Geospatial Health 2023; volume 18:1158

Spatial clustering of colorectal cancer in Malaysia

Sharifah Saffinas Syed Soffian,[1] Azmawati Mohammed Nawi,[1] Rozita Hod,[1] Khairul Nizam Abdul Maulud,[2,5] Ahmad Tarmizi Mohd Azmi,[2] Mohd Hazrin Hasim Hashim,[3] Huan-Keat Chan,[4] Muhammad Radzi Abu Hassan[4]

[1]Department of Community Health, Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur; [2]Earth Observation Centre, Institute of Climate Change, Universiti Kebangsaan Malaysia, Bangi; [3]Insitute for Public Health, National Institute of Health, Bandar Setia Alam, Shah Alam; [4]Clinical Research Center, Sultanah Bahiyah Hospital, Alor Setar; [5]Department of Civil Engineering, Faculty of Engineering and Built Environment, Universiti Kebangsaan, Malaysia

Abstract

The rising trend of Colorectal Cancer (CRC) incidence has become a global concern. Spatial determinants may play an important role as suggested by registered geographical variations of CRC incidence. The current study was designed to identify the spatial distribution pattern of CRC at the neighbourhood level in Malaysia by geocoding the addresses of CRC cases registered by the National Cancer Registry between 2010 and 2016. Cluster analysis was performed to examine the spatial dependence of CRC cases as well as group differences with regard to socio-demographic characteristics. Identified clusters were categorized into urban and rural areas based on the population background. Most of the 18,405 individuals included in the study were male (56%) and people aged between 60 and 69 years (30.3%). Among patients with available information on their CRC stage, 71.3% presented for care late (at stages III or IV of the disease). The Malaysian states shown to have CRC clusters were Kedah, Penang, Perak, Selangor, Kuala Lumpur, Melaka, Johor, Kelantan and Sarawak. Spatial autocorrelation detected significant clustering (Moran's $I = 0.244$, $p < 0.01$, Z-score >2.58). The CRC clusters in Penang, Selangor, Kuala Lumpur, Melaka, Johor and Sarawak occurred in urbanized areas, while those in Kedah, Perak and Kelantan were in rural areas. Factors associated with urban CRC clusters as shown by Odds Ratio (OR) included late-stage presentation (1.27, CI 1.15-1.41); post-mortem diagnosis (0.82, CI 0.76-0.89); and adenocarcinoma type of the cancer (0.81, CI 0.67-0.98). We conclude that the presence of several clusters in urbanized and rural areas implies the impact of ecological determinants at the neighbourhood level. These findings can be used to guide the policymakers in resource allocation and cancer control.

Correspondence: Azmawati Mohammed Nawi, Department of Community Health, Faculty of Medicine, Universiti Kebangsaan Malaysia 56000 Kuala Lumpur, Malaysia.
E-mail: azmawati@ppukm.ukm.edu.my

Key words: colorectal cancer; spatial cluster; geographical variation; ecology; Malaysia.

Acknowledgements: the Authors would like to thank the Universiti Kebangsaan Malaysia (UKM) for funding this study (FF-2021-121). Thank you to PLAN Malaysia for the input of boundaries data. We also thank the team for their commitment and tireless efforts in ensuring that manuscript was well executed.

Conflict of interest: the Authors declare no conflict of interest.

Funding: none.

Received for publication: 28 September 2022.
Revision received: 14 February 2023.
Accepted for publication: 14 February 2023.

*Geospatial Health 2023; 18:1158
doi:10.4081/gh.2023.1158*

Introduction

Risk factors identified for Colorectal Cancer (CRC) in previous studies include obesity, physical inactivity, family history of CRC, low fibre-dietary intake, old age and smoking (Chazelas *et al.*, 2019; Gibson *et al.*, 2020; Gram *et al.*, 2020; Li *et al.*, 2021). A few diseases, such as inflammatory bowel disease and Lynch syndrome (Brouwer *et al.*, 2017; Pesola *et al.*, 2020) also warrant screening for CRC. Although there is a positive association between these identified risk factors and CRC, the selective nature of individual-level determinants limits the extent by which policy action changes can take place.

Whenever possible, primary prevention should be the key strategy to contain the risk factors of a disease. People living in the same neighbourhood interact with each other and are likely to share a similar exposure, behaviour and lifestyle (Goshayeshi *et al.*, 2019; Soffian *et al.*, 2021). Cancer clusters are often linked to occupational exposure and to chemical pollutants, which has led to restrictive legislation in some cases (Pang *et al.*, 2020; Um *et al.*, 2020), but the potential relationship between residential neighbourhood and the clustering pattern of CRC has not been widely explored (Andrilla *et al.*, 2020; Halimi *et al.*, 2020).

Mapping could provide insights into the geographical variations in CRC and assist surveillance and control of the disease. In Low- and Middle-Income Countries (LMICs) where resources are limited, the identification of spatial clusters of CRC allows stakeholders to focus on areas requiring more attention than non-affected, adjacent regions, thus resulting in more cost-effective interventions.

In Malaysia, CRC is the most common cancer in males (National Cancer Institute, 2018). Age-Standardized incidence Rates (ASRs) of 14.6 per 100,000 men and 11.1 per 100,000 females have been recorded (Chandran *et al.*, 2020). Diagnosis at late stages occurred in more than two-thirds of all Malaysians living with CRC between 2007 and 2016 (National Cancer Institute, 2018). Despite the free-of-charge screening services offered in all public primary healthcare settings since 2014, the annual uptake remains below 1% (Chandran *et al.*, 2020). The under-diagnosis of CRC is partly due to lack of public awareness and ineffective intervention schemes that leave many in high-risk groups unattended. As information of the spatial epidemiology of CRC in Malaysia is limited, this study aimed to identify the local geographic patterns of CRC between 2010 and 2016.

Materials and Methods

Study area and data collection

This study concerns the CRC distribution in Malaysia, an upper middle-income country located in the south-eastern part of Asia. The country covers an area of approximately 330, 534 km^2 (Department of Survey & Mapping Malaysia, 2017) and consists of Peninsular Malaysia and East Malaysia, which are separated by the South China Sea. Land borders include Thailand, Singapore, Indonesia and Brunei. There are 13 states and three federal territories where East Malaysia includes one federal territory (Labuan) and two states (Sabah and Sarawak), while there are two federal territories (Kuala Lumpur and Putrajaya) and 11 states in Peninsular Malaysia.

A cross-sectional study was conducted based on CRC cases registered by the National Cancer Registry (NCR) in Malaysia between 2010 and 2016. The address for each CRC case was geocoded and aggregated to the "mukim", the smallest administrative unit in Malaysia. The NCR is a nationwide population-based registry belonging to the Ministry of Health, which traces all CRC cases notified by both public and private hospitals through a manually operated reporting system since 2007 (Azizah *et al.*, 2019). All residents in Malaysia diagnosed with cancers in the colon and/or rectum (ICD-10 codes: C18-C20) were included in the analysis. There were 18,552 CRC cases in Malaysia between 2010 and 2016; however 147 cases were excluded from spatial analyses due to incomplete residential address information. Out of that figure, 14,701 cases were identified in the urban-rural clusters and further analysed for associated factors.

Base maps construction

The base map of Malaysia was constructed using the official administrative cartography obtained from the Department of Town and Country Planning (PLAN Malaysia), corresponding to the central year of the analysis period. The residential address for each individual case was geocoded and categorized by state and mukim. Another map with similar boundaries containing information regarding land use was constructed and used as an overlay. Each state was named in the map to facilitate the description of the results and the discussion. All data were integrated in the World Geodetic System 1984 (WGS) map projection. ArcGis 10.8.1 software (ESRI, Redlands, CA, USA) was used for mapping and data visualization.

Population

Information on the demographics and vital status of the population was obtained via an online database from the Department of Statistics Malaysia (DOSM) based on data collected from the 2010 Census. It included total population, age groups, gender information, Gross Domestic Product (GDP) per capita by state and the percentage of individuals below the poverty line (monthly income of RM980 (USD225) as defined by the DOSM). Neighbourhoods with populations of ≥10 000 people with at least 60% of the population aged ≥15 years engaged in non-agricultural activities are classified as urbans (DOSM, 2019). Rural areas are defined as non-urban locations comprising all types of settlements, such as villages, small towns and populous congregations of less than 10,000 people with agricultural characteristics and rich in natural resources (PLAN Malaysia, 2023).

Statistical analysis

The ASRs for CRC were based on the total population in each state of Malaysia, adjusted to sex and age-group, respectively. A multivariate regression model considering CRC urban-rural clustering as the dependent variable was created. The independent variables consisted of age (<50 years/≥50 years old) at diagnosis; sex (male/female); vital status at diagnosis (alive/dead); stage (early stage/late stage/unknown); and histological type (adenocarcinoma/other). The classification of CRC follows the tumour, node and metastasis (TNM) staging, where stage I refers to the invasion of primary tumour through the *muscularis mucosa* and *muscularis propria* of the intestinal wall; stage II to primary tumour involvement of pericolorectal tissues or invasion of other adjacent organs or structures; stage III invasion and involvement of local lymph nodes; and stage IV metastasis to one or more other sites in addition to the other pathologies mentioned (Weiser, 2018).

The spatial CRC information studied involved all states in Peninsular and East Malaysia and were based on polygonal data. Natural-break classification with three classes was used for the thematic maps. The cut-off for low case density was ≤56 cases, moderate density was defined as numbers between 57 and 234, whereas high-density areas referred to >235 cases within a mukim. We minimized the average deviation of each class from the class mean as much as possible, while also maximizing the variance between classes.

Non-geocoded CRC cases were excluded from the spatial analysis. Socio-demographics and clinical data for any CRC case identified as belonging to urban-rural clusters were analysed using chi-square and multivariate logistic regression analyses. Spatial autocorrelation was measured with Moran's *I*. Data analysis was performed using the SPSS version 21.0 for Windows (https://www.ibm.com). Factors associated with any urban-rural cluster found were explored using forward stepwise logistic regression analysis (Low *et al.*, 2020), with the results presented as odds ratios (ORs) and 95% confidence intervals (CIs). The final model was also tested for interaction and multicollinearity and confirmed with the Hosmer-Lemeshow goodness-of-fit test (Petersen, 1996).

We used Kernel Density Estimation, which is widely used for the detection of clustering pattern in the cancer epidemiology field by accounting for the average location over a certain number of points, estimating density and factoring in smoothing parameters to obtain a useful view of study areas (Kelsall & Diggle, 1995). The Kernel functions are symmetric around zero and integrate to one. The smoothed risk surfaces were determined based on the reference grids made to cover the study area. The smoothed intensity was calculated by the difference of the distances between each point on the reference grid and the case locations. The intensity of points at each grid point was estimated using the quartic (biweight) kernel type for symmetrical patterns. Fixed bandwidths were applied to control the overall patterns of the underlying spatial distribution. An initial bandwidth was selected based on the average nearest distance between points and cases. Analyses were performed with varying bandwidths using direct optimization to find the bandwidth that minimizes the estimated mean square error. Cross-validation resulted in relatively small bandwidths because of the large sample size. Considering the urban-rural classification with delineation at the state-level for comparison, a 10-km radius was selected as the initial bandwidth of the kernel, using a range from 0.5 to 50 km. Results of subsequent searches over the bandwidth range were compared and the 0.5-km radius bandwidth was chosen to avoid both over-smoothing and under-smoothing the density surface.

Getis-Ord Gi statistics (Getis & Ord, 1992; Ruktanonchai *et al.*, 2014) were used to identify spatial CRC clusters. A high score on this index with a low *p*-value indicates clustering. We analyzed the features of each neighbour mukim looking for clustering tendencies. A fixed 3-km distance band was decided on to examine the underlying spatial relationships based on data skewness whereby a minimum of eight neighbours are recommended for reliable Z-scores. Neighbouring features inside the specified critical distance were given a weight of one and cluster *p*-values were adjusted for multiple testing using the False Discovery Rate (FDR) correction (http://desktop.arcgis.com). The results from Kernel Density Estimation and Getis Ord Gi showed similar spatial patterns of CRC distribution across urban-rural disparities.

Results

The number of newly diagnosed CRC cases over the 7-year study period showed a gradual rising trend with a sudden rise from 2014 onwards (Figure 1); the lowest increase was recorded in 2011 (12.3%) and the highest in 2016 (17.1%). The mean age of people living with CRC at the point of diagnosis was 61.8 years with a standard deviation (SD) of ±12.7. Individuals in the 60-69 years age group accounted for almost one-third (30.3%) of the CRC population and the CRC incidence was higher in men. Of the cases with available stage information, more than 60% were diagnosed at a late stage (III and IV). Newly diagnosed CRC cases with histologically confirmed adenocarcinoma type represented 89.4% of the total number of cases. Additionally, only 36.1% of reported CRC patients were alive at the time of diagnosis (Table 1).

The spatial distribution of the ASR for CRC in both males and females are shown in Figures 2 and 3. The highest ASRs was recorded in Penang State, with 23.2/100,000 for males and 18.7/100,000 for females. Meanwhile, Perak State accounted for the lowest ASR for males with 10.9/100,000, whereas Labuan Federal Territory accounted the lowest for females at 2.8/100,000. Despite adjustment for age and sex, the incidence of CRC in the urban areas was found to be persistently higher than in the rural areas.

Geographical variations in the CRC incidence were observed in Malaysia. The spatial autocorrelation showed a significant clustering pattern with Moran's *I*: 0.244 (p <0.01, Z-score >2.58). States with CRC clusters included Kedah, Penang, Perak, Selangor, Kuala Lumpur, Melaka, Johor, Kelantan and Sarawak (Figures 4 and 5). Eight spatial clusters of CRC were seen in Peninsular Malaysia and only one in East Malaysia. The CRC clusters in Penang, Selangor, Kuala Lumpur, Melaka, Johor and Sarawak were located in urbanized areas, while those in Kedah, Perak and Kelantan were in rural areas.

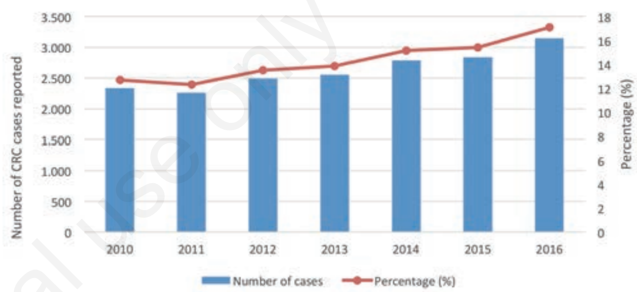

Figure 1. Trend of colorectal cancer incidence in Malaysia 2010 – 2016.

Figure 2. Spatial distribution of the age-standardized incidence rate (ASR) for CRC in Malaysian males per 100,000 at the state level 2010-2016.

Figure 3. Spatial distribution of the Age-Standardized incidence Rate (ASR) for CRC in Malaysian females per 100,000 at the state level 2010-2016.

High CRC incidence is commonly linked to high indices of socioeconomic status (Rabeneck *et al.*, 2020). In the urbanized state areas, where high-density population areas mix with average-density population areas, such as 7,365 and 1,664 people per km^2, respectively, and where the economy is industry-driven, western lifestyles have been rapidly adopted. The GDP per capita by states in the urban areas are up to ten times higher than in the rural areas (DOSM 2019), and a variety of services, including food and beverages, are available. While the reported poverty level in the urban areas range between 2 and 8%, they are much lower than in the rural areas (10-12%) (DOSM 2019). This has an impact on the quality of life and the lifestyle of many urban dwellers should be of concern in relation to CRC. Nevertheless, the study identified two distinctive geographical features of spatial CRC cluster in Malaysia (Figure 6). The summary of characteristics for respective urban and rural CRC clusters is presented in Table 2.

Following the comparison of demographics profile between CRC clusters in the urbanized and rural areas, the study observed statistically significant differences with regard to the status of CRC patients at diagnosis (Table 3). The odds of a post-mortem positive diagnosis were 18% less likely in urban clusters (OR: 0.82, 95%CI 0.76, 0.89) compared to those living in the rural clusters. However, CRC patients in the urban clusters were 1.27 times more likely to present with late stages of the disease (OR: 1.27, 95% CI 1.15,1.41) and 85% with unknown stages (OR: 1.85, 95%CI 1.67,2.06). In fact, 19% of people living with CRC in the urban

Table 1. Distribution of CRC cases in Malaysia with associated variables.

Characteristic		CRC cases (out of 18,405) No.	%
Year	2010	2,333	12.7
	2011	2,263	12.3
	2012	2,489	13.5
	2013	2,551	13.9
	2014	2,787	15.1
	2015	2,836	15.4
	2016	3,146	17.1
Age group	<50 years	2,959	16.1
	≥ 50 years	15,446	83.9
Gender	Male	10,351	56.2
	Female	8,054	43.8
CRC stage	I	862	4.7
	II	2,265	12.3
	III	3,601	19.6
	IV	4,174	22.7
	Unknown	7,503	40.7
Histological type	Adenocarcinoma	16,454	89.4
	Other	1,951	10.6
Status at diagnosis	Alive	6,615	35.9
	Dead	11,731	63.7
	Unknown	59	0.3

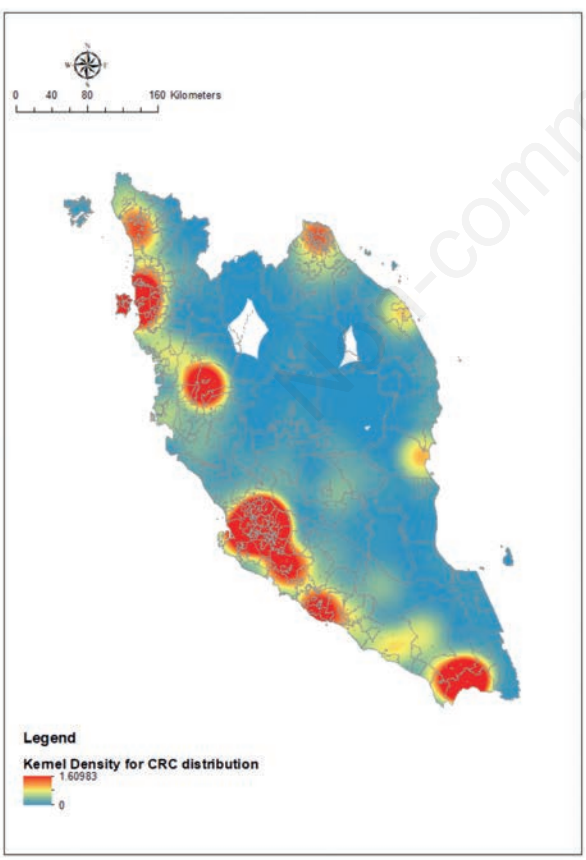

Figure 4. Heatmap showing the relative concentration of CRC cases in Peninsular Malaysia 2010-2016.

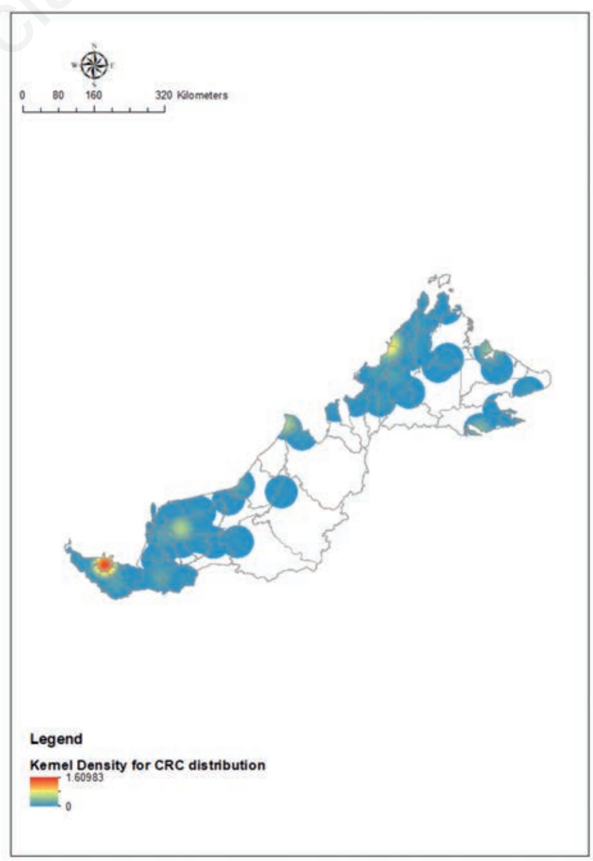

Figure 5. Heatmap showing the relative concentration of CRC cases in East Malaysia 2010-2016.

cluster were less likely to be diagnosed with histological type adenocarcinoma (OR: 0.81, 95%CI 0.67,0.98). The findings reflected the poor prognosis of CRC patients among the urban dwellers despite of readily available treatment facilities. Further studies that focus on the underlying factors influencing late-stage presentation at the specific areas may provide insight in understanding the matter. However, there was no statistically difference between age and sex on the one hand and the CRC cluster categories on the other.

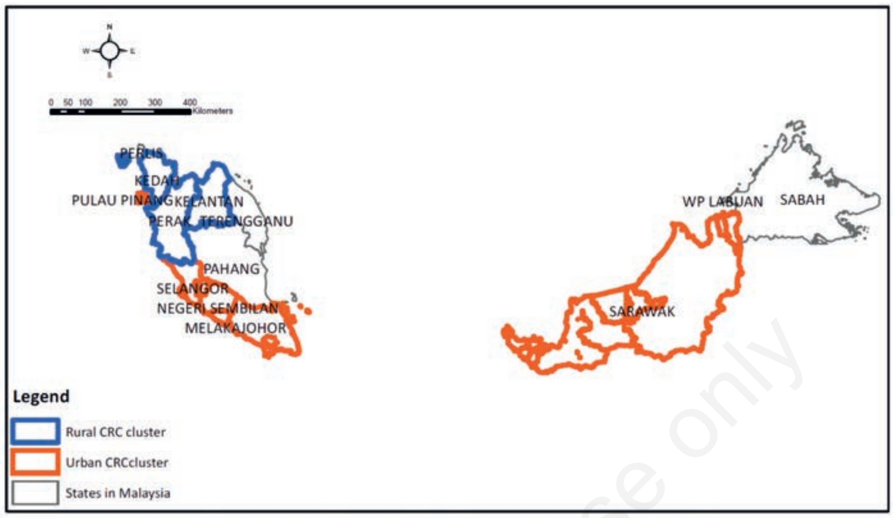

Figure 6. Distribution of urban-rural CRC clusters among the Malaysian states.

Table 2. Characteristics of CRC clusters found in Malaysia.

Cluster description[a]	Urban	Rural
States involved	Penang, Selangor, Kuala Lumpur, Melaka, Johor, Sarawak	Kedah, Perak, Kelantan
Population size x 1,000 (no.)	2,738.7-6,291.5	901.1-2,119.7
Population density (per km^2)	1,664-7,365	22-224
GDP[b] contribution to country (%)	9.7- 23.0	1.8-3.3
Economic type	Industry-based	Agricultural
Below poverty line (%)[c]	2-8	10-12

[a]DOSM 2019; [b]gross domestic product; [c]poverty line cut off at household monthly income below RM980 (USD 225).

Table 3. Association of population sociodemographics and the urban-rural CRC clusters*

Parameter	Crude OR	p-value	95% CI	Adjusted OR*	p-value	95% CI
Age group						
<50 years	1	-	-	-	-	-
≥50 years	1.03	0.56	0.93, 1.14	-	-	-
Sex						
Female	1	-	-	-	-	-
Male	1.06	0.10	0.98, 1.14	-	-	-
Status at diagnosis						
Alive	1	-	-	1	-	-
Dead	0.82	<0.05	0.76, 0.89	0.82	<0.05	0.76, 0.89
Stage						
Early	1	-	-	1	-	-
Late	1.28	<0.05	1.16, 1.42	1.27	<0.05	1.15, 1.41
Unknown	1.87	<0.05	1.69, 2.08	1.85	<0.05	1.67, 2.06
Histological type						
Adenocarcinoma	1.13	<0.05	0.99, 1.27	0.81	<0.05	0.67, 0.98
Others	1	-	-	1	-	-

*n=14,701 cases; OR, odds ratio; *adjusted OR calculated using forward stepwise in multiple logistic regression analysis.

Discussion

Evidence of an indirect influence of built environment in the aetiology for CRC is mounting (Soffian *et al.*, 2021; Tian *et al.*, 2018; Wray & Minaker, 2019). Although the most common attributes of the built environment explored include spatial accessibility, residential density, land use and green spaces, this study identified a higher degree of clustering in urban areas than in rural areas based on population density alone. The sudden rise from 2014 onwards reflects the initiation of opportunistic screening using immunochemical faecal occult blood test (iFOBT) in the majority of public primary care centres in Malaysia (Chandran *et al.* 2020).

CRC is predominantly reported in upper middle- to high-income countries and often associated with urbanization and increased economic status. The rising pattern of CRC incidence demonstrated in this study reflects an adaptation to new lifestyles following the move towards higher standards of living seen in a middle-income country like Malaysia. Based on spatial analysis, we observed a significant CRC clustering trend in many parts of the country. This is consistent with previous findings by localized CRC spatial studies which identified CRC clustering patterns in urbanized areas of Penang and Kuala Lumpur (Samat *et al.*, 2013; Shah *et al.*, 2014), characterized by high availability of public and private healthcare facilities offering CRC screening and diagnostic testing. That late-stage presentation was nearly 30% more likely reported in urban cluster highlights the alarming problem of late-stage presentation, which is the main concern. Indeed, that fact that more than half of the CRC cases presented with late stages of the disease (stages III and IV) does not reflect the timely treatment and effective screening efforts as evidenced in many developed countries (Shaukat *et al.*, 2021). Examination of the degree of accessibility to healthcare facilities and the level of expert requirement needed, particularly in highly CRC clustered areas, may provide a better understanding and thus serve policy makers with possible targeted strategies for early detection of the disease.

Low screening uptake and public awareness on CRC screening remains the challenging issue in many countries (Bujang *et al.*, 2021; Gimeno-García *et al.*, 2011; Sung *et al.*, 2019). Moreover, it indicates that health-seeking behaviour is a cross-cutting issue regardless of the economic background. In the presence of international and local CRC screening guidelines, preventive strategies should focus on targeted populations in specified geographical regions.

Adenocarcinoma was the most prevalent histological form of CRC observed in the study. However, CRC cases in urban clusters elsewhere have shown other types of colon cancer to be more likely linked to worse prognosis (Li e*t al*., 2019; Zhang *et al.,* 2022). Likewise, post-mortem diagnosis in urban clusters was 23% less likely than in other places. Provided that CRC is a complex and multifactorial disease, it is worth to explore the influence of ecological factors in urban areas compared to rural areas that possibly could influence cluster aggregation.

The steadily rising CRC incidence since 2010 in both sexes was predominantly seen in those older than 50 years. Although the ASRs for CRC in males was found to be typically higher than females, the interstate homogeneity could possibly relate to certain sex-dependent factors in the CRC pathophysiology of the latter. On the other hand, a recent molecular study of patients with advanced stage CRC has identified a novel modulating gene influential in CRC progression, specifically in females (Xu *et al.*, 2020). Similarly, Hasakova *et al.*, (2018) in their study revealed positive relationship between sex-dependent genetic factors and the prognostic outcome of CRC. While sex appears less significant for cluster development in urbanized areas in our study, inclusion of females is important in the risk stratification for screening eligibility.

Although this cross-sectional study design had a limited ability to explain the plausible relationship between CRC and the immediate ecological risk factors, the findings identified cluster patterns suggesting potential ecological risk factors in both the urban and rural areas. Another limitation is that the geocoding of CRC cases may not be completely accurate due to incomplete postal addresses. For cancer prevention and planning programmes, further research examining the influence of built environment and hotspots for CRC is warranted.

Conclusions

The presence of significant, strong clustering of CRC in urban and rural areas implies the potential influence of ecological determinants at the neighbourhood level. Identification of such factors provides insights for policymakers in the context of healthy settings and resource allocation.

References

Andrilla CHA, Moore TE, Man Wong K, Evans DV, 2020. Investigating the impact of geographic location on colorectal cancer stage at diagnosis: a national study of the SEER cancer registry. J Rural Health 36:316-25.

Azizah AM, Hashimah B, Nirmal K, Siti Zubaidah AR, Puteri NA, Nabihah A, Sukumaran R, 2019. Malaysia national cancer registry report 2012-2016.

Brouwer JGM, Makama M, Van Woudenbergh GJ, Vasen HFA, Nagengast FM, Kleibeuker JH, Kampman E, 2017. Inflammatory potential of the diet and colorectal tumor risk in persons with Lynch syndrome. Am J Clin Nutr 106:1287-94.

Bujang NNA, Lee YJ, Mohd Zain SAS, Aris JH, Md Yusoff FA, Suli Z, Abu Hassan MR, 2021. Factors associated with colorectal cancer screening via immunochemical fecal occult blood test in an average-risk population from a multiethnic, middle-income setting. JCO Glob Oncol 7:333-41.

Chandran A, Mustapha FI, Tamin NSI, Hassan MRA, 2020. Overview of colorectal cancer screening programme in Malaysia. Med J Malaysia 75:235-39.

Chazelas E, Srour B, Desmetz E, Kesse-Guyot E, Julia C, Deschamps V, Druesne-Pecollo N, 2019. Sugary drink consumption and risk of cancer: Results from Nutrinet-Santé prospective cohort. BMJ 366:l2408.

Department of Statistics Malaysia (DOSM). 2019. Available online at: https://www.dosm.gov.my/v1/index.php? r=home/community

Department of Survey and Mapping Malaysia. 2017. Available online at: https://www.jupem.gov.my/ms/peta-laman

ESRI ArcGis Desktop – ArcMap. http://desktop.arcgis.com/en/arcmap/ Accessed 04 Feb 2023.

Getis A, Ord JK. 1992. The analysis of spatial association by use of distance statistics. Geog Anal 24:189-206

Gibson DC, Prochaska JD, Yu X, Kaul S, 2020. An examination between census tract unhealthy food availability and colorectal cancer incidence. Cancer Epidemiol 67:101761.

Gimeno-García AZ, Quintero E, Nicolás-Pérez D, Jiménez-Sosa A, 2011. Public awareness of colorectal cancer and screening in a Spanish population. Public Health 125:609-15.
Goshayeshi L, Pourahmadi A, Ghayour-Mobarhan M, Hashtarkhani S, Karimian S, Dastjerdi RS, Eghbali B, 2019. Colorectal cancer risk factors in north-eastern Iran: A retrospective cross-sectional study based on geographical information systems, spatial autocorrelation and regression analysis. Geospat Health 14:219-28.
Gram IT, Park SY, Wilkens LR, Haiman CA, Le Marchand L, 2020. Smoking-related risks of colorectal cancer by anatomical subsite and sex. Am J Epidemiol 189:543-53.
Halimi L, Bagheri N, Hoseini B, Hashtarkhani S, 2020. Spatial analysis of colorectal cancer incidence in Hamadan Province, Iran: a retrospective cross-sectional study. Appl Spat Anal Policy 13:293-303.
Hasakova K, Vician M, Reis R, Zeman M, Herichova I, 2018. Sex-dependent correlation between survival and expression of genes related to the circadian oscillator in patients with colorectal cancer. Chronobiol Int 3: 1423-34.
Kelsall JE, Diggle PJ, 1995. Non-parametric estimation of spatial variation in relative risk. Stat Med 14:2335-42.
Li H, Boakye D, Chen X, Hoffmeister M, Brenner H, 2021. Association of body mass index with risk of early-onset colorectal cancer: systematic review and meta-analysis. Am J Gastroenterol 116:2173-83.
Low EE, Demb J, Liu L, Earles A, Bustamante R, Williams CD, Provenzale D, Kaltenbach T, Gawron AJ, Martinez ME, Gupta S, 2020. Risk Factors for Early-Onset Colorectal Cancer. Gastroenterology 159:492-501.
National Cancer Institute. 2018. Malaysian study on cancer survival (MySCan). National Cancer Institute, Ministry of Health Malaysia, Vol. 4.
Pang Y, Kartsonaki C, Guo Y, Chen Y, Yang L, Bian Z, Bragg F, 2020. Socioeconomic status in relation to risks of major gastrointestinal cancers in chinese adults: A prospective study of 0.5 million people. Cancer Epidemiol Biomarkers Prev 29:823-31.
Pesola F, Eloranta S, Martling A, Saraste D, Smedby KE, 2020. Family history of colorectal cancer and survival : A Swedish population-based study. J Intern Med 287: 723-33.
Peterson NJ. 1996. Evaluation of the Hosmer-Lemeshow global goodness-of-fit statistics for mixed variable logistic regression models. The University of Texas School of Public Health
PLAN Malaysia Department of Town and Country Planning. 2023. Available online at: https://www.planmalaysia.gov.my/
Rabeneck L, Chiu H and Senore C. 2020. International perspective on the burden of colorectal cancer and public health effects. Gastroenterology 158:447-52.
Ruktanonchai CW, Pindolia DK, Striley CW, Odedina FT, Cottler LB. 2014. Utilizing spatial statistics to identify cancer hot spots: a surveillance strategy to inform community-engaged outreach efforts. Int J Health Geogr 13:39.
Samat N, Knight A, Shattar A, Sulaiman Y, Manan AA, Weng CN, 2013. investigating geographic distribution of colorectal cancer cases: an example from Penang State, Malaysia. Asian Social Science 9:38-46.
Shah SA, Neoh HM, Rahim SSSA, Azhar ZI, Hassan MR, Safian N, Jamal R, 2014. Spatial analysis of colorectal cancer cases in Kuala Lumpur. Asian Pac J Cancer Prev 15:1149-54.
Shaukat A, Kahi CJ, Burke CA, Rabeneck L, Sauer BG, Rex DK, 2021. ACG clinical guidelines: colorectal cancer screening 2021. Am J Gastroenterol 116:458-79.
Soffian SSS, Nawi AM, Hod R, Chan HK, Hassan MRA, 2021. Area-level determinants in colorectal cancer spatial clustering studies: a systematic review. Int J Environ Res Public Health 18:1-26.
Sung JJ, Chiu HM, Jung KW, Jun JK, Sekiguchi M, Matsuda T, Kyaw MH, 2019. Increasing trend in young-onset colorectal cancer in Asia: More cancers in men and more rectal cancers. Am J Gastroenterol 114:322-29.
Tian Y, Li J, Zhou T, Tong D, Chi S, Kong X, Ding K, Li J. 2018. Spatially varying effects of predictors for the survival prediction of nonmetastatic colorectal cancer. BMC Cancer 18:1-14.
Um K, Park CS, Yoo C, Ahn YS, Kim M, Jeong KS, 2020. Risk factors including night shift work of colorectal polyp. Ann Occup Environ Med 32:e26.
Wray AJD, Minaker LM, 2019. Is cancer prevention influenced by the built environment? A multidisciplinary scoping review. Cancer 125:3299-311.
Weiser MR. 2018. AJCC 8th Edition: Colorectal Cancer. Ann Surg Oncol 25:1454-5.
Xu P, Richter J, Blatz A, Gärtner F, Alberts R, Azoitei A, Makori WA, 2020. Downregulation of ORP3 correlates with reduced survival of colon cancer patients with advanced nodal metastasis and of female patients with grade 3 colon cancer. Int J Mol Sci 21:5894.
Zhang Y, Chen Y, Huang J, Wu X, Tang R, Huang Q, Xu Y, Peng X, Fu K and Xiao S. 2022. Mucinous histology is associated with poor prognosis in locally advanced colorectal adenocarcinoma treated with postoperative first-line adjuvant chemotherapy: a systematic review and meta-analysis. Eur J surg Oncol 48:2075-81.