RESEARCH ARTICLE

Spatial Analysis of Colorectal Cancer Cases in Kuala Lumpur

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Abstract

Background: In Malaysia, data from the Malaysian Health Ministry showed colorectal cancer (CRC) to be the second most common type of cancer in 2007-2009, after breast cancer. The same was apparent after looking at males and females cases separately. In the present study, the Geographic Information System (GIS) was employed to describe the distribution of CRC cases in Kuala Lumpur (KL), Malaysia, according to socio-demographic factors (age, gender, ethnicity and district). Materials and Methods: This retrospective review concerned data for patients diagnosed with colorectal cancer in the years 1995 to 2011 collected from the Wilayah Persekutuan Health Office, taken from the cancer notification form (NCR-2), and patient medical records from the Surgical Department, Universiti Kebangsaan Malaysia Medical Centre (UKMMC). A total of 146 cases were analyzed. All the data collected were analysed using ArcGIS version 10.0 and SPSS version 19.0. Results: Patients aged 60 to 69 years accounted for the highest proportion of cases (34.2%) and males slightly predominated 76 (52.1%), Chinese had the highest number of registered cases at 108 (74.0%) and staging revealed most cases in the 3rd and 4th stages. Kernel density analysis showed more cases are concentrated up in the northern area of Petaling and Kuala Lumpur subdistricts. Spatial global pattern analysis by average nearest neighbour resulted in nearest neighbour ratio of 0.75, with Z-score of -5.59, p value of <0.01 and the z-score of -5.59. Spatial autocorrelation (Moran's I) showed clustering significant with p<0.01, Z score 3.14 and Moran's Index of 0.007. When mapping clusters with hotspot analysis (Getis-Ord Gi), hot and cold spots were identified. Hot spot areas fell on the northeast side of KL. Conclusions: This study demonstrated significant spatial patterns of cancer incidence in KL. Knowledge about these spatial patterns can provide useful information to policymakers in the planning of screening of CRC in the targeted population and improvement of healthcare facilities to provide better treatment for CRC patients.

Keywords: Spatial analysis - GIS - colorectal cancer - Kuala Lumpur

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Introduction

Colorectal cancer (CRC) is an important public health problem that is on the rise all over the world. Incidence rates are substantially higher in men than in women (American Cancer Society, 2011), where it is the third most common cancer in men (663,000 cases, 10.0% of the total) and the second in women (571,000 cases, 9.4% of the total). About 608,000 deaths from colorectal cancer are estimated worldwide, accounting for 8% of all cancer deaths, making it the fourth most common cause of death from cancer. Majority of the cases occur in developed regions. In the case for Malaysia, a rapidly developing country located in Southeast Asia, data from the Malaysian Health Ministry showed that CRC is the 2nd most common type of cancer from 2007-2009, about 12.6% from all cases, after breast cancer. The same trend is seen after looking at males and females cases separately where it is also the 2nd most common cancer in both sexes respectively (MOH, 2009).

Risk factors of CRC include inherent genetic factors and dietary habits. In genetic studies, DNA methylation and nucleotide synthesis of the 5,10-Methylene-tetrahydrofolate reductase (MTHFR) gene has been reported to play a role in the etiology of colorectal adenomas, where individuals with the MTHFR TT genotype (particularly the elderly) with low intakes of folate, vitamin B12, and vitamin B6 had an increased risk of the cancer (Ulrich et al., 1999). Another study found that single nucleotide polymorphisms (SNPs) in the 8q24 chromosomal region were associated with colorectal cancer susceptibility and therefore puts an individual at

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higher risk of developing colon cancer (Hutter et al., 2010). For dietary habits, macronutrients and micronutrients have been reported to enhance or inhibit carcinogenesis in the colon and rectum. High level sucrose intake with sedentary lifestyles (Slattery et al., 1997), consumption of red meat and processed meat (Norat et al., 2005; Larson and Wolk, 2006) were significantly associated with increased CRC risk, while fish and fiber intake were inversely associated with the disease (Bingham et al., 2003; Norat et al., 2005). As dietary habits are associated with socioeconomic status and also, to some extent, urbanization (Fukuda et al., 2005), researchers have attempted to identify geographical clusters of CRC using Geographic Information System (GIS). GIS can be defined as the technology of gathering, storing, manipulating and visualizing geographical information; its usage in epidemiological studies include measurement of empiric data and identification of spatial relationships between variables associated with health. GIS can be used in the investigation of many aspects of healthcare access and health outcomes (Graves, 2008).

For CRC, Japanese researchers succeeded in identifying spatial clusters with high mortality rates, where this societal cluster had a high socioeconomic index-representing high income and education level together with high population density, which were urban characteristics. These findings were consistent with those of a previous study indicating a positive relationship between mortality from CRC and socioeconomic index of urbanisation (Fukuda et al., 2005).

Another study (Pollack et al., 2006) in California showed 57% of overall cases of colorectal cancer were diagnosed at a late stage. Californians diagnosed with late-stage colorectal cancer were more likely to be Hispanic and living in areas of lower socioeconomic status. GIS helped to identify two areas where the observed number of late-stage cancers was different than the expected numbers from the distribution in the rest of the state. This would help in the organization of prevention and control activities targeted at the areas with higher than expected late-stage colorectal cancer rates shown through GIS (Rushton et al., 2004).

In this study, GIS will be employed to describe CRC cases in Kuala Lumpur (KL), Malaysia, according to socio-demographic factors (age, gender, ethnicity and district). CRC distribution in KL will also be analyzed via spatial patterns and clustering analysis.

Materials and Methods

The place of study is the state of Wilayah Persekutuan, which covers both Kuala Lumpur and Putrajaya. The state covers an area of 292 km square. The total number of population is about 1,722,500 in the year 2010 (Dept of Statistics Malaysia 2010). This is a retrospective review where data on patients diagnosed with CRC from the year 1995-2011 was collected from the Wilayah Persekutuan Health Office, taken from the cancer notification form (NCR-2), and patient's medical records from the Surgical Department, Universiti Kebangsaan Malaysia Medical Centre (UKMMC). Ethical approval for the study has been obtained from the UKM Ethics Committee and registered under the National Medical Research Register (NMRR) NMRR-10-1345-6960. Data gathered for this study purpose was approved by the Wilayah Persekutuan Health Office and Universiti Kebangsaan Malaysia Medical Centre.

Inclusion criteria for this study are Malaysians residing in the Wilayah Persekutuan state who have been diagnosed as CRC positive via histological findings that were confirmed by a pathologist. Subjects were excluded if their records from the NCR-2 form or medical records were incomplete. All the data collected were analysed using ArcGIS 10 and SPSS version 19 while the co-ordinates of patient's residence studied were identified by using Google Earth. For the data analyses performed using SPSS, categorical variables were presented as frequencies and percentages.

Spatial analysis with average nearest neighbour, Global Moran's I, kernel density and hotspot analysis (Getis-Ord Gi) were used. Average nearest neighbour analysis will indicate if cases are really clustered or merely by random or dispersed. Global Moran's I generates a z-score, describing the degree of spatial concentration or dispersion that will reveal if it is clustered, dispersed or random based on both feature locations and feature values. Getis-Ord Gi statistic will give a Z score value which tells us where features with either high or low values cluster spatially. The larger the Z score value, the more extreme the clustering of hot spot, while with smaller Z score value, the clustering of low values or cold spot will be more intense. This is based on census blocks in the study area.

Results

The total number of registered CRC cases in KL was 146 from 1995 to 2011. There was a sudden increase of 48 (32.9%) cases in 2007, however with the following years showed a decreasing trend in registered cases. Highest

Table 1. Distribution of Colorectal Cancer Cases by Age, Gender and Ethnicity in Kuala Lumpur

Characteristics		No. of cases (n=146) n (%)
Age	20-29	4 (2.7)
	30-39	4 (2.7)
	40-49	17 (11.6)
	50-59	28 (19.2)
	60-69	50 (34.2)
	70-79	35 (24.0)
	80-89	7 (4.8)
	90 and above	1 (0.7)
Gender	Male	76 (52.1)
	Female	70 (47.9)
Ethnic	Malay	28 (19.2)
	Chinese	108 (74.0)
	Indian	8 (5.5)
	Others	2 (1.4)
Staging (n=75)	1	5 (6.7)
	2	18 (24.0)
	3	28 (37.3)
	4	24 (32.0)

number of registered cases in KL was 48 in 2007, while the lowest number of recorded cases was 1 in 1995, 1998 and 2003, respectively. Figure 1 describes the distribution of cases by subdistricts in KL. Most of these cases were from residential areas, especially in the area of Petaling.

Table 1 describes the distribution of CRC in KL by age, gender, ethnicity and staging of disease. Patients aged 60 to 69 years old represented 34.2% of of the study population; this age group has the highest number of cases. There were only minimal differences in gender distribution, with slightly higher cases in males (76 cases, 52.1%) compared to females. On the distribution of cases by ethnicity, Chinese has the highest number of registered cases (108 cases, 74.0%) compared to other ethnicities. "Others" ethnic group was the lowest with 2 (1.4%) cases and Indians rank 2nd lowest with 8 (5.5%) cases.

Figure 2 shows the distribution of cases according to their ethnicity. The Chinese cases appeared to be scattered all around KL. Staging of the cases revealed more cases in the 3rd and 4th stages of CRC. The total number of 3rd

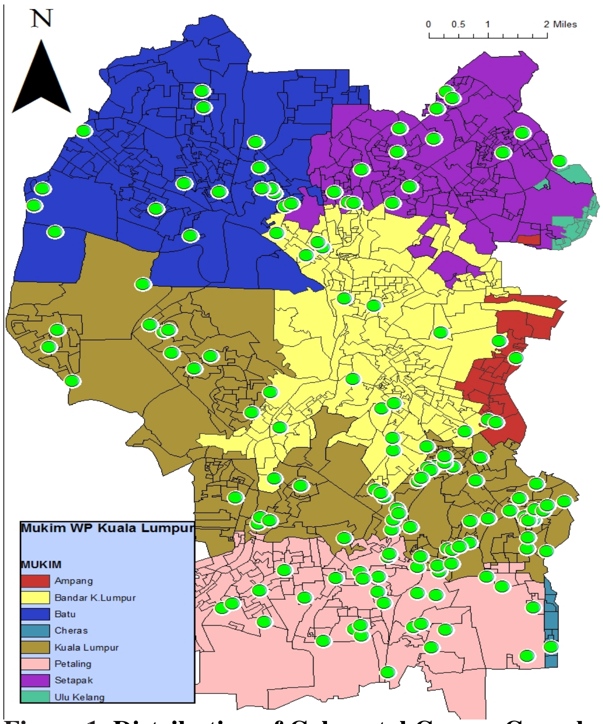

Figure 1. Distribution of Colorectal Cancer Cases by Subdistricts in Kuala Lumpur

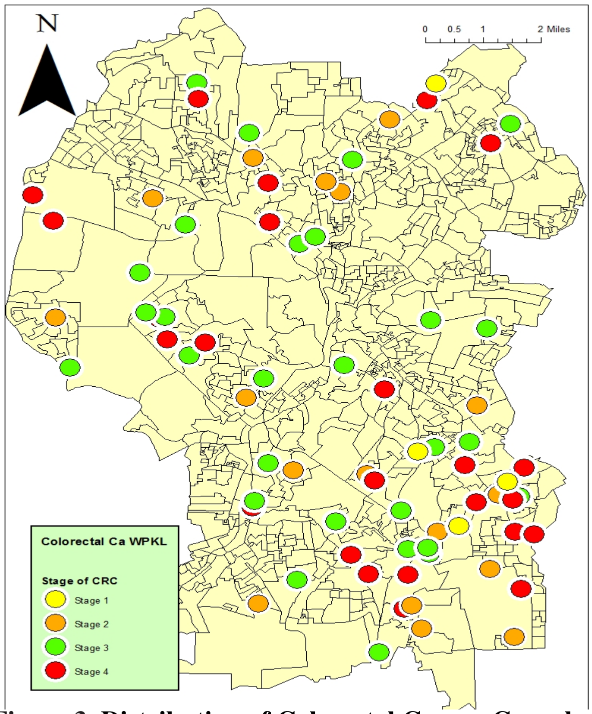

Figure 3. Distribution of Colorectal Cancer Cases by Disease Stage in Kuala Lumpur

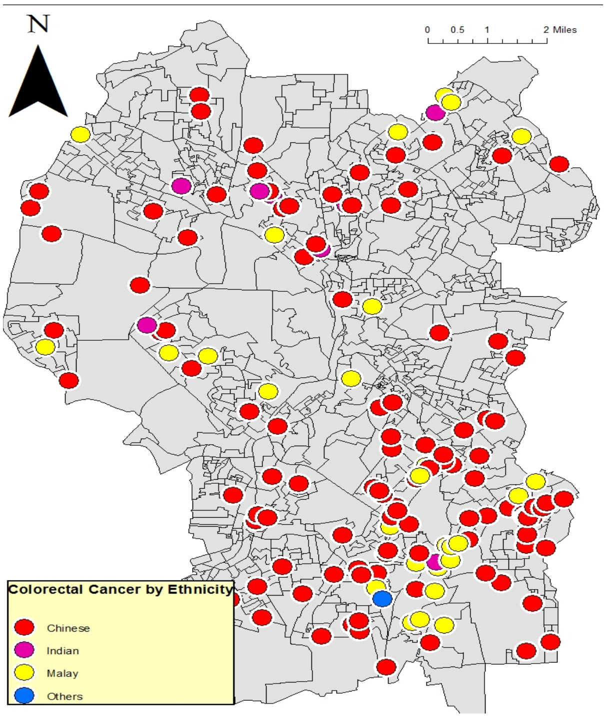

Figure 2. Distribution of Colorectal Cancer Cases by Ethnicity in Kuala Lumpur

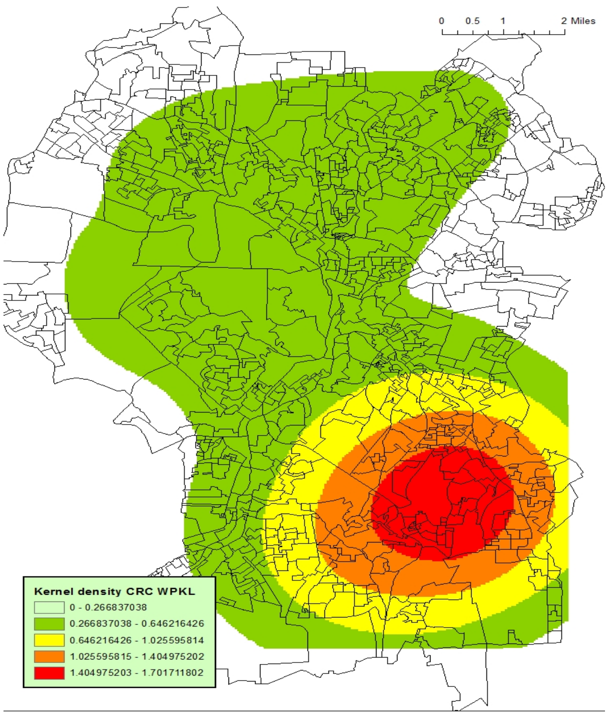

Figure 4. Distribution of Colorectal Cancer Cases by Kernel density in Kuala Lumpur

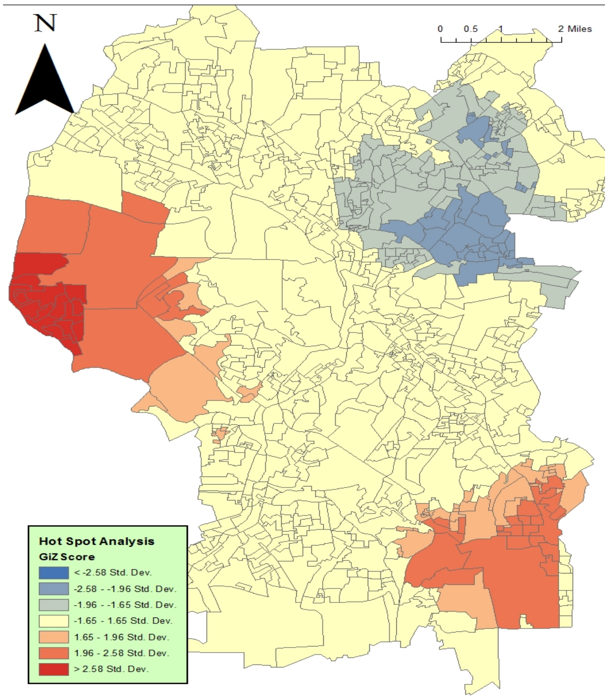

Figure 5. Hot Spot Analysis of Colorectal Cancer Cases in Kuala Lumpur

stage cases was 28 cases (37.3%) while 24 cases for the 4th stage (32.0%); this is described spatially in Figure 3.

In Figure 4, Kernel density analysis showed that more cases are concentrated up in the northern area of Petaling and KL subdistricts. Spatial global pattern analysis by average nearest neighbour showed a nearest neighbour ratio of 0.75, with Z-score of -5.59 and p value of <0.01. This shows there is less than 1% likelihood that this clustered pattern could be the result of random chance. Spatial autocorrelation (Moran's I) showed clustering significant with p<0.01, Z score 3.14 and Moran's Index of 0.007. Hot and cold spots were identified when the clusters were mapped with hotspot analysis (Getis-Ord Gi). It is possible that those areas of hot spots at the northeast and southwest areas are due to the high density of population (Figure 5).

Discussion

GIS has been utilised since 150 years ago in public health to analyse and compare data related to a disease in a particular area. Diseases such as cholera and dengue have been mapped to rule out the relationship between the diseases and other environmental and spatial characteristics (Narimah et al., 2010). Currently, GIS is also used in some settings to map cancer epidemiology data especially by race, ethnicity, gender, disease and accessibility of healthcare (Graves, 2008). A study to observe the variation of prostate cancer average with annual age-adjusted in UK found geographic variation in cancer incidence across three states. They are distinguishable regarding their particular social, political, economic, health care and environmental systems (Gregorio et al., 2006). Another study in Tehran showed some evidences of clustering of childhood cancer (retinoblastoma and leukaemia) in the inner city of Tehran and it may be indicative of a stronger contribution of environmental factors to the aetiology of childhood cancer in this population (Mosavi-Jarrahi et al., 2007). In the United States, cancer cases that have been notified to registries are routinely entered into GIS, and trends are monitored over time. However, in Malaysia, records from the national cancer registry are only presented in tabular form to provide the statistical data on the cases. These data lack the spatial component and limits the use of GIS to analyse cancer cases (Narimah et al., 2010). In this study, we used GIS to explore the distribution of recorded CRC cases in the country's capital, KL.

Increasing age is has been found to be the strongest non-modifiable risk factor for colorectal cancer incidence and mortality (Morisson et al., 2011). In Malaysia, the incidence of colorectal cancer increases with age with the overall incidence rate being 14.5 per 100,000 population (MOH, 2006). More than 90 per cent of the colorectal cancer cases occur in the age of 40 and above and rarely occur in younger age group (Malaysia Oncological Society, 2006). These findings correlate with our study where colorectal cases were seen highest in those aged 60-69 years old. The mechanism can be due to molecular and pathophysiologic changes that occur throughout life which progressively modify molecular homeostasis of colonic epithelial cells leading to neoplasia. Ageing also increases epithelial proliferation in human colon (Holt et al., 2009).

Globally, majority of the highest colorectal cancer incidence rates among males were observed in Europe, North America, and Oceania. High rates were also noted in Japan and Singapore and this is most likely due to environmental or lifestyle factors (Center et al., 2009). In the United States (US), age-standardised data shows the male to female ratio in colorectal cancer varies from 1.2:1 to 1.7:1 (Payne, 2007). In Malaysia, the incidence is slightly higher among males, 16.2 per 100,000 compared to females, 12.7 per 100,000 population (MOH, 2006). Various research findings have suggested that biological factors play a part in differences between men and women in colorectal cancer risk. For example the incidence of right-sided colon cancer is higher among women, while men more often have cancer of the left colon and rectal cancer (Payne, 2007).

In this study, rate of colorectal cancer in males (52.1%) were found to be slightly higher compared to females (47.0%) for patients in Wilayah Persekutuan. This is also similar to another study (Murphy et al., 2011) which showed that colorectal cancer incidence rates generally are higher among males, than females, at all anatomic subsites.

Colorectal cancer has been described as an 'equal opportunity disease' where it has equal distribution in affecting men and women (Osias et al., 2001). However, there are still important differences between both groups in their risk of developing colorectal cancer. By looking at the bigger picture, risk factors for colorectal cancers such as exposure to dietary and lifestyle related risk factors can influence the number of cases among males and females. For instance, studies suggest the effect of red meat on CRC risk is stronger in men than in women while in another large cohort study, no significant interaction by sex for either red or processed meat were reported (Murphy et al., 2011).

In the US, incidence rates of colorectal cancer showed clear racial or ethnic differences (Ollberding et al., 2011). In Malaysia, the incidence is highest among the Chinese where the incidence rate is 23.8 per 100,000 population, and lower in Indians and Malays, where the incidence rate was 9.1 per 100,000 and 6.9 per 100,000 respectively (MOH, 2006).

This study showed the Chinese population had the highest rate of colorectal cancer cases in Malaysia (74%), followed by the Malays (19.2%), Indians (5.5%) and others (1.4%). This is similar to a Malaysian study that showed Chinese race were significant independent predictive factors for colorectal cancer (Goh et al., 2005) and another research in Singapore (Lim et al., 2002) that showed Chinese population exhibits much greater rates compared with the Malay population. In this case, genetic factors play possible role in aetiology of colorectal cancer (Sung et al., 2005).

The study showed more cases diagnosed at a later stage, which were stage 3 (37.3%) and stage 4 (32.0%). This finding was similar with other countries which further emphasizes the need for early detection through screening. With mass screening we hope to see more of earlier stage diagnosis and decrease the incidence of later stage. In Netherlands, a study on spatial distribution of colorectal staging showed variation in stage specific incidences, except for stage 3 and 4 (Elferink et al., 2012).

We found significant clustered cases of CRC in KL, where more studies into environmental risks will be needed to explain the spatial variation obtained in our study (Mohebbi et al., 2008).

According to the cluster analysis, CRC hot spots were located in the northwest areas of KL. Generally, the northwest areas have high-priced lands and expensive residential houses. Most of the population there are known to have a high socioeconomic status. Based on studies done linking socioeconomic factors and CRC, high levels of socioeconomic status have been associated with the development of cancer (Mohebbi et al., 2008; Rohani-Rasaf et al., 2013).

Meanwhile, from cold spots were located in the cluster analysis at the northeast areas in KL. This area is known to be crowded with many types of low cost houses and flats. The majority of the population here ranges from low to medium socioeconomic status. Another reason contributing to the low incidence of CRC cases at these cold spots can be due to lack of mass screening to detect CRC among the population. The incidence of Stage I CRC will be increased if mass screening is done (Elferink et al., 2012) and this can reduce the later stages of CRC among the targeted population by implementing early treatment.

When looking at the Kernel density and other hotspot areas, the southeast area of KL has a high density of cases as well. This might be due to more patients with CRC staying in these areas and have better access to health care services. This will enable those living in that area to get earlier diagnosis of CRC by medical professionals at the healthcare centres.

In conclusion, this study demonstrated significant spatial patterns of cancer incidence in KL. Knowledge about these spatial patterns can provide useful information to policymakers in the planning of screening of CRC in the targeted population and improvement of healthcare facilities to provide better treatment for CRC patients.

In this study we did not include surrounding environmental exposure risks in our analysis. Due to the limited number of recorded cases from 1995-2011, the study cases were limited and without matched controls. A larger, case-control study including environmental exposure risk analysis will be needed to fully explain the occurrence of CRC clusterings and the contributing environmental factors towards the disease.

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