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Time trend and geographical distribution of colorectal cancer incidence before and after COVID-19 pandemic in southern Iran: an interrupted time series analysis

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ABSTRACT

Aim: This study aimed to assess the trend and geographical distribution of colorectal cancer (CRC) in Fars province from 2011 to 2024, and its changes during COVID-19.

Background: Research has indicated that the risk of CRC varies significantly across different regions of the world.

Methods: From 2011 to 2024, data from 1,453 CRC patients who were registered in the Shiraz Colorectal Cancer Surgery (SCORCS) program were analyzed. Using R software (v4.2.0), we applied interrupted time series analysis to evaluate the impact of COVID-19 on CRC incidence and mortality. Spatial distribution was examined with ArcGIS (v10.4.1), and Moran's I test was used to determine high- and low-risk regions. A 5% significance level was applied to all analyses.

Results: In this study, 56.2% of the patients were men and 43.8% were women. Most patients (49%) were between 30 and 59 years old. Rectal cancer was slightly more common (57.7%) than colon cancer (41.8%), and only a very small number (less than 0.5%) had both. About half of the patients were classified as T3, and over 80% already had metastasis. At the pandemic onset, both outcomes showed a significant immediate increase, followed by a significant post-pandemic decline in slope. Among the studied areas, Kazerun and Jahrom had the highest incidence rate, while Zarqan and Kazerun showed the highest mortality rate.

Conclusion: This study shows that CRC incidence and mortality declined during COVID-19, likely due to restrictive policies. However, the high rates in some cities of Fars province highlight the need for targeted interventions to reduce the disease burden.

Keywords: Colorectal cancer, Geographical distribution, Trend, Fars province, COVID-19.

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Introduction

Colorectal cancer (CRC) begins in either the colon or the rectum. Depending on the location, it may be called colon cancer or rectal cancer. These two types are often grouped because they have many features in common (1). According to the International Agency for Research on Cancer, Asia accounted for 966,399 cases of CRC in 2022, representing 50.2% of all global cases. Most of these cases occurred in East Asian countries, where 517,106 cases were reported; In contrast, Iran has one of the highest incidence rates of CRC among countries in the EMRO region (2).

Research has shown that the risk of CRC varies significantly across different regions of the world, with some reports indicating that the risk in one

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country may be up to 25 times higher than in another. In general, high-income countries such as the United States, New Zealand, and Canada report higher incidence rates, while developing countries are facing a rising trend in CRC cases. These regional differences are largely attributed to environmental, social, and behavioral factors, among which environmental factors play the most important role in the development and spread of the disease (3). Based on the latest report by the International Agency for Research on Cancer (2022), CRC accounted for 9.4% of all cancers in Iran. It ranks as the fourth most common cancer among Iranian men and the third most common among women. With a population of approximately 86 million, Iran recorded 12,899 cases of CRC in 2022 (4). Moreover, the incidence and prevalence of CRC have been rising over the past decade (5), and projections suggest that both incidence and mortality rates will continue to rise in Iran from 2021 to 2050 (6).

The risk of CRC varies across different regions of Iran. Based on available data, the northern, northwestern, and parts of the western and central provinces are considered high-risk areas. For instance, some studies have identified East Azerbaijan as a high-risk province, while South Khorasan, Kerman, and Sistan and Baluchestan are classified as low-risk regions (3, 7). According to the latest national report from the National Cancer Registry Program (2018), CRC was the fifth most common cancer among the general population of Fars Province. However, when analyzed by gender, it ranked as the fourth most common cancer among both men and women. In Fars Province, the crude incidence rate and age-standardized incidence rate (ASR) per 100,000 population were reported as 15.44 and 16.03 in men, and 13.6 and 13.09 in women, respectively (8).

Given the significance of the COVID-19 pandemic and its impact on the management of many non-communicable diseases, cancer (particularly CRC) faced substantial challenges in the identification of new cases. Considering the importance of this issue, the present study was conducted to determine the impact of the COVID-19 pandemic on the diagnostic process of CRC across different stages of the disease. Additionally, the study aims to examine the geographical distribution of CRC cases and related deaths, and to identify hot and cold spots in terms of incidence and mortality.

Methods

Study area and study design

This was a retrospective hospital registry study with ecological analyses of aggregated data. Ecological studies are observational in nature and examine the relationship between exposures and health outcomes at the population level rather than the individual level. They rely on the analysis of aggregated data. Fars Province, the study area, is located in the southwest of Iran and consists of 37 counties. According to the most recent estimates, the province has a population of approximately 5,039,732, with 50.5% male and 49.5% female residents.

Data source and processing

This was an ecological study using data from the Colorectal Research Center at Shiraz University of Medical Sciences. The dataset was derived from a population-based registry program which installed in January 2007 at Shahid Faghihi Hospital, a tertiary-level specialized center for surgical treatment. This registry was established at this hospital as a province-wide, registry for CRC. The registry includes data on patients admitted to the CRC section of Shahid Faghihi Hospital with a confirmed diagnosis of colon cancer (CC) or rectal cancer (RC). The diagnosis of CRC was confirmed based on the pathology report of intestinal tissue samples obtained to surgery. The registry contained no duplicate records, and only incident CRC cases were included. Only patients residing in Fars province were retained in the analysis, and county assignment was based on the patient's registered residence address.

Metastasis was defined as the involvement of the liver, lungs, or any other distant organs. A total of 1,453 patients were included in this study, comprising 607 patients with colon cancer and 839 patients with rectal cancer. Data extracted from the registry included patients' demographic characteristics and the date of diagnosis (according to the pathology report). Staging was determined using the American Joint Committee on Cancer (AJCC) staging system (7th edition), categorized from stage I to stage IV. Follow-up assessments were conducted at 1, 2, and 4 weeks after surgery, followed by

evaluations at 3 months, 6 months, 1 year, and annually thereafter for up to 10 years or until death. Deaths were confirmed by a physician and recorded as CRC-related if applicable. The analytical framework of this study is shown in Figure 1.

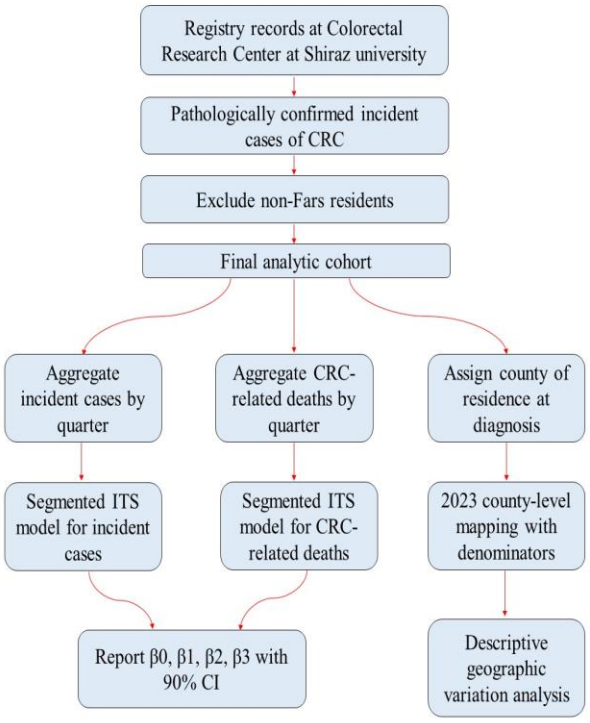

Figure 1. Flowchart of the study design and analytical process

Statistical analysis

Geographical distribution

To estimate the incidence of CRC in each county of Fars Province, statistical analyses were conducted using Microsoft Excel. A color-coded quartile classification was used to visualize the geographical distribution of CRC across the 37 counties. The incidence variation and spatial autocorrelation between counties were assessed using the Getis-Ord Gi statistic and Moran's I test, respectively. In the color spectrum, the first quartile (Q1) represents counties with the lowest incidence, while the fourth quartile (Q4) indicates those with the highest incidence. The spatial distribution map was generated using ArcMap GIS software, version 10.2. A p-value < 0.05 was considered statistically significant.

Interrupted time series

In Interrupted Time Series (ITS) studies, a specific outcome is monitored over time to detect underlying trends. At a known time point, an event, such as the COVID-19 pandemic, interrupts this trend, enabling researchers to evaluate its impact. The counterfactual represents the hypothetical scenario in which the intervention did not occur, and the pre-existing trend would have continued unchanged. By comparing the observed post-intervention data to this counterfactual, the effect of the intervention can be estimated. The standard ITS regression model includes four main parameters: 1) β_0 shows the baseline level of the outcome at time zero. 2) β_1 indicates the slope (trend) before the intervention. 3) β_2 measures the immediate change in the level of the outcome following the intervention. 4) β_3 captures the change in the post-intervention trend, modeled through the interaction between time and the intervention. This relationship is formally expressed in Formula 1 (9 ,10).

Formula 1: $\text{Outcome} = \beta_0 + \beta_1(\text{time}) + \beta_2(\text{level}) + \beta_3(\text{time} \times \text{level}) + \varepsilon$

In this study, the interruption point was the onset of the COVID-19 pandemic. We assessed the trend of incidence and deaths before and after the pandemic in Fars province. Data were aggregated into 3-month (quarterly) intervals, resulting in 52 equally spaced observations over the 13-year study period. The interruption point was defined as the first quarter of 2020 (January to March), coinciding with the official start of the COVID-19 pandemic in Iran. A Poisson regression model with a log link and population offset was used, and all model assumptions were checked.

Results

Descriptive results

The basic demographic characteristics of patients diagnosed with colon cancer (CC) or rectal cancer (RC) are presented in Table 1. Of the 1,453 registered patients, 43.8% were female, and 56.2% were male. More than 97% of the patients were over 30 years of age. Among them, 41.8% had colon cancer, 57.7% had rectal cancer, and less than 0.5% were diagnosed with cancer involving both the colon and rectum. Approximately 50% of the patients were diagnosed at T3 stage or higher, and about 19% had evidence of cancer spread to other organs. In addition, over 30% of the patients were diagnosed at stage III.

Table 1. Primary characteristics of patients with CRC admitted in Shahid Faghihi Hospital.

Factors		Number	Percent (%)	95% CI
Sex	Female	636	43.8%	41.2 - 46.3
	Male	817	56.2%	53.6 - 58.7
Age	6 to 19	1	0.1%	0 - 0.2
	20 to 29	32	2.2%	1.4 - 2.9
	30 to 59	712	49%	46.4 - 51.5
	Over 60	708	48.7%	46.1 - 51.2
Cancer type	Colon	607	41.8%	39.2 - 44.3
	Rectal	839	57.7%	55.2 - 60.2
	Colon& Rectal	7	0.5%	0.1 - 0.8
Tumor size based on T	T0	19	1.3%	0.7 - 1.8
	Tis	6	0.4%	0 - 0.7
	T1	82	5.6%	4.4 - 6.8
	T2	367	25.3%	23 - 27.4
	T3	716	49.3%	46.7 - 51.8
	T4	131	9%	7.5 - 10.4
	TX	2	0.1%	0 - 0.3
	Unknown	130	9%	7.4 - 10.4
Cancer stage	0	27	1.9%	1.2 - 2.7
	I	344	23.6%	21.5 - 25.9
	II	408	28%	25.7 - 30.5
	III	443	30.5%	28.1 - 32.9
	IV	97	6.7%	5.4 - 8
	Unknown	134	9.2%	7.7 - 10.8
Metastasis	Yes	271	18.6%	16.6 - 20.7
	No	1149	79.1%	76.9 - 81.1
	Unknown	33	2.3%	1.5 - 3.2
Lymph node involvement	N0	815	56.1%	53.5 - 58.6
	N1	358	24.6%	22.4 - 26.8
	N2	144	9.9%	8.3 - 11.4
	NX	6	0.4%	0 - 0.7
	Unknown	130	9%	7.4 - 10.4
The outcome of cancer	Alive with disease	91	6.3%	5 - 7.5
	Alive without disease	969	66.7%	64.2 - 69.1
	Death from disease	316	21.7%	19.6 - 23.8
	Death from other diseases	29	2%	1.2 - 8.7
	Lost to follow up	37	2.5%	1.7 - 3.3
	Unknown	11	0.8%	0.3 - 1.2

Table 2. Incidence trend and death trend that have compared before and after COVID-19.

Parameters	Incidence								Death	
	Tumor size categories				Cancer stage categories					
	Tis, T1, T2	p	T3, T4	p	0, I, II	p	III, IV	p	coefficients	p
β_0	4.08	<0.001	3.63	0.004	5.73	<0.001	1.57	0.0781	0.71	0.091
β_1	0.16	<0.001	0.32	<0.001	0.26	<0.001	0.22	<0.001	0.20	<0.001
β_2	2.34	<0.001	11.55	<0.001	8.57	<0.001	12.31	<0.001	10.86	<0.001
β_3	-0.22	<0.001	-0.44	0.133	-0.61	<0.001	-0.80	<0.001	-0.91	<0.001

All parameters were measured at a 0.05 significance level.

Interrupted time series

The results of the interrupted time series (ITS) analysis are presented in Table 2. According to this analysis, the incidence of CRC, stratified by tumor size and disease stage, showed a significant immediate level change after the start of the COVID-19 pandemic. For example, the incidence of tumors at stages T3 and T4 experienced a sharp rise of 11.55 cases ($p < 0.001$) after the onset of COVID-19, indicating a substantial growth. Similarly, the trend in mortality also demonstrated a comparable sudden increase following the beginning of the pandemic.

These findings highlight the considerable impact of the COVID-19 pandemic on the diagnosis and outcomes of CRC. Figure 2 shows the trend of CRC incident cases in Fars province from 2011 to 2023, stratified by several categories, comparing the pre- and post-COVID-19 periods.

In addition, we also observed a significant change in slope in the post-pandemic period. Despite the initial rise, the post-pandemic trend of CRC incidence showed a significant decline in slope compared to the pre-pandemic period in all categories, indicating that the rate of increase slowed down considerably after the pandemic. Similarly, the trend in mortality also demonstrated both a comparable sudden increase at the pandemic onset and a

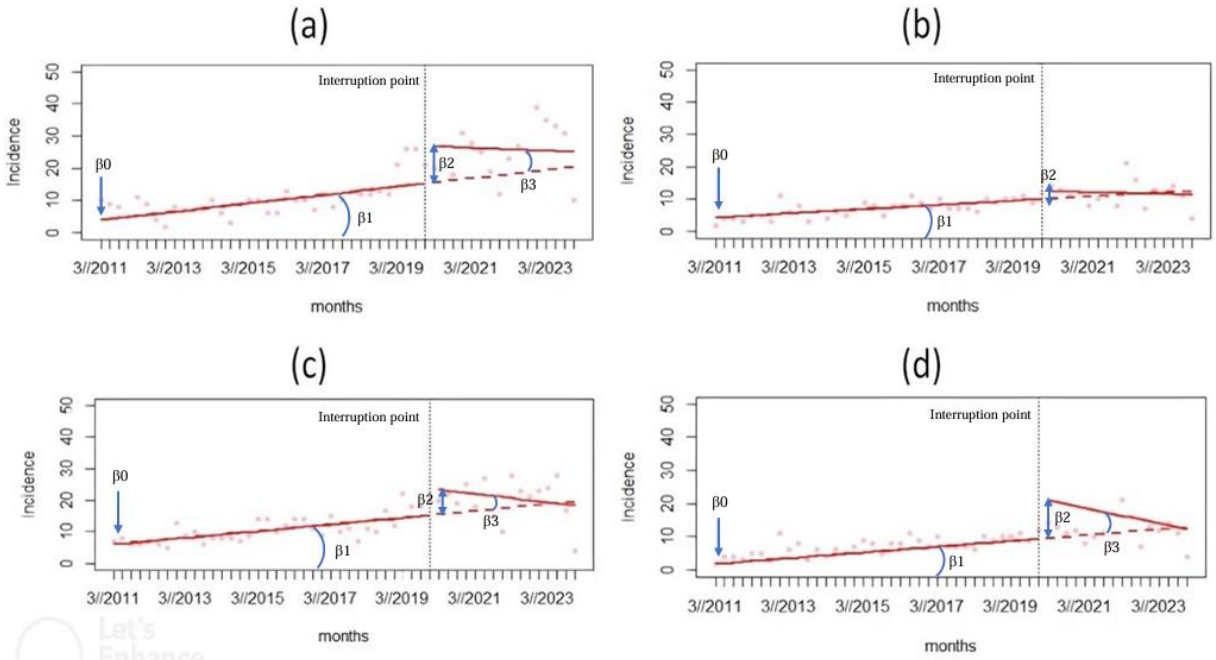

Figure 2. Incidence trend of CRC in Fars province from 2011 to 2023, which have compared before and after COVID-19. (a: incidence trend of CRC based on T3 and T4.b: incidence trend of CRC based on Tis, T1 and T2.c: incidence trend of CRC based on stage 0, stage I and stage II. d: incidence trend of CRC based on stage III, stage IV); β_0: baseline level of the outcome at time zero; β_1: trend before the pandemic; β_2: change in the level of the outcome; β_3 change in slope.

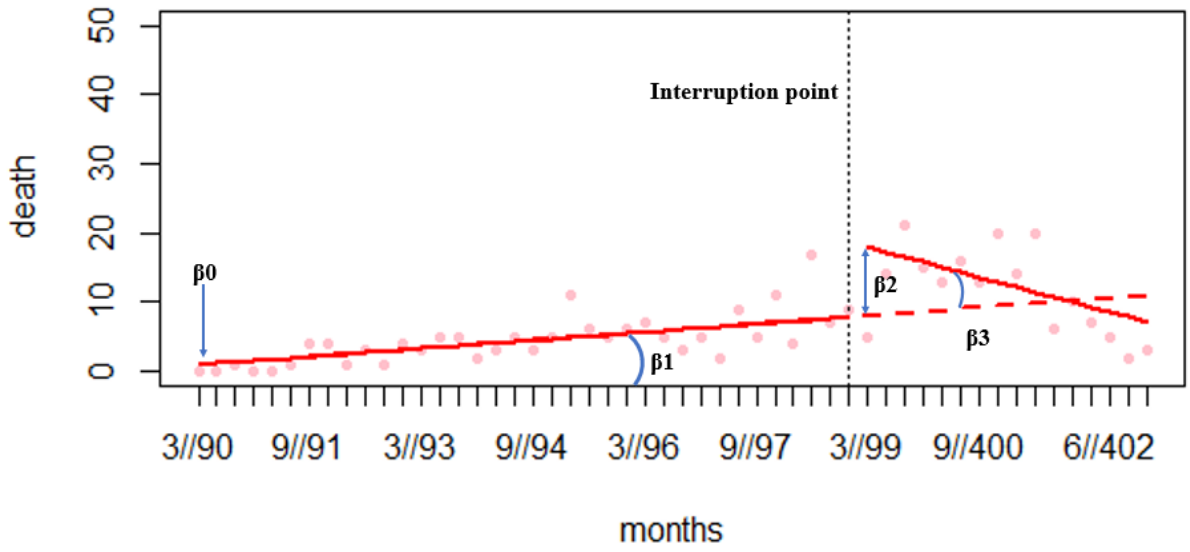

Figure 3. Death trend of CRC in Fars province from 2011 to 2023, which have compared before and after COVID-19. β_0: baseline level of the outcome at time zero; β_1: trend before the pandemic; β_2: change in the level of the outcome; β_3 change in slope.

subsequent significant decline in slope during the post-pandemic period. Figure 3 illustrates the mortality trend of CRC in Fars province from 2011 to 2023 before and after the COVID-19 pandemic.

Geographical distribution

After reviewing CRC data, Kazerun, Jahrom, and Larestan had the highest incidence rates per 100,000 people in 2023 among the counties in Fars Province, with 27.1, 17.8, and 13.6 respectively. The hot spot in the incidence rate was located in Kazerun (p=0.928), which was not statistically significant. No cold spots were identified; however, some cities in eastern Fars Province, including Bavanat, Kharameh, Bakhtegan, and Neyriz, had an incidence rate of zero.

Zarqan, Kazerun, and Jahrom had the highest rates of CRC death among the counties in Fars Province, with 5.6, 2.3, and 2.2 respectively. The hot spot in the death rate was located in Zarqan County (p=0.634), which was not statistically significant and no cold spot was identified (Figure 4).

Discussion

In this study, data from CRC patients who underwent surgical treatment in Fars Province over the past 13 years were analyzed. The number of male patients was slightly higher than that of female patients, and the number of rectal cancer cases was slightly greater than colon cancer cases. Only a small proportion of patients were diagnosed with both colon and rectal cancer. Most patients were diagnosed and treated at advanced stages of the disease. Following the onset of the COVID-19 pandemic, a decrease in the overall incidence and mortality trends of CRC was observed. However, this reduction varied across different aspects of the disease. For instance, the decline was more pronounced in stage III and stage IV CRC cases. In terms of geographical distribution, the highest incidence rates were recorded in Kazerun, Jahrom, and Larestan, respectively. While the highest death rates were recorded in the cities of Zarqan and Kazerun, respectively. No statistically significant hot spots or cold spots were identified for either incidence or mortality rates, indicating that the disease has no spatial clustering in Fars province.

The higher number of rectal cancer cases compared to colon cancer in this study might be attributed to the fact that this center serves as a national referral center for rectal cancer treatment (11). Additionally, the slightly higher number of male patients with CRC compared to female patients is consistent with the GLOBOCAN 2022 data (4) and may be influenced by hormonal differences, particularly male sex hormones (12). Furthermore, the absence of an organized screening program may have contributed to the late-stage diagnosis and treatment of many patients (13). A combination of factors including environmental exposures, cultural and ecological conditions, genetic predisposition, and socioeconomic disparities may explain why certain counties, such as Kazerun and Jahrom, have reported the highest incidence rates of CRC in Fars Province (14, 15). Notably, Kazerun was identified as a hot spot in this study, which is in line with the findings of a prior study conducted in the same region (15).

In our study, the incidence of CRC decreased during the onset of the COVID-19 pandemic. This decline may be associated with the strict public health measures implemented by governments to control the spread of the virus, which coincided with delays in the diagnosis of many cancers, including CRC. Additionally, our findings are in line with previous studies that have reported a reduction in CRC incidence during the post-COVID-19 period compared to the pre-pandemic period (16, 17). Our study also found a decrease in mortality from CRC following the onset of the pandemic. This decline could be attributed to a reduction in the number of patients visiting hospitals for diagnosis and treatment during this time (11). However, this finding contrasts with a study conducted in the United States, where a slight increase in mortality was reported. That increase was partly associated with an 80%–85% decline in screening volume after the government declared public health emergency measures to combat COVID-19 (18).

This study has several limitations. First, the findings are based solely on data from Shiraz city and may not be generalizable to the entire country. Regional differences in healthcare access, environmental exposures, socioeconomic status, and referral patterns could affect the incidence and outcomes of CRC. Due to the nature of observational studies, particularly ecological studies, causal

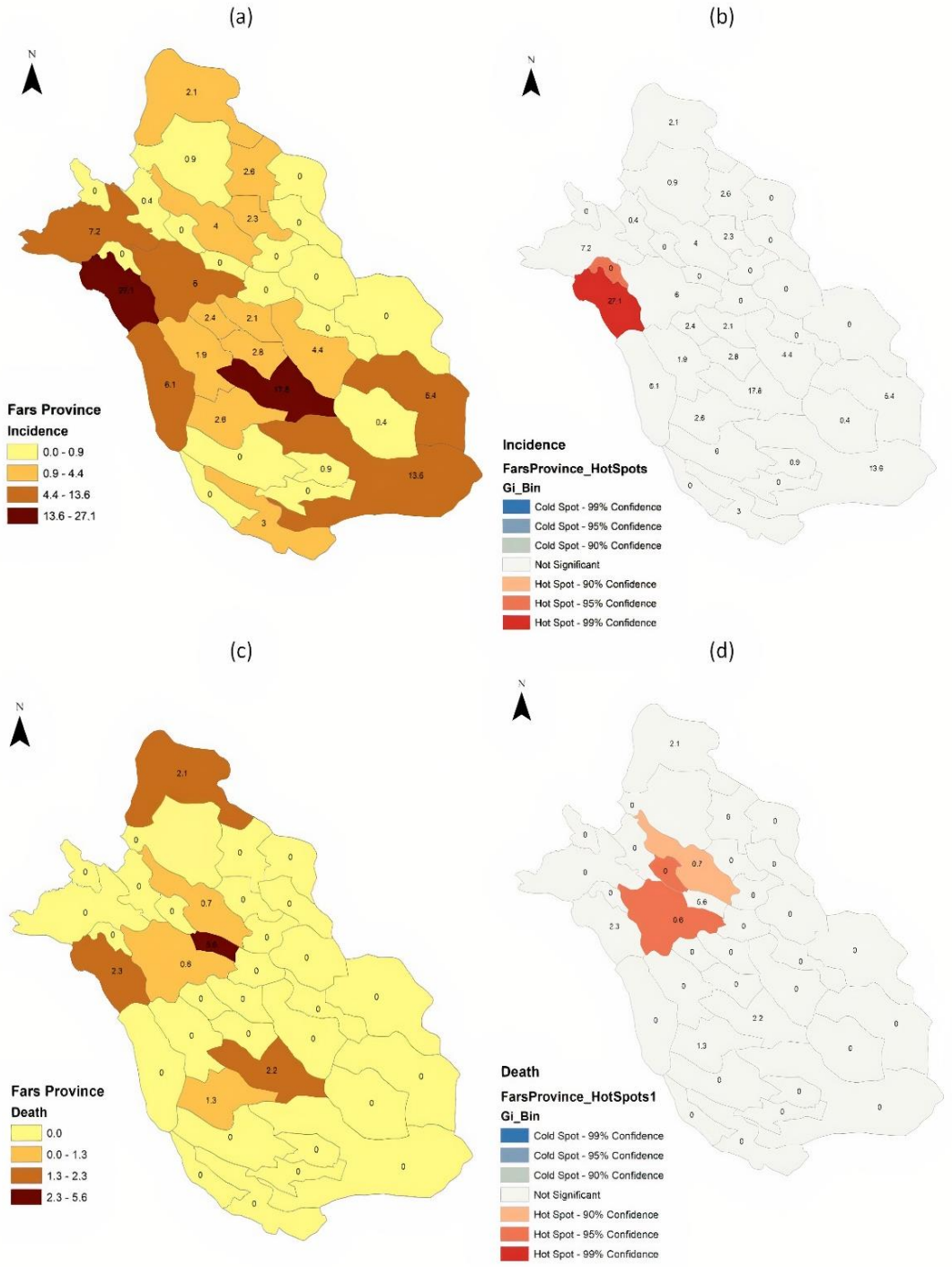

Figure 4. Geographical distribution and geographical correlation of CRC across Fars province in 2023. (a: incidence rate of CRC in Fars province. b: geographical correlation of incidence rate with p-value 0.928 and z-score 0.089.c: death rate of CRC in Fars province: geographical correlation of patients who died due to CRC with p-value 0.634 and z-score -0.475.

relationships cannot be inferred. Therefore, it is recommended that future studies be conducted on a larger, multi-center or national scale to enhance the generalizability of the findings and provide a more comprehensive understanding of CRC epidemiology across Iran.

Conclusion

The observed decline in CRC incidence and mortality during the COVID-19 pandemic, likely attributable to restrictive public health measures and disruptions in routine healthcare services, highlights the need for preparedness plans to ensure continuity of cancer care during public health emergencies. Furthermore, the notably high incidence and mortality rates of CRC in certain cities of Fars province underscore the importance of region-specific strategies and targeted interventions to improve early detection, access to care, and cancer prevention efforts.

Conflict of interests

There is no conflict of interest for authors of this article.

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Ethical approval

This project was found to comply with ethical standards by the Ethics Committee of Yazd University of Medical Sciences and was approved with the number IR.SSU.SPH.REC.1403.166.

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