction

Coronavirus disease 2019 (COVID-19) as one of the fatal epidemics that has spread globally, and the World Health Organization declared it a pandemic on March 11, 2020 (Sohaylie et al., 2022). However, not all people are affected by COVID-19 equally (Leventelis et al., 2024), and COVID-19 patients with pre-existing comorbidities have worse consequences (Bulka et al., 2022). Epidemiological evidence demonstrates that one of the factors that causes various types of pre-existing comorbidities is direct exposure to pesticides and chemical fertilizers (Flynn et al., 2021). Accordingly, this paper aims to investigate the spatial relationship between the use of pesticides and chemical fertilizers and the infection rate of COVID-19 and its mortality in the East-Azarbayjan province of Iran.

Data and Method

Three main categories of data were used in this study: 1) The pesticides and chemical fertilizers data obtained from the Ministry of Agriculture. 2) COVID-19 data were obtained from Tabriz University of Medical Sciences. 3) We obtained the rural district shapefile of the province from the Ministry of Road and Urban Development.

In this study, 34 variables were used, including 16 agricultural variables and 18 COVID-19 variables. The variables were categorized into four primary categories: 1) independent spatial variables; 2) independent spatiotemporal variables; 3) dependent spatial variables; and 4) dependent spatiotemporal variables. The Minimum-maximum method was applied to normalize the data (Auwul et al., 2021). Spatial autocorrelation assessment is used to determine whether the relationship between dependent and independent variables varies spatially or not (Ballard & Bone, 2021). In addition, after specifying 25 km as the distance band using the Calculate Distance Band from the Neighbor Count tool, the inverse distance squared method was used to conceptualize the spatial relationship (Goodchild, 1986). The multicollinearity is assessed by the variance inflation factor (Ballard & Bone, 2021).

To explore the spatial relationship between agrochemical exposure and COVID-19 infection and mortality, the Geographically Weighted Regression model was used (Brunsdon et al., 1998). Before running the model, the bandwidth parameter that specifies the neighboring features and controls the degree of smoothing in the model (Fotheringham et al., 2003) was determined, using the method that was applied by Tokey, 2021. The Gaussian method was selected as the distance decay function (Hadayeghi et al., 2010). A continuous model was selected as the model type parameter (Fraser et al., 2012). To determine the neighborhood's size, the user-defined method was selected in the neighborhood selection method (Liu & Strobl, 2022).

Results and Discussion

The results can be interpreted from two aspects: 1) to explore the effects of different types of agrochemicals on COVID-19, and 2) to explore which COVID-19 indicators are influenced most by the agrochemicals.

According to the findings, increasing the sum of herbicides is significantly associated with the hotspots of the mortality to infection (MTI) ratio. In addition, the trend, average, peak, and peak period of the MTI ratio increase as the sum of herbicides increases. The same is true about the peak period and hotspots of death due to infection (DDI). Overall, the DDI and MTI ratio factors are higher in areas where herbicides are highly used.

Except of the peak period of the DDI, hotspots of potassium use have a significant positive relationship with all of the COVID-19 indicators. The peak period of infection and MTI ratio are prolonged in hotspots. In addition, the hotspots are highly correlated to the hotspots of infection, DDI, and MTI ratio. Further, the peak, average, and trend of the MTI ratio increase intensely in the hotspot areas. Moreover, increasing in sum of potassium has a significant positive relationship with hotspots of infection, DDI, and MTI ratio. As a result, using potassium may also indirectly increase COVID-19 infection, DDI, and MTI ratio.

Hotspots of insecticide and phosphate use indicated significant positive correlations with the COVID-19 indicators. However, their correlations were lower than those of the herbicides and potassium with COVID-19. Insecticide hotspots had positive correlations with hotspots of the DDI and the MTI ratio. Peak periods of infection and the MTI ratio go longer in the hotspot areas. The peak and average of the MTI ratio increase in the insecticide hotspots. In addition, phosphate hotspots are correlated with the high peak, average, and trend of the MTI ratio. Furthermore, peak periods of infection and DDI increase in hotspot areas. As a result, the use of insecticides and phosphates may indirectly increase infection, DDI, and MTI ratios. In contrast, we found no relationships between the use of fungicides and nitrates and the COVID-19 indicators.

Conclusion

Areas of high total use and hotspots of herbicides and potassium were significantly positively correlated with an increase in COVID-19 intensity in both infection and mortality. High usage of phosphate and insecticides, as well as their hotspots, were associated with high COVID-19 infection and death in most indices. There is no evidence of a relationship between increasing COVID-19 infection and mortality and high fungicide and nitrate use. In general, the findings of this study revealed a positive spatial relationship between the use of pesticides and chemical fertilizers and an increase in COVID-19 infection and mortality.

Keywords: Agrochemicals, Coronavirus, Spatial relationship, Geographically Weighted Regression.

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نشریه کاربرد سنجش از دور و سیستم اطلاعات جغرافیایی در علوم محیطی
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بررسی رابطه فضایی بین قرارگیری در معرض مواد شیمیایی کشاورزی و ابتلا و مرگ ناشی از کرونا

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اطلاعات مقاله

نوع مقاله:
مقاله پژوهشی

تاریخ دریافت: ۱۴۰۴/۰۱/۱۵
تاریخ بازنگری: ۱۴۰۴/۰۸/۲۳
تاریخ پذیرش: ۱۴۰۴/۱۰/۰۶
تاریخ انتشار: ۱۴۰۴/۱۰/۱۴

کلیدواژه‌ها:
مواد شیمیایی کشاورزی،
کرونا،
روابط فضایی،
رگرسیون وزن‌دار جغرافیایی.

چکیده

هدف: عوامل محیطی مختلف منجر به اختلاف در تعداد ابتلا به کووید-۱۹ و مرگ و میر آن در مناطق مختلف شده است. افراد مبتلا به بیماری‌های زمینه‌ای، میزان عفونت و مرگ و میر بیشتری دارند. استفاده از سموم کشاورزی و کودهای شیمیایی یکی از عوامل اصلی شیوع بیماری های زمینه‌ای است. بنابراین، آن‌ها ممکن است به طور غیر مستقیم در افزایش ابتلا و مرگ و میر ناشی از COVID-19 نقش داشته باشند. بر این اساس، بررسی رابطه فضایی بین استفاده از آفت‌کش‌ها و کودها و ابتلا به کووید-۱۹ و مرگ و میر آن هدف اصلی این مقاله است.

روش‌ها: در این راستا، از مدل رگرسیون وزن‌دار جغرافیایی برای بررسی روابط در بخش روستایی استان آذربایجان شرقی استفاده شد.

یافته‌ها: یافته‌ها رابطه فضایی معنی‌داری را بین استفاده از علف‌کش‌ها، پتاسیم، فسفات و حشره‌کش‌ها و افزایش ابتلا به COVID-19 و به‌ویژه مرگ‌ومیر نشان داد. مناطقی که از استفاده زیاد و نقاط داغ علف کش و پتاسیم استفاده می‌شود با افزایش مرگ و میر COVID-19 ارتباط مثبت معنی داری داشت. استفاده زیاد از فسفات و حشره‌کش‌ها و همچنین نقاط داغ آن‌ها، در بیشتر شاخص‌ها با ابتلای بالای COVID-19 و مرگ همراه بود. اما ضرایب آنها کمتر از علف کش ها و پتاسیم بود. هیچ مدرکی دال بر ارتباط بین افزایش ابتلا به کووید-۱۹ و مرگ و میر و استفاده از قارچ کش و نیترات وجود ندارد.

نتیجه‌گیری: یافته‌های این مطالعه رابطه فضایی مثبتی را بین استفاده از مواد شیمیایی کشاورزی و افزایش آلودگی و مرگ‌ومیر کووید-۱۹ نشان داد.

استناد: احمدی، حامد؛ بیرقی خطیبی، ندا؛ ارگانی، میثم و قنبری، ابوالفضل (۱۴۰۵). بررسی رابطه فضایی بین قرارگیری در معرض مواد شیمیایی کشاورزی و ابتلا و مرگ ناشی از کرونا. *کاربرد سنجش از دور و سیستم اطلاعات جغرافیایی در علوم محیطی*، ۶ (۱۸)، ۳۵-۱۸.
http//doi.org/10.22034/rsgi.2025.66478.1131

ناشر: دانشگاه تبریز.

Introduction

Throughout history, several epidemics have posed serious threats to human societies (Cao & Liu, 2024). Coronavirus disease 2019 (COVID-19) emerged as one of the most severe global health crises of recent decades, and the World Health Organization (WHO) declared it a pandemic on March 11, 2020 (Sohaylie et al., 2022). Since then, its rapid spread and high disease burden have had profound social, health, and economic consequences worldwide (Isazadeh et al., 2021). Importantly, the impacts of COVID-19 have not been uniform across populations (Leventelis et al., 2024). Individuals with pre-existing comorbidities experience substantially worse outcomes, including higher hospitalization, intensive care admission, and increased mortality (Bulka et al., 2022). A large body of evidence indicates that conditions such as diabetes, cardiovascular diseases, respiratory disorders, chronic kidney and liver diseases, cerebrovascular disease, hypertension, and immune suppression significantly heighten vulnerability to COVID-19 infection and its fatal consequences (Bhinder et al., 2022; Chen et al., 2024; Chen et al., 2021; Hussain & Sharma, 2024; Kadirvelu et al., 2022; Kim et al., 2021; Wu et al., 2021).

Pre-existing comorbidities can arise from various environmental exposures, among which agricultural pesticides and chemical fertilizers (CFs) have been repeatedly identified as important contributors. Epidemiological studies have demonstrated that chronic or repeated exposure to these agrochemicals—either through direct contact or through residuals in food—can increase the likelihood of developing a wide spectrum of chronic diseases (Flynn et al., 2021). Numerous studies have linked pesticide exposure to Alzheimer’s and Parkinson’s diseases, chronic kidney disease, respiratory disorders, cardiovascular diseases, thyroid abnormalities, reproductive and fetal disorders, autoimmune conditions, hypertension, diabetes, dermal diseases, cancer, and several neurodegenerative conditions (Costa et al., 2020; Hoang et al., 2021; Kaur et al., 2020; Lulla et al., 2016; Mandic-Rajcevic et al., 2019; Parks et al., 2022; Rebouillat et al., 2022; Requena et al., 2019; Sagiv et al., 2022; Schmidt, 2020; Suarez-Lopez et al., 2018; Sung et al., 2022). Although fewer studies have examined the health impacts of CFs, available evidence clearly indicates their potential pathogenicity. Nitrogen fertilizers, phosphate fertilizers, and nitrate compounds have been associated with endocrine disruption, reproductive abnormalities, cancer, metabolic disorders, cardiovascular diseases, and certain congenital and fetal conditions (Ahada & Suthar, 2018; Ahmed et al., 2017; Alfthan et al., 2015; Bindraban et al., 2020; Hossain et al., 2022; Hui et al., 2021; Jayasumana et al., 2015; Zhai et al., 2017).

Taken together, prior literature consistently shows that exposure to pesticides and chemical fertilizers (CFs) can elevate the risk of developing comorbidities that are strongly associated with adverse COVID-19 outcomes. Importantly, the relationship between agrochemical exposure and COVID-19 is indirect: these substances do not contribute to the transmission of SARS-CoV-2, but they may increase susceptibility to infection and mortality by exacerbating underlying health conditions known to worsen COVID-19 severity. This conceptual pathway is strongly supported by evidence from other environmental health studies. In particular, numerous epidemiological investigations have documented that long-term exposure to air pollution—including fine particulate matter (PM2.5) and nitrogen dioxide (NO2)—is associated with increased rates of COVID-19 infection, hospitalization, and mortality (Cole et al., 2020; Conticini et al., 2020; Wu et al., 2021). Mechanistic explanations suggest that chronic exposure to these pollutants worsens pre-existing respiratory and cardiovascular conditions, thereby amplifying the severity of COVID-19 outcomes (Hermanns et al., 2024; Ma et al., 2025). These findings provide a well-established precedent for understanding how environmental exposures can indirectly influence COVID-19 severity and lend further plausibility to the hypothesis that agrochemical use may act as a similar indirect factor through its effects on comorbidities.

Despite extensive research on factors influencing COVID-19, the spatial dimension of this indirect pathway—linking the distribution of agricultural pesticides and CFs to spatial variations in COVID-19 infection and mortality—has received limited attention. To address this gap, the present study investigates the spatial relationship between the use of pesticides and CFs and COVID-19 infection rate, death due to infection (DDI), and mortality-to-infection ratio in the rural districts of East Azerbaijan Province, Iran.

Methodologically, the study employs a seven-step analytical framework: (1) data collection and preprocessing, (2) variable quantification, (3) data standardization, (4) spatial autocorrelation analysis, (5) assessment and mitigation of multicollinearity, (6) optimal bandwidth selection, and (7) application of the Geographically Weighted Regression (GWR) model to explore local spatial relationships between agrochemical use and COVID-19 outcomes.

Materials and Methods

Study area

East-Azerbaijan province is located in the north-west of Iran (Latitude: 4068578 to 4366776 & Longitude: 507395 to 796480). The province has the greatest contribution to agricultural production in the country (Planning and Budget Organization of Iran_The agriculture, forestry and fisheries chapter, 2017). Southwest, central and east central of the province had the largest number of sowing seeds between 2000 and 2018. In addition, East-Azerbaijan is one of the most highly COVID-19-infected provinces in Iran. According to data obtained from the Health Vice-Chancellor of East-Azerbaijan province, from 1 April 2020 to 28 February 2022, 183,217 people were infected and 9,898 people died due to COVID-19. Fig. 1 indicates population, cultivation and COVID-19 conditions in the province based on the rural districts (RDs).

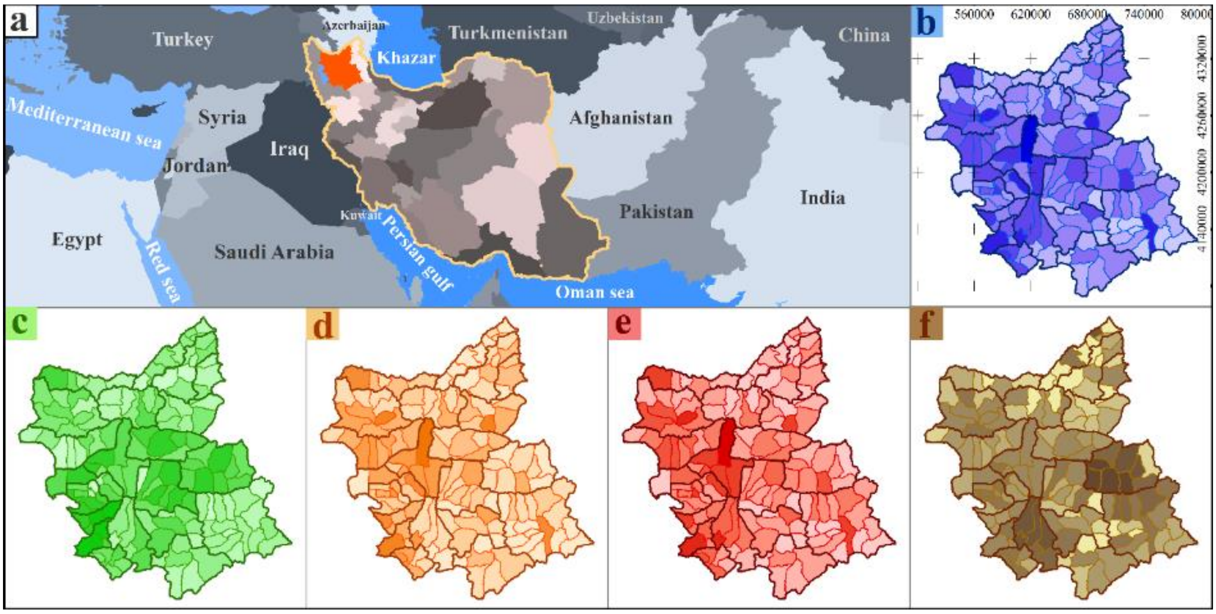

Fig 1. Study area: a) Location in the country, b) Population distribution (2017), c) Seed sowing (2000-2018), d) Number of infected people to COVID-19 (Apr 2020-Feb 2022), e) Number of COVID-19-related deaths (Apr 2020-Feb 2022), and f) mortality to infection (MTI) ratio (Apr 2020-Feb 2022).

Data collection and preprocessing

Three main categories of data were used in this study: 1) The consumed pesticides and CFs (PCF) data (kilogram per hectare) obtained from Ministry of Agriculture (the East- Azerbaijan Agricultural Organization) for a 19-years duration from 2000 to 2018 based on each year and for 142 RDs. Pesticides were categorized into three groups: herbicides, insecticides and fungicides. CFs were also categorized into three groups: phosphate, potassium, and nitrate. 2) COVID-19 data including the number of infected and dead people due to Covid-19. These data were obtained from Tabriz University of Medical Sciences (the Health Vice-chancellor of East- Azerbaijan province) for a 23-month duration from 1 April 2020 to 28 February 2022 based on each month and RD. 3) We obtained the RDs' shapefile of the province from the Ministry of Road and Urban Development (General Directorate of Roads and Urban Development in East Azerbaijan province). Then, the pesticides, CFs and COVID-19 data were joined to the shapefile in order to conduct a spatial analysis. Of note, the RD where Tabriz city is located was eliminated from all analyses. Because, it is an overpopulated city and its COVID-19 data is not comparable to the other RDs.

Variables description

In this study, 34 variables were selected to analyze the spatial relationship between use of the agricultural PCF (16 variables) and COVID-19's infection and mortality (18 variables). The data for all variables were extracted from the primary data. The variables are categorized into two dependent (COVID-19) and independent (pesticides and CFs) variables. Moreover, they are categorized into two spatial and spatiotemporal variables. The following are the four primary categories of variables:

1. *Independent Spatial variables:* Sum of Herbicide (SH), Sum of Insecticide (SI), Sum of Fungicide (SF), Sum of Phosphate (SPH), Sum of Nitrate (SN), Sum of Potassium (SP), Sum of Pesticides (SPES), and Sum of CFs (SCF). All of the variables represent the total amount of pesticides and CFs utilized throughout the study period.

2. *Independent Spatiotemporal variables:* Hotspot intensity of Herbicide (HH), Hotspot intensity of Insecticide (HI), Hotspot intensity of Fungicide (HF), Hotspot intensity of Phosphate (HPH), Hotspot intensity of Nitrate (HN), Hotspot intensity of Potassium (HP), Hotspot intensity of Pesticides (HPES), and Hotspot intensity of CF (HCF). To quantify the Hotspot intensity, a space-time cube was created for each variable and then the Emerging Hot Spot Analysis was performed (Ahmadi et al., 2022).

3. *Dependent Spatial variables:* Monthly peak of the COVID-19's infection (PI), Peak period of the COVID-19's infection (PPI), Monthly min of the COVID-19's infection (MI), SUM of the COVID-19's infection (SI), Trend of the COVID-19's infection (TI), Peak of the death due to COVID-19 (PD), Peak period of the death due to COVID-19 (PPD), Min of the death due to COVID-19 (MD), SUM of the death due to COVID-19 (SD), Trend of the death due to COVID-19 (TD), Peak of the MTI ratio (PM), Peak period of the MTI ratio (PPM), Min of the MTI ratio (MM), Average of the MTI ratio (AM), and Trend of the MTI ratio (TM).

4. *Dependent Spatiotemporal variables:* Hotspot Intensity of the COVID-19's Infection (HI), Hotspot Intensity of the death due to COVID-19 (HD), and Hotspot Intensity of the MTI ratio (HM).

Normalizing the data values

Given that the original values' ranges differ among the different variables (Wang & Wu, 2020), prior to analyzing the spatial relationships, all datasets were normalized to make them comparable (Auwul et al., 2021), perform the analysis dimensionless (Konstantinoudis et al., 2021) and reduce the effect of outliers (Xu & Zhang, 2021). For this purpose, Minimum-maximum method was applied. It keeps the original data values' relationships and lets the user define the Max-Min (Auwul et al., 2021). All data sets were scaled between 0-100.

Moran's I

Spatial autocorrelation assessment is used to determine whether the relationship between dependent and independent variables varies spatially or not (Ahmadi et al., 2024). Moran's I is a widely used index for measuring the statistical significance of the spatial autocorrelation (Moran, 1950) by evaluating the spatial patterns between the features and their attributes according to rejection of the null hypothesis (Ebdon, 1985). If it is rejected, then the pattern is clustered or dispersed and is statistically significant (Andy, 2005). The rejection is computed by the z-score (standard deviation) and the p-value (probability) (M. Goodchild, 1986). If the z-score is higher than 2.58 or lower than -2.58, and the p-value is lower than 0.01, then the observed spatial pattern is not random and the spatial autocorrelation is statistically significant (Griffith, 1987). In addition, after specifying 25 km as the distance band using Calculate Distance Band from the Neighbor Count tool, the inverse distance squared method was used to conceptualize the spatial relationship (M. F. Goodchild, 1986).

Variance Inflation Factor (VIF)

Eliminating independent variables that have a high correlation with any other independent variables is an essential procedure before model estimation (Wheeler & Tiefelsdorf, 2005) due to multicollinearity (Páez et al., 2011). Collinearity is assessed by the VIF, which measures the degree to which the presence of dependence among the independent variables inflates the variance of the estimated regression coefficient (Ballard & Bone, 2021). The VIF of all independent variables should be less than 10 to ensure multicollinearity is not an issue (Wang & Wu, 2020).

Geographically Weighted Regression (GWR) model

In previous studies, many different types of models have been used to investigate spatial relationships. Traditional models such as spatial error models (SEM) and ordinary least squares (OLS) regression presume that there is a linear and spatially constant relationship between the dependent and independent variables, and so they estimate global statistics for the entire area (Ali et al., 2007). Thereby, the effect of local variation is essentially ignored (Singh & Masquelier, 2018). In contrast, to get the local impact, a GWR model calculates the local regression coefficients by assigning higher weight to the nearby features (Brunsdon et al., 1998). The critical contribution of GWR is to then investigate the relationship between the dependent and independent variables on the local scale, by constructing a separate equation for the neighborhoods of the subject feature (McMillen, 1996). The formulation of GWR is available in (Stewart Fotheringham et al., 1996).

Before running GWR, the Bandwidth parameter that specifies the neighboring features and controls the degree of smoothing in the model (Fotheringham et al., 2003) was determined, using the method that was applied by (Tokey, 2021). Then, the Gaussian method was selected as the distance decay function due to the characteristics of the studied variables (Hadayeghi et al., 2010). This method assigns decreasing weights outside of the determined bandwidth features and never reaches to zero (Charlton et al., 2009). Because the dependent variable involves a wide range of values, a continuous model was selected as the model type parameter (Fraser et al., 2012). To determine the neighborhood's size, the user defined method was selected in the Neighborhood selection method (Liu & Strobl, 2022).

Results

Spatial autocorrelation analysis

Spatial autocorrelation of the variables was calculated by the Global Moran's I. The results are shown in Table 1. The Moran's index for all of the variables is more than the expected index (-0.007143), which indicates a clustered pattern. However, because the z-score is between +2.58 and -2.58 and has a high p-value, some of the variables have a random pattern and are not statistically significant at the 1 percent level. Such variables were excluded from the model.

Table 1. Results of the spatial autocorrelation analysis

Category	Variable	Moran's Index	Expected Index	Z-Score	P-Value	Statistical significance
Independent-Pesticides	SH	0.825	-0.007143	13.16	0.000	S
	SI	0.668		11.06		
	SF	0.451		7.22		
	SPES	0.731		11.79		
	HH	0.855		13.4		
	HI	0.953		14.86		
	HF	0.771		12.07		
	HPES	0.834		13.03		
Independent- CFs	SPH	0.968		15.17		

Category	Variable	Moran's Index	Expected Index	Z-Score	P-Value	Statistical significance
	SN	0.947		15.06		
	SP	0.338		5.75		
	SCF	0.927		14.62		
	HPH	0.748		11.69		
	HN	0.816		12.74		
	HP	0.82		12.81		
	HCF	0.796		12.44		
Dependent-Infection	PI	0.063		1.13	0.256	NS
	PPI	0.826		12.91	0.000	S
	MI	0.054		1.09	0.274	NS
	SI	0.074		1.34	0.179	
	TI	0.048		0.93	0.351	
	HI	0.564		8.86	0.000	S
Dependent-DDI	PD	0.052		0.99	0.321	NS
	PPD	0.165		2.69	0.007	S
	MD	-0.003		0.05	0.958	NS
	SD	0.061		1.12	0.259	
	TD	0.046819		0.89	0.372	
	HD	0.736		11.53	0.000	S
Dependent-MTI ratio	PM	0.312		5.59		
	PPM	0.413		6.58		
	MM	-0.003		0.06	0.944	NS
	AM	0.353		5.91	0.000	S
	TM	0.334		5.62		
	HM	0.542		8.55		

* Significant at 1 percent level

* Not statistically significant

Multi-collinearity problem

VIF was used to assess potential multi-collinearity of all the independent variables. The independent variables with a VIF greater than 10 were removed, one by one, starting with the variable with the highest VIF until all VIFs were below 10. To avoid the variables becoming redundant, multi-collinearity was examined independently in the two categories of pesticides and CFs. As a result, SPES, HPES, SPH, SCF, HN, and HF, were excluded from the model.

Optimal bandwidth determination

There is no definite way to determine the optimal bandwidth, however, testing different bandwidths and evaluating some of the influential indices may help to determine it. Accordingly, the bandwidth was tested for three to fifteen neighborhoods. Higher local R^2 and lower AICc are preferable when determining the optimal bandwidth. As the neighborhood number increases, both the local R^2 and the AICc decrease and vice versa. Consequently, a high number of neighborhoods leads to a better AICc and a worse local R^2 and vice versa. Therefore, it is important to maintain a balance between these two parameters. In this study, six neighborhoods were selected as the optimal bandwidth because it provides an acceptable local R^2 and a significantly decreased AICc.

Exploring the spatial relationship between using of the PCF and COVID-19

The PCF's overall effect

After assessing spatial autocorrelation and potential multi-collinearity, ten independent variables remained and were categorized into pesticides (6) and CFs (4) groups. In addition, nine dependent variables remained and were categorized into infection (2), death due to mortality (DDI) (2), and MTI ratio (5 variables) groups. The GWR model was then performed 18 times, separately for each dependent variable and each group of independent variables. According to Table 2, the R^2 and Adjusted R^2 ($AdjR^2$), which quantify a model's goodness of fit, are generally more than 0.5. This indicates that more than fifty percent of the dependent variables’ changes are explained by the independent variables. There is just an exception including PPD in CFs, where the R^2 is significantly less than 0.5. In addition, $AdjR^2$ for PPD and PPM in both groups of the independent variables are much lower than 0.5, and the discrepancy between their R^2 and $AdjR^2$ values is considerable. This shows that the variances of the independent variables are unable to adequately explain the dependent variable.

Furthermore, the AICc is considerably affected by change in the dependent variable. The dependent variables related to the MTI ratio have the lowest AICc. They provide a better fit to the observed data. However, the AICc is not an absolute indicator for measuring the goodness of fit and should be assessed alongside the local R^2 and the standard residuals. The standard residual was utilized to assess the GWR models' local goodness of fit. The results are shown in Figures 2 to 3. If the standard residual in the most of the units exceeds 2.58, the model is biased and has lost at least one key independent variable. The results show that just a few units in all of the models have exceeded 2.58. Therefore, none of the models are biased, and all of them are trustworthy.

Table 2. Overall results of the GWR model

Independent variables	Dependent variables	R-squared	AdjR2	AICc
Pesticides	PPI	0.95	0.909	1081.95
	HI	0.717	0.489	1364.33
	PPD	0.52	0.132	1313.28
	HD	0.783	0.608	1305.17
	PM	0.824	0.682	1008.33
	PPM	0.642	0.354	1252.58
	AM	0.831	0.695	1088.92
	TM	0.84	0.711	1063.38
	HM	0.822	0.679	1215.01
CFs	PPI	0.91	0.861	1117.63
	HI	0.657	0.467	1344.92
	PPD	0.403	0.066	1298.58
	HD	0.746	0.605	1280.99
	PM	0.741	0.598	1016.15
	PPM	0.573	0.336	1231.04
	AM	0.729	0.579	1109.03
	TM	0.754	0.617	1077.86
	HM	0.759	0.625	1211.62

Exploring the spatial relationship between the pesticides and COVID-19

Nine GWR models were run based on each dependent variable involving: PPI, HI, PPD, HD, PM, PPM, AM, TM, and HM. SH, SI, SF, HH, HI, and HF were included in all of the models as the independent variables. The results are shown in Fig. 2 and Table 3. Columns 1 and 2 in Fig. 2 show the standard residuals and local R^2 distributions, respectively. The local regression coefficients of the independent variables are shown in columns 3-8. The regression coefficients represent the strength and type of spatial relationship between each dependent variable and independent variable. In other words, the regression coefficient indicates how many units the dependent variable increases or decreases as the independent variable increases one unit. Positive and negative values denote direct and inverse spatial relationships, respectively. A-I rows in Fig. 2 also shows the results of each GWR model for the dependent variables individually. The number of RDs with positive or negative coefficients, as well as their means, were calculated to determine the total local regression coefficient of each independent variable.

We estimated coefficients between the dependent and independent variables in this study. The number of RDs with positive and negative coefficients (N) and the mean positive and negative coefficient of the RDs (M) in the entire province were calculated for each model and independently for each independent variable to determine the type of coefficients. The results are shown in Table 3. To establish whether the coefficient is positive, the following guidelines were used:

1. If both of the M and N are positive for the positive coefficient, and at least one of them is significantly higher, the coefficient is significantly positive.
2. If both of the M and N are positive for the positive coefficient, and neither of them is significantly higher, the coefficient is positive.
3. It is positive if the Ms are close together or if the positive coefficient's M is somewhat lower than the negative coefficient's M and its N is very high.
4. It is positive if the Ns are close together or if the positive coefficient's N is somewhat lower than the negative coefficient's N and its M is very high.

Before looking at the coefficients, it is worth noting that the local R^2 for the majority of the models is greater than 50 percent, showing that the dependent variables are well described by the independent variables. A few models have local R^2 values below 50 percent, yet the results are reliable due to the reliability of their standard residuals.

The investigating of different models indicates different outcomes. However, to avoid being confusing, we go over the positive relationships. In most of the models, SH and HI indicate positive or significantly positive coefficients. In addition, HH indicates a positive or significantly positive coefficients in some of the models. Eventually, HF, SI and SF indicate positive or significantly positive coefficients in just a few of the models. From another point of view, SI has its positive coefficients with the variables related to COVID-19 infection. Moreover, SH, HI and HH have their main positive coefficients with the variables related to mortality to infection ratio. The detailed results are provided in the Fig. 2 and Table 3.

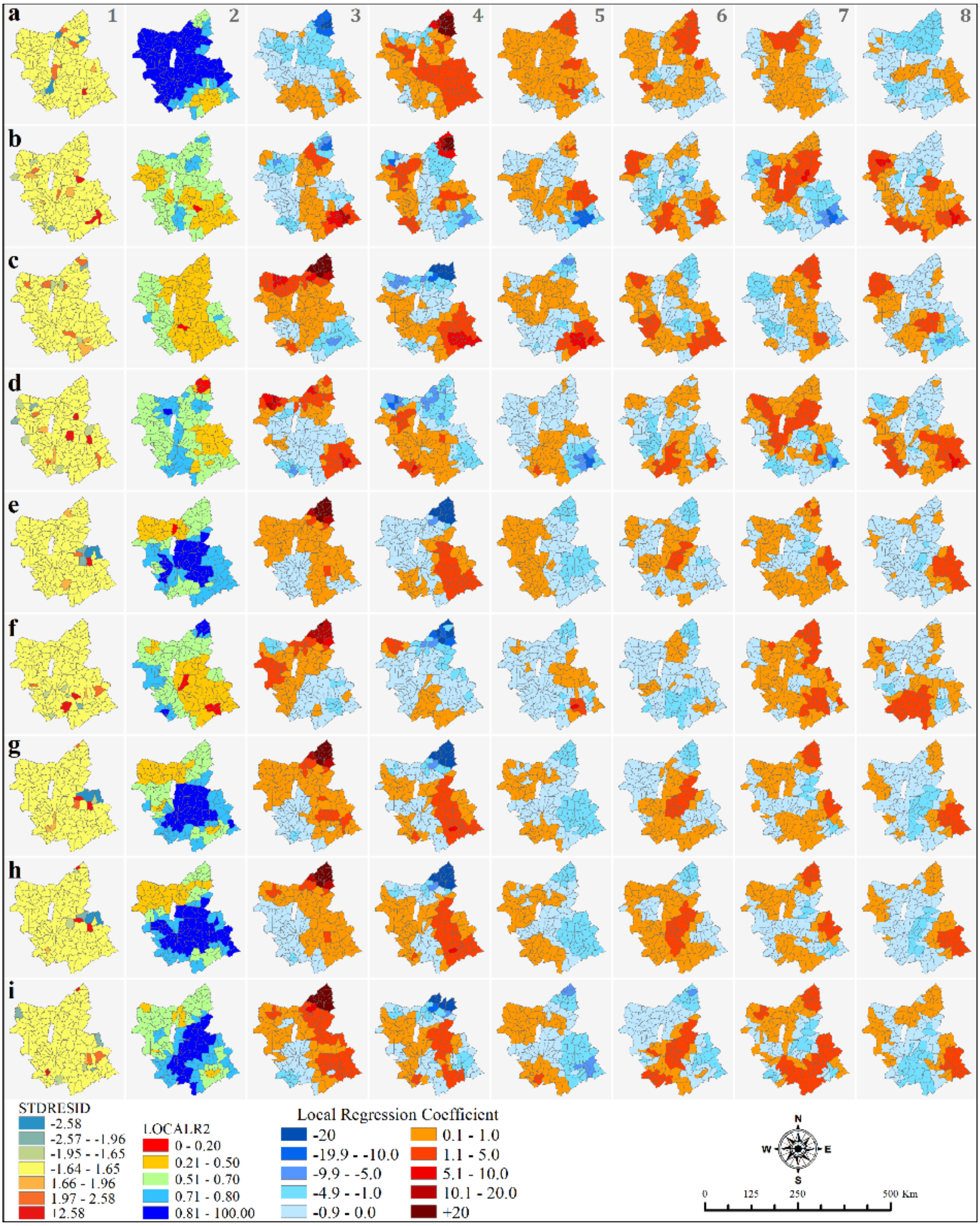

Fig 2. Local distribution of standard residuals, local R2, and the regression coefficients, separately for each dependent and independent variables (Pesticides): a) PPI, b) HI, c) PPD, d) HD, e) PM, f) PPM, g) AM, h) TM, i) HM; and 1) Std. residual, 2) local R2, 3) Coefficient of SH, 4) Coefficient of SI, 5) Coefficient of SF, 6) Coefficient of HH, 7) Coefficient of HI, 8) Coefficient of HF

Table 3. Total results of local regression coefficient in spatial relationship between the pesticides and COVID-19

Dependent variables (GWR models)	Type of coefficient	SH		SI		SF		HH		HI		HF	
		Count	Mean	Count	Mean	Count	Mean	Count	Mean	Count	Mean	Count	Mean
PPI	Positive	40	0.39	120	3.85	123	0.68	104	0.61	108	0.31	29	0.31
	Negative	101	2.64	21	0.82	18	0.34	37	0.31	33	0.32	112	0.90
HI	Positive	57	1.61	80	3.27	66	0.42	71	0.92	73	1.18	89	1.53
	Negative	84	1.86	61	2.02	75	1.54	70	0.91	68	2.76	52	0.5
PPD	Positive	101	7.53	75	1.48	77	1.14	94	0.83	65	1	57	0.76
	Negative	40	1.73	66	16.51	64	0.97	47	1.24	76	0.93	84	0.71
HD	Positive	70	2.01	78	0.88	45	0.31	64	0.59	90	1.04	84	1.36
	Negative	71	0.81	63	3.16	96	1.05	77	0.95	51	1.72	57	0.58
PM	Positive	95	3.8	64	1.11	66	0.04	61	0.39	94	0.34	35	0.81
	Negative	46	0.14	77	6.52	75	0.95	80	0.41	47	0.27	106	0.21
PPM	Positive	84	2.84	30	0.58	31	0.76	28	0.43	116	1.03	74	0.74
	Negative	57	0.86	111	2.99	110	0.36	113	0.75	25	0.27	67	0.46
AM	Positive	99	4.77	78	1.13	43	0.09	76	0.69	80	0.55	51	0.63
	Negative	42	0.37	63	10.63	98	0.97	65	0.54	61	0.47	90	0.58
TM	Positive	87	6.16	94	0.97	55	0.08	103	0.55	70	0.5	51	0.59
	Negative	54	0.27	47	16.64	86	1.08	38	0.85	71	0.4	90	0.51
HM	Positive	102	8.39	73	0.95	58	0.26	55	1.22	91	1.18	63	0.72
	Negative	39	0.74	68	18.69	83	1.93	86	0.98	50	0.91	78	0.88

Exploring the spatial relationship between the CFs and COVID-19

The spatial relationships between CFs and COVID-19 were explored using the same dependent variables in the pesticides. However, four variables SN, SP, HPH, and HP were included as independent variables in all of the models. The results are shown in Fig. 3 and Table 4. The local R^2 for PPI is greater than 80 percent and for most of the other models is greater than 50 percent with the exception of PPD and PPM, which had local R^2 lower than 50 percent. Nonetheless, the results are reliable due to the reliability of their standard residuals, despite the poorer goodness of fit.

According to the results, HP and HPH indicate positive and significantly positive coefficients in most of the models. Unlike, SN and SP just have the positive and significantly positive coefficients in the few models. From another point of view, HP and HPH have their positive coefficients with all of the variables including the variables related to COVID-19 infection, Death due to infection, and mortality to infection ratio. Additionally, SP and SN have mainly their positive coefficient with COVID-19 infection and death due to infection. The detailed results are provided in the Fig. 3 and Table 4.

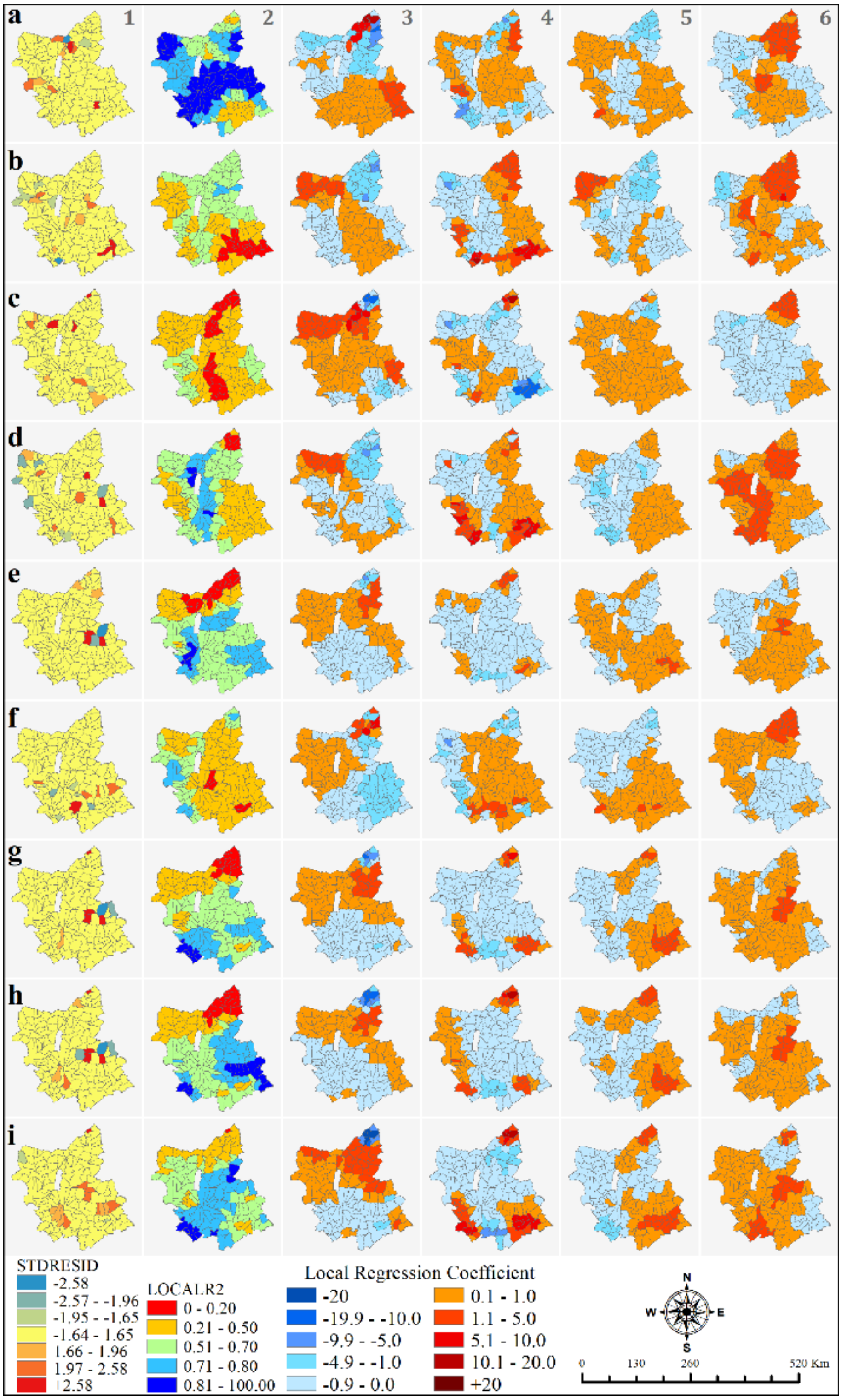

Fig 3. Local differences of standard residuals, local R2, and the regression coefficients, separately for each dependent and independent variables (CFs): a) PPI, b) HI, c) PPD, d) HD, e) PM, f) PPM, g) AM, h) TM, i) HM; and 1) Std. residual, 2) local R2, 3) Coefficient of SN, 4) Coefficient of SP, 5) Coefficient of HPH, 6) Coefficient of HP

Table 4. Total results of local regression coefficient in spatial relationship between the CFs and COVID-19

Dependent variables (GWR models)	Type of coefficient	SON		SOP		HOPH		HOP	
		Count	Mean	Count	Mean	Count	Mean	Count	Mean
PPI	Positive	77	1.78	74	0.54	89	0.3	70	1
	Negative	64	1.55	67	1.54	52	0.76	71	0.44
HI	Positive	67	0.59	80	1.92	40	0.46	96	0.98
	Negative	74	1.15	61	0.58	101	0.61	45	0.44
PPD	Positive	108	1	52	0.9	126	0.3	31	0.88
	Negative	33	2.19	89	1.54	15	0.73	110	0.42
HD	Positive	48	0.64	89	1.8	61	0.42	123	1
	Negative	93	0.97	52	0.41	80	0.75	18	0.25
PM	Positive	64	0.36	33	0.55	94	0.28	78	0.21
	Negative	77	0.42	108	0.25	47	0.14	63	0.05
PPM	Positive	56	0.98	88	0.52	72	0.35	80	0.76
	Negative	85	0.86	53	1.29	69	0.36	61	0.22
AM	Positive	71	0.45	35	1.28	62	0.56	120	0.32
	Negative	70	0.86	106	0.36	79	0.18	21	0.04
TM	Positive	57	0.43	54	1.01	74	0.55	107	0.32
	Negative	84	1.1	87	0.34	67	0.17	34	0.09
HM	Positive	76	1.2	53	3.13	62	0.86	111	0.68
	Negative	65	2.53	88	0.72	79	0.5	30	0.25

Discussion

The spatial relationship of pesticides and CFs with COVID-19 were explored in two different categories. The results can be interpreted from two aspects: 1) to explore the effects of different types of PCFs on COVID-19, and 2) to explore which COVID-19 indicators are influenced most by the PCFs.

According to the findings, increasing the sum of herbicides is significantly associated with MTI ratio hotspots. In addition, the trend, average, peak and peak period of the MTI ratio increase as the sum of herbicides increases. The same is true about the peak period and hotspots of the DDI. However, there is no evidence that increasing the sum of herbicides increase COVID-19 infections. Moreover, the use of herbicides is highly associated with the long peak period of DDI, and high average and trend of the MTI ratio. Overall, the DDI and MTI ratio factors are higher in areas where herbicides are highly used. As a result, it is likely that high use of herbicides has contributed to increased COVID-19 mortality.

Except of the peak period of the DDI, hotspots of potassium use have a significant positive relationship with all of the COVID-19 indicators. The peak period of infection and MTI ratio are prolonged in hotspots. In addition, the hotspots are highly correlated to the hotspots of infection, DDI, and MTI ratio. Further, the peak, average, and trend of the MTI ratio increase intensely in the hotspot areas. Moreover, increasing in sum of potassium has a significant positive relationship with hotspots of infection, DDI, and MTI ratio. As a result, using potassium may also indirectly increase COVID-19 infection, DDI, and MTI ratio.

Hotspots of insecticide and phosphate use indicated significant positive correlations with the COVID-19 indicators. However, their correlations were lower than those of the herbicides and potassium with COVID-19. Insecticide hotspots had positive correlations with hotspots of the DDI and the MTI ratio. Peak periods of infection and the MTI ratio go longer in the hotspot areas. Peak and average of the MTI ratio increase in the insecticide hotspots. In addition, phosphate hotspots are correlated with the high peak, average and trend of the MTI ratio. Furthermore, peak periods of infection and DDI increase in hotspot areas. As a result, use of insecticides and phosphates may indirectly increase infection, DDI, and MTI ratios. In contrast, we found no relationships between the use of fungicides and nitrates and the COVID-19 indicators.

Among the nine COVID-19 indicators, the peak period of infection had the highest positive correlation with all of the dependent variables. In the other words, they may cause (among other factors) the peak period to be prolonged. This is deduced from the number and intensity of independent variables that have a positive correlation with the dependent variable. Moreover, the PPI, MTI ratio, DDI, and AM hotspots had the most positive associations with the all of the independent variables. This clearly shows that COVID-19 mortality is high in areas where pesticides and CFs are highly used.

Based on our review, this is the first study to explore the spatial relationship between the use of pesticides and CFs and COVID-19 infection and mortality. Although there is no comparable research to which we can compare our findings, many studies have reported positive correlations between various diseases and exposure to different kinds of pesticides and CFs (Xun et al., 2022). It has also been reported that COVID-19 infection and mortality are higher among the people with underlying diseases than among those without such risk factors (Liao et al., 2021; Reyes-Sánchez et al., 2022; Semenzato et al., 2021). Consequently, it is possible that PCFs use may increase COVID-19 infection and mortality, indirectly.

This study explored the relationship between the use of pesticides and CFs and COVID-19's infection and mortality. This study has some limitations. According to our findings, there is a positive spatial relationship between using pesticides and CFs and COVID-19 infection and mortality. However, pesticides and CFs are unlikely to directly lead to COVID-19. Previous research has established that there may be a relationship between exposure to pesticides and CFs and a number of different diseases. In addition, underlying diseases are a risk factor for COVID-19 mortality. Future studies should investigate whether the rate of underlying diseases such as cancer, Parkinson's Disease, respiratory diseases, diabetes, high/low blood pressure, neurodegenerative diseases and other diseases is high in the study area of this study. Data regarding the distribution of underlying diseases in the study area are unavailable, a main limitation of the present study. Other limitations include: a lack of literature exploring the relationship between the use of CFs and different diseases which could potentially help estimate the impact of CFs on the underlying diseases, and their indirect relationship with the COVID-19; the inability to compare the present study's results with others due to the lack of comparable studies in this field; and the unavailability of data in the whole country to explore the relationship patterns and the affecting factors. Despite its limitations, this study is the first of its kind on the subject and offers a fresh perspective on the parameters that influence COVID-19 infection and mortality. Future studies should conduct comparable research using different models, variables, and areas to compare with the findings of this study and address the shortcomings.

Conclusion

A GWR model was used in this study to explore local spatial relationships between pesticide and CFs use and COVID-19 infection and death. The following are the main findings:

1. Areas of high total use and hotspots of herbicide and potassium were significantly positively correlated with an increase in COVID-19 mortality, as well as its peak and peak period, average, trend, and hotspots.
2. High usage of phosphate and insecticides, as well as their hotspots, were associated with high COVID-19 infection and death in most indices. Their coefficients, however, were lower than those of herbicides and potassium.
3. There is no evidence of a relationship between increasing COVID-19 infection and mortality and high total fungicide and nitrate use and hotspots.

4. Overall, the highest positive relationships of pesticide and CFs use were with the prolonged peak period of infection, mortality to infection ratio hotspots, death due to infection hotspots, and average mortality to infection ratio hotspots.
5. The association of pesticide and CFs hotspots with increasing COVID-19 indicators was stronger than the association of areas with high total use with COVID-19 indicators.

In general, the findings of this study revealed a positive spatial relationship between the use of pesticides and CFs and increasing in COVID-19 infection and mortality.

Acknowledgements

We appreciate the assistance of Dr. Adibkia, the Vice Chancellor for Education and Research, Tabriz University of Medical Sciences, helping in obtaining the COVID-19-related data. We also are thankful Dr. Imani and Mr. Nobari, the heads of Statistics and Information of East Azerbaijan Agricultural Organization, regarding help in obtaining the pesticides-related and CF-related data.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sector.

Data availability

Datasets and codes related to this article can be downloaded at https://prod-dcd-datasets-cache-zipfiles.s3.eu-west-1.amazonaws.com/vmyw6nwn7p-1.zip, an open-source online data repository hosted at Mendeley Data.

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