ORIGINAL ARTICLE

SPATIAL ANALYSIS OF CERVICAL CANCER INCIDENCE IN IRAQ DURING 2010-2015

Muzahem Mohammed AL-Hashimi¹ and Safwan Nathem Rashed¹

¹Department of Statistics and Informatics, College of Computer science & Mathematics, University of Mosul, Mosul, Iraq

Corresponding author: Muzahem Mohammed AL-Hashimi

Email: muzahim_alhashime@uomosul.edu.iq

ABSTRACT

Cervical cancer is the most common cancer in Iraq. This study aimed to examine the spatial pattern and high-risk clusters of cervical cancer in different areas of Iraq (except the Kurdish region) during the period 2010-2015. The age-adjusted incidence rates (AAIRs), age-specific incidence rates (ASIRs), and annual percent changes (APCs) were calculated for 2010-2015. We used three techniques of spatial statistical analysis which are Global spatial autocorrelation, Getis-Ord Gi statistic, and Anselin Local Moran's I statistic to investigate spatial clustering and outliers. Over the period 2000-2015, 1037 cases were diagnosed with AAIR of incidence of (3.521 per 100,000). Depending on AAIRs, we found cervical cancer incidence was highest (8.212 per 100,000) in the age group of 60-69 years old. The APC of cervical cancer age-specific rates has significantly risen for the age groups 60-69 only. We identified spatial high-risk clusters for incidence. The cluster was mainly located in the center of Iraq (Baghdad, Najaf, Kerbala, and Babil provinces), the central-eastern part of Iraq (Diyala province), and the southern part of Iraq (Basrah province). While the provinces in the northern and northeastern parts of Iraq, as well as the western province, had relatively lower AAIRs from cervical cancer. A spatial cluster pattern for the incidence of cervical cancer in Iraq was revealed, which will be valuable for improving the allocation of health resources in Iraq.*

Keywords: Cold spots, hotspots, spatial outliers, cervical cancer, Iraq.

INTRODUCTION

Globally, cervical cancer was the fourth most commonly diagnosed cancer (after breast cancer, colorectal cancer, and lung cancer) and the fourth leading cause of death in women¹. Based on GLOBOCAN 2020 estimates, 604,000 new cases of cervical cancer and 342,000 deaths reported worldwide in 2020². Cervical cancer incidence rates are related to the age with the highest incidence seen in elderly women (55-69 years of age) in lower-resource countries, whereas in highest source countries, a maximum of incidence reached around the age of 40 year¹. Globally, the average age of diagnosis of cervical cancer was 53 years. Cervical cancer incidence rates are highly varying across regions. The age-standardized rate was highest in eastern, southern, or western Africa (ASR>40 per 100,000 women)¹. The lowest ASR values (ASR<5 per 100,000 women) were reported in western Asia or the western part of central-south Asia.

The worldwide variations in cervical cancer incidence might be attributed to Human papillomavirus (HPV) infection, differences in exposure to risk factors, inequalities in access to adequate screening, and cancer treatment facilities^{1,2}.

As shown in Figure 1, Iraq is located in the Middle East, in southwestern Asia. Iraq has common borders with the following countries: Iran in the west; Jordan and Syria in the east; Kuwait and Saudi Arabia in the south; and Turkey in the north. Iraq has 18 provinces (113 districts). The total area of Iraq is 437,072 square kilometer³. The estimated population of Iraq as of mid-year 2020, according to UN data, is 40,222,493.

Spatial statistical analysis is ordinarily used in epidemiology and health studies⁵. Understanding the Spatial analysis of disease in a population may reveal valuable information about disease causes and controls⁶. Disease

maps are a visual representation and an efficacious tool for displaying a large volume of geographical data. They used to view patterns of diseases for a specific geographic region⁷.

This study aimed to examine the spatial pattern and high-risk clusters of cervical cancer in different areas of Iraq during the period 2010-2015 (except the Kurdish region).

Figure 1: World Iraq Map⁴

MATERIALS AND METHODS

Data

This study covers all provinces except the Kurdish region (Erbil, Duhok, and Al-Sulaymaniyah provinces) with 83 districts in the country during 2010-2015. Data for incident cases of cervical cancer (ICDO-3: C53) by age (total 7 age groups, 20-29, 30-39, ..., 80+ years) in women, for each district between 2010 and 2015, come from the Iraqi Cancer Registry (ICR). The ICR is located in Baghdad, the capital of Iraq. The registry was founded in 1974 through close cooperation of the Ministry of Health and Iraqi Cancer Society. The ICR provided the data of cancer patients throughout the country. Data on cancer cases were collected from all hospitals (public and private), clinics, radiotherapy and pathology departments, and labs in all provinces of Iraq. The dataset

included the registry number, name, age at diagnosis, gender, nationality, occupation, residence code, type and cancer sites, grade, stage, treatment, the hospital name, and location were registered. The completed records were entered into the "Alphabetical Index" to prevent duplication⁸. Between 2010 and 2015, the female population in Iraq, by district and 5-year age group obtained from the Central Organization for Statistics in the Ministry of Planning. This data was used to calculate age-adjusted incidence rates (AAIRs), using the direct method. SAS 9.4 was used to calculate the AAIRs. Maps were created using ArcGIS v.10.6 software. Statistical significance was assumed at $p < 0.05$. Examining the spatial pattern of cervical cancer AAIRs is critical to government efforts to understanding and targeting cervical cancer.

STATISTICAL METHODS

Global spatial autocorrelation - Moran's I

Global spatial autocorrelation - Moran's I used to assess the overall spatial patterns of cervical cancer in Iraq. In other words, global Moran's I measures the spatial autocorrelation of districts and the cervical cancer AAIRs simultaneously. The global index of spatial autocorrelation is defined as⁹:

$$I = \frac{n \sum_i \sum_j W_{ij} (X_i - \bar{X})(X_j - \bar{X})}{\sum_i \sum_j W_{ij} (X_i - \bar{X})^2}$$

Where:

X_i and X_j = the AAIRs of cervical cancer for districts i and j ;

$\bar{X}$ = the average of AAIRs of cervical cancer for the districts in the study area;

W_{ij} = the element of spatial weight matrix between district i and district j ; and

n = the total number of districts observed (a total of 83 districts were observed).

A value for I that is significantly greater than 1, a strong positive spatial autocorrelation, indicates a clustered pattern (i.e., similar cervical cancer AAIRs founded together). The value $I = 0$ indicates that the cervical cancer AAIRs was randomly distributed in the study area, and a value for I that is significantly less than 1, a strong negative spatial autocorrelation, indicates a dispersed pattern (i.e., nearby districts have very different cervical cancer AAIRs)¹⁰.

Getis-Ord G_i^* statistic

Global spatial autocorrelation was applied to determine whether the feature locations and feature attributes are relevant, but it cannot precisely identify where such attributes are clustered. Thus, we used Getis-Ord G_i^* statistics to detect different cold spots, hotspots, and high risk across Iraq that represent clusters of districts with significantly low or high AAIRs

cervical cancer. The Getis-Ord G_i^* index calculated as follows¹¹:

$$G_i^* = \frac{\sum_{j=1}^n W_{ij} X_j - \bar{X} \sum_{j=1}^n W_{ij}}{S \sqrt{\frac{n \sum_{j=1}^n W_{ij}^2 - (\sum_{j=1}^n W_{ij})^2}{n-1}}}$$

Where:

X_i and X_j the AAIRs of cervical cancer for districts i and j ;

$\bar{X}$ = the average of AAIRs of cervical cancer for districts in the study area;

W_{ij} = the element of spatial weight matrix between district i and district j ;

n = number of districts; and

S = the standard deviation of the AAIRs of cervical cancer in the study area.

The Getis-Ord G_i^* tool creates a z-score and p-value for every district, where $z > 1.96$ and ($p < 0.05$) indicate the stronger the intensity spatial clustering of the hotspot, and $z < -1.96$ with ($p < 0.05$) indicate the stronger the intensity spatial clustering of the cold spot. A z score near zero indicates no apparent spatial clustering¹¹.

The Anselin Local Moran's I

The local Moran I statistic indicates the similitude of a district comparative with its neighbors. As a result, in neighborhoods where both the district and its neighbors have high AAIRs, the Local Moran statistic will be positive demonstrating that the specific district is similar (i.e., 'high'). Similarly, in neighborhoods where both the district and its neighbors have low AAIRs, the Local Moran statistic also will be positive demonstrating that the district is similar to its neighbors (i.e., 'low'). When the Local Moran statistic is positive, this is an indicator of similarity, not the absolute value of the intensity variable¹².

The Anselin Local Moran's I statistic delineates significant spatial clusters of districts with low or high AAIRs as well as spatial outliers. Clusters of districts with high AAIRs and their neighbors who have high AAIRs (high-high) were regarded as "hotspots". Similarly, clusters of districts with low AAIRs and their neighbors who have low AAIRs (low-low) were regarded as "cold spots".

Conversely, the local Moran's I delineates districts with higher AAIRs while the neighbors have lower AAIRs (high-low), as well as districts with lower AAIRs while the neighbors have higher AAIRs (low-high). The Anselin Local Moran's I is defined as¹³:

$$I_i = \frac{(x_i - \bar{x}) \sum_j w_{ij} (x_j - \bar{x})}{S^2}$$

Where:

x_i = the AAIRs of cervical cancer for the i th district;

$\bar{x}$ = the average of AAIRs of cervical cancer for the districts in the study area;

x_j = the AAIRs of cervical cancer for the j th district;

w_{ij} = the element of spatial weight matrix between district i and district j ;

n = number of districts; and

S = the standard deviation of the AAIRs of cervical cancer in the study area.

RESULTS

Descriptive analysis

From 2010 to 2015, 1037 cervical cancer cases (except the Kurdish region) registered in ICR, accounting for approximately 1.63% of the total female cancer cases in Iraq. Cervical cancer is the most common type of cancer among females in Iraq. The AAIRs of cervical cancer was (3.52/100,000) with the highest rate in 2014 (3.80/100,000). Cervical cancer incidence was highest (8.21/100,000) in the age group of 60-69 years old (Table 1, Figure 2). Of the 83 total Iraq districts, 699 (67.40%) incidences occurred in 29 districts, and the remaining 338 (32.60%) in 54 districts. The five districts with the highest ASIRs of cervical cancer were Rissafa with 7.26/100,000, AL-Sadir with 7.23/100,000, AL-Hilla with 7.06/100,000, AL-Mahmoodiya with 5.30/100,000, and AL-Ammarah with 5.01/100,000 (Figure 3). Mapping the incidence

rates revealed that the districts with the lowest cervical cancer rates were those with relatively low population densities.

Table 1: Age-specific incidence rates (per 100,000) by age group in Iraq during the period 2010-2015

Age group	ASIRs
20-29	0.16
30-39	0.93
40-49	4.00
50-59	6.99
60-69	8.21
70-79	7.48
80+	4.93

Figure 2: Age-specific incidence rates (per 100,000) by age group per year in Iraq during the period 2010-2015

Trend

The joinpoint regression model indicated that the AAIRs of cervical cancer have an insignificant raised trend with an APC of 2.58% between 2010 and 2015 (Figure 4). The APC of cervical cancer age-specific rates has significantly risen for the age groups 60-69 only (APC=11.93%, $P=0.01$; 95% CI= 3.5% to 21.0%) (Table 2).

Figure 3: The geographical distribution of cervical cancer incidence (per 100,000) by districts in (2010-2015)

Table 2: Trend analysis for cervical cancer in Iraq by age group, 2010-2015

age groups	APC%	P-value	95% CI	
			Lower	Upper
20-29	-9.71	0.142	-22.7	5.5
30-39	-13.04	0.102	-27.6	4.5
40-49	-3.01	0.519	-14.0	9.3
50-59	-0.69	0.899	-13.8	14.5
60-69	11.93*	0.016	3.5	21.0
70-79	6.31	0.082	-1.2	14.4
80+	12.40	0.104	-3.7	31.2

Figure 4: Joinpoint analyses of the AAIRs of cervical cancer incidence in Iraq, 2010-2015. APC, Annual Percentage Change.

Spatial autocorrelation

The global spatial autocorrelation analyses (Global Moran's I) of cervical cancer incidence showed significant clusters for the years 2010 to 2015 in the observed 83 districts (Moran's $I = 0.250, z = 3.85, p < 0.01$), which indicated that incidence rates of cervical cancer were strongly

spatial clustered. Throughout Iraq, districts with similar cervical cancer rates tend to cluster closely together than we would expect by random chance for the years 2010 to 2015.

Hot and cold spots - Getis - Ord G_i^*

To recognize the location of a cluster of districts with the high incidence rate of cervical cancer, namely hot spots of cervical cancer incidence, the Getis-Ord G_i^* statistic was done for cervical incidence of 83 districts from 2010 to 2015 (Figure 5). Four clusters were identified, three hotspots (high incidence–high incidence clusters) and one cold spot (low incidence–low incidence clusters). Cold spots clustered in Al-Anbar province (Rawa and Al-Kaim districts). Hotspots of cervical cancer incidence clustered in Baghdad (Al-Karkh, Al-Risafa, Al-Adhamiya, Al-Sadir, and Al-Mada'in districts), Diyala (Baquba district), Babil (Al-Hilla, Al-Mussayab, and Al-Mahaweel districts), Al-Najaf (Al-Najaf and Al-Kufa districts), Karbala (Al-Hindiya district), and Basrah provinces (Abu Al-Khaseeb district).

Figure 5: Hot and cold spots of cervical cancer ASIRs in Iraq (2010 to 2015).

Anselin Local Moran's I- Spatial outliers

The district-level Anselin Local Moran's *I* measures for cervical cancer incidence were computed, and the significant cluster (high- high, low-low, high-low, and low- high) is shown in Figures 6. The high-high type indicates clustering of cervical cancer incidence, whereas the low-low type indicates clustering of cervical cancer incidence. The significant hotspots and cold spots detected by the Getis Ord *G**statistic were confirmed by Anselin Local Moran's *I* statistic. Hotspots were seen in Baghdad (Al-Karkh, Al-Risafa, Al-Adhamiya, Al-Sadir, and Al-Mada'in districts), Diyala (Baquba district), Babil (Al-Mussyab and Al-Mahaweel districts), Al-Najaf (Al-

Kufa district), Karbala (Al-Hindiya district), and Basrah provinces (Abu Al-Khaseeb and Al-Zubair districts). Cold spots appeared in Al-Anbar (Rawa, Al-Kaim, and Heet districts), Diyala (Al-Khalis district), Nineveh (Al-Mosul district), and Maysan provinces (Qalat Saleh). There were 3 districts (Al-Ramadi, Haditha, and Tikrit districts) identified as the high-low category of a spatial outlier, where cervical cancer AAIRs were high but were surrounded by districts with low AAIRs. Conversely, there was one district (Abu-Graib) identified as the low-high category of a spatial outlier, where cervical cancer AAIR was low but was surrounded by districts with high AAIRs.

Figure 6: Clusters and spatial outliers in AAIRs of cervical cancer (2010-2015).

DISCUSSION

In this study, we investigated geographic variation in the cervical cancer rates in Iraq using the 2010-2015 Iraqi Cancer Registry Database. To our knowledge, in Iraq, this is the first study to explore geospatial patterns of cervical cancer in

Iraq applying three techniques of spatial statistics. Global spatial autocorrelation (Moran's *I*) was applied to examine the spatial similarity across districts regarding cervical cancer AAIRs. Two Local spatial autocorrelations to investigate clusters of districts with low or high AAIRs, the Getis-Ord *G** statistic to investigate hot and cold

spots, and the Anselin Local Moran's *I* statistic to investigate spatial outliers.

The AAIrS of cervical cancer are relatively low in Iraq and the Middle East countries. The AAIrS of cervical cancer in Iraq (except three Kurdish provinces) was 3.521/100,000 population during 2010-2015, with a peak of (9.25/100,000) in the age group of 60-64 years old. Compared with the AAIrS in Iraq, the most recent study of cervical cancer incidence among nationals of the Gulf Cooperation Council States during 1998-2012 showed higher AAIrS (per 100,000 female population) in the Gulf Cooperation Council (4.5), United Arab Emirates (6.4), Qatar (6.4), Oman (5.3), and Bahrain (4.1)¹⁴. Compared to the other countries in the Middle East, Iraq has the highest AAIrS of cervical cancer than that in Saudi Arabia (1.9) and Kuwait (2.6) during 2008-2012, Jordan (2.0) during 2000-2013, and Iran (2.14) during (1990-2016)¹⁵. The GLOBOCAN 2020 estimates of incidence (AAIrS per 100,000 female population) showed that Iraq has incidence lower than the global incidence rate (13.3) and lower than that in Eastern Africa (40.1), Melanesia (28.3), South America (15.4), South-Eastern Asia (17.8), Eastern Asia (10.8), Northern America (6.2), Australia/New Zealand (5.6), and Western Asia (4.1)².

During the study period, incidence rates for cervical cancer increased insignificantly. Our analysis shows a statistically significant increase in incidence in the age group 60-69 years (this result is consistent with that reported by Hassan et al.¹⁶), while no significant changes were reported in the other age groups.

We identified spatial high-risk clusters for incidence. The cluster was mainly located in the center of Iraq (Baghdad, Najaf, Kerbala, and Babil provinces), the central-eastern part of Iraq (Diyala province), and the southern part of Iraq (Basrah province). While the provinces in northern and northeastern parts of Iraq, as well as the western province, had relatively lower AAIrS from cervical cancer. This result is consistent with that reported by Ameen et al.¹⁷. In this work, most of 488 patients with cervical carcinoma were referred to Radiotherapy and Nuclear Medicine Hospital in Baghdad for chemotherapy/radiotherapy in 1999-2009 were from Baghdad, Basrah, Babil, Messan, and Al-Najaf and the lowest from the North of Iraq. However, within those provinces generally

classified as having low or high AAIrS, there is a large variability at the province level.

However, knowing the reasons for the geographical difference in cervical cancer incidence in Iraq is beyond the scope of this article. The causes of this geographic pattern of cervical cancer in Iraq are unknown. According to Hull et al.¹⁸, a persistent infection with the sexually transmitted human papillomavirus is the most common cause of cervical cancer. However, other factors that lead to the prevalence of cervical cancer include geography, social status, traditional procedures, healthcare availability, screening levels, smoking and HIV co-infection, and the use of oral contraceptives. In Iraq, A study by Hassan et al.¹⁶ showed that usage of oral contraceptives and chlamydia infection is the most risk factor for cervical cancer. Al Niyazee et al.¹⁹ have found a higher prevalence of invasive squamous cervical cancer and cervical intraepithelial abnormality. Another study showed a considerable relationship between the histological outcome of the patient and persistent HPV infection²⁰. Ameen et al.¹⁷ showed that most cases of patients with carcinoma of the cervix in Iraq in late-stage due to the absence of a screening program. Another explanation for higher incidences in some districts may be because oncology centers are located in the provinces for these districts, and the cases arising in the province are registered, whereas other provinces do not fully record cases. However, the causes behind the higher incidences in some districts should be investigated further.

CONCLUSION

We identified spatial high-risk clusters for incidence. The cluster was mainly located in the center of Iraq (Baghdad, Najaf, Kerbala, and Babil provinces), the central-eastern part of Iraq (Diyala province), and the southern part of Iraq (Basrah province). While the provinces in northern and northeastern parts of Iraq, as well as the western province, had relatively lower AAIrS from cervical cancer. We observed an insignificant increasing trend during the study period.

ACKNOWLEDGMENTS

We would like to express our thanks to the staff of the Iraqi Cancer Board-Ministry of Health for their effort in providing data access. We are grateful to the University of Mosul, for supporting our work.

CONFLICT OF INTEREST

We declare that we have no conflicts of interest

to disclose regarding this manuscript.

FUNDING

This manuscript received no specific grant from any funding agency in the public or commercial sectors.

REFERENCES

1. Arbyn M, Weiderpass E, Bruni L, et al. Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. *Lancet Glob Health*. 2020; 8(2):e191-203.
2. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209-49.
3. Ibp I. Iraq country study guide, Volume 1. Strategic information and developments.
4. <https://library.wur.nl/WebQuery/wurpubs/fulltext/464098>
5. Su SC, Kanarek N, Fox MG, et al. Spatial analyses identify the geographic source of patients at a National Cancer Institute Comprehensive Cancer Center. *Clin. Cancer Res*. 2010;16(3):1065-72.
6. Ruankaew N. GIS and epidemiology. *J. Med. Assoc. Thai. = Chotmai het thangphaet*. 2005;88(11):1735-8.
7. Boscoe FP, Ward MH, Reynolds P. Current practices in spatial analysis of cancer data: data characteristics and data sources for geographic studies of cancer. *Int. J. Health Geogr*. 2004;3(1):28.
8. Annual Statistical Report 2015. Planning Directorate, Ministry of Health/Environment, Republic of Iraq 2016: 4-5.
9. Wong DW. Statistical analysis of geographic information with ArcView GIS and ArcGIS, 2005.
10. Anselin L. Local indicators of spatial association—LISA. *Geogr. Anal*. 1995;27(2):93-115.
11. Khan D, Rossen LM, Hamilton BE, et al. Hot spots, cluster detection and spatial outlier analysis of teen birth rates in the US, 2003-2012. *Spat. Spatio-temporal Epidemiol*. 2017;21:67-75.
12. Levine N. Hot spot analysis of zones. N Levine, CrimeStat: Spatial Statistics Program for the Analysis of Crime Incident Locations, Version. 2013;4:242960-95.
13. E.S.R. Institute. ArcGIS desktop: release 10. Redlands CA: Environmental Systems Research Institute; 2011.
14. Alkhalawi E, Al-Madouj A, Al-Zahrani A. Cervical Cancer Incidence and Trends among Nationals of the Gulf Cooperation Council States, 1998-2012. *Gulf J. Oncol*. 2019;1(31):7-13.
15. Riahi S, Mokhtari AM, Vali M, et al. Incidence and mortality rate of cervix cancer in Iran from 1990 to 2016: A systematic review and meta-analysis. *J. contemp. med. sci*. 2019;5(1):1-7.
16. Hassan MR, Gatea AA, Hassan HR. Prevalence of cervical cancer and associated factors among women in Baghdad/Iraq. *World J Pharm Res*. 2018;7(11):178-86.
17. Ameen NS, Helmi ZR. The characteristics women with cervical cancer referred for radiotherapy and/or chemotherapy. *Iraqi Postgrad Med J*. 2013;12:321-8.
18. Hull R, Mbele M, Makhafole T, et al. Cervical cancer in low and middle-income countries. *Oncology Letters*. 2020;20(3):2058-74.
19. Al Niyazee AA, Abedalrahman SK, Saleh LA. Prevalence of cytological abnormality of cervical papanicolaou smear. *Middle East J. Fam. Med*. 2019;7(10):16.
20. Abdul-Samad MN, Kandala NJ. The molecular detection of HPV infection in samples of Iraqi women with abnormal cervical smears. *Iraqi Journal of Science*. 2018;1995-2004.