

The Spatial patterns of liver cancer in Libya: Standardized Morbidity Ratio and Poisson- Gamma Model, Based Analysis of Cancer Registry Data, 2020

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الملخص

تم استخدام النماذج الإحصائية المكانية أو طرق بايز على نطاق واسع لتحليل ودراسة أنماط التوزيعات الجغرافية لمرض نادر أو منطقة جغرافية صغيرة. مرض السرطان يعتبر مشكلة صحية متزايدة باستمرار والسبب الأكثر شيوعاً للوفيات الطبية حول العالم. بالإضافة إلى ذلك ، فإن مرض السرطان هو الأكثر انتشاراً للأمراض في ليبيا. تتمثل أهداف هذه الدراسة في تحليل وتحديد المخاطر العالية والمنخفضة غير العادية لليبيا كنمط وباعتبارها عملية (رسم خرائط سرطان الكبد) بناءً على نسبة الاعتلال المعيارية (SMR) ، وهي نهج تقليدي لقياس الخطر النسبي لهذا المرض. وكذلك استخدام نموذج بواسون جاما (Poisson-gamma). أيضاً، لفهم وتقييم العلاقة بين مرض سرطان الكبد ومخاطره العالية في منطقة الدراسة. تم استخراج مناطق الدراسة باستخدام نظام المعلومات الجغرافية. بعد ذلك ، تم ربط بيانات حالات سرطان الكبد المرصودة وبيانات السكان لإجراء التحليل باستخدام برنامج WinBUGS. تبدأ هذه الدراسة بمراجعة موجزة لهذه النماذج ، بدءاً من طريقة SMR متبوعةً بنموذج Poisson-gamma ، والذي نطبقه بعد ذلك على حالات الإصابة بسرطان الكبد في ليبيا. تتم مقارنة جميع النتائج باستخدام الخرائط والجداول. خلصت الدراسة إلى أن نموذج بواسون-جاما يعطي تقديرات مخاطر نسبية أفضل مقارنة بالطريقة الكلاسيكية (SMR). يمكن لنموذج بواسون-جاما (Poisson-gamma) التغلب على مشكلة SMR في حالة عدم وجود سرطان كبد ملاحظ في المنطقة.

الكلمات المفتاحية: رسم خرائط المرض ، ليبيا ، سرطان الكبد ، طريقة SMR ، تقدير المخاطر النسبية (RR)، نموذج بواسون قاما (Poisson-gamma)

Abstract

The spatial statistical models or Bayesian methods have been used widely to analyze and study the patterns of geographical distributions for a rare disease or

small geographical area. Cancer is the ever-increasing health problem and most common cause of medical deaths around the world. Additionally, cancer has the highest prevalence of diseases in Libya. Libya, as the study area, was selected to perform this research and to estimate its relative risk for liver cancer. Cancer data and population censuses of the country for the time period 2020 were used in this study. The objectives of this study are analyzing and identifying the unusual high and low risk of Libya as a pattern and as the process (the liver cancer mapping) based on the Standardized Morbidity Ratio (SMR), a traditional approach to measuring the relative risk of the disease, and Poisson-gamma model. Also to understand and assess the relationship of liver cancer disease and its high risk of a study area. Regions of the study were extracted by using GIS system. Then, observed liver cancer cases data and the population data were coupled to perform the analysis using WinBUGS software. This study starts with a brief review of these models, starting with the SMR method and followed by the Poisson-gamma model, which we then apply to liver cancer incidence in Libya. All results are compared using maps and tables. The study concludes that the Poisson-gamma model gives better relative risk estimates compared to the classical method. The Poisson-gamma model has can overcome the SMR problem when there is no observed liver cancer in an area.

Keywords: Libya, Liver Cancer, SMR Method, Disease Mapping, Relative Risk Estimation, Poisson-gamma Model.

1. INTRODUCTION AND RESEARCH AIM

Cancer is the ever-increasing health problem and most common cause of medical deaths around the world; cancer disease impacts everyone "the rich or poor people, the old or young, women or men and kids. There are several risk factors that cause cancer. Worldwide, alcohol use, physical inactivity, tobacco use and unhealthy diet are the main cancer risk factors, as well as some chronic infections are known as risk factors for cancer, which have main relevance in low- and middle-income countries, including, Libya. In Libya, cancer is the one of the most cause of mortality and morbidity after a car accident and cardiovascular disease [(Singh and Al-Sudani, 2001). Therefore, cancer is a significant problem in public health in Libya (Aglia et al., 2014; El Mistiri et al., 2010). For instance, liver cancer has the highest prevalence of disease digestive cancer in Libya, in specially, it has high incidence in west and north regions of Libya (Alramah et al., 2019; Alhdiri et al., 2016; Bodalal et al., 2014; Bodalal & Bendaraf, 2014; Alragig et al., 2015).

Medically, liver cancer is cancer that usually starts in the cells that line the inside of the liver. i.e. Just cancers that begin in the liver are called liver cancer. This cancer can occur along the liver and it can occur anywhere along the liver. It occurs when cells in the liver mutate and grow uncontrollably. Abnormal cells that accumulate to form cancers in the liver that can grow to invade nearby structures and spread to other parts of the body. A “liver cancer risk factor” is anything that increases the risk of developing liver cancer. Many of the most important risk factors for liver cancer are beyond the control, such as age, family history, and medical history. Also, there are some risk factors you can control, such as overweight, low physical activity, and alcohol consumption.

The current study was proposed due to the lack of data on incidence and mortality for liver cancer in Libya. We aimed to examine the distribution of overall liver cancer malignancies diagnosed in Libyan healthcare system with respect to descriptive cancer epidemiology indicators. Therefore, the main aim of this research is the liver cancer mapping for describe geographic of disease risk and identifying unusual high and low risk areas. The areas or regions of Libya vary in size, shape, and population size (Fig. 1). In this study, we discuss and demonstrate the most common methods used in the study of disease mapping, which are classical method that known as Standardized Morbidity Ratio (SMR) and Poisson-gamma model. We will focus on its application to liver cancer data in Libya. This study is organized as follows. First, in Section 2, we review and describe the classical method in estimating relative risk using SMR method. This includes the definition of SMR and its drawbacks. Then we move to describe and overview of the earliest application of Bayesian methodology, that called as “Poisson-gamma model” which is applied and used by Lawson et al. (2003), will be in Section 2. Section 3 describes the cancer data used in our application and presented findings. As well as several results presented in this section based on these two methods, which are applied to observed liver cancer data in Libya in order to demonstrate and identify a better method of estimating liver risk. Finally, we close with some discussion and conclusion in Section 4.

2. METHODOLOGY

2.1. Standardized Mortality Ratio Method

In disease mapping, SMR is the commonest statistics used in spatial studies. The main aim of the SMR is to estimate the RR of a certain disease in a certain map,

which may be interpreted as the probability that a person within a specified region contracts the disease divided by the probability that a person in the population contracts the disease. In the field of epidemiology studies, SMR represents either standardized mortality ratio or the standardized morbidity ratio, when mortality refers to death while morbidity refers to the incidence.

However, in general notation, suppose that O_i , where $i=1, 2, \dots, H$ (H indexes the areas or regions. In other words, geographical regions or regions), indicates the observed cases of a certain disease of the study, and let E_i represents the expected cases or counts based on the known risk factors. Using these values as obtained from the available data, we can calculate the relative risk θ_i for area i , which is the SMR defined as

$$SMR = \hat{\theta}_i = \frac{O_i}{E_i} \quad (1)$$

Samat and Percy (2008) used the Equation (1) for the SMR in their study and applied it to dengue disease mapping in Malaysia. According to Lawson et al., (2003), although SMR is used commonly as measure to estimate the true relative risk, but at the same time, it has some problems associated with the use of it. SMR is based on a ratio estimator, the mean and variance of SMR are very highly dependent on expected count E_i . Furthermore, if there are areas with no observed count data, mathematically the SMR is necessarily zero (see Equation 2). Meza (2003) showed that this problem of SMR makes the interpretation of SMR difficult, and it should be done with caution and also who points out other problems of using SMR, which that the SMR is a reliable measure of relative risk for large geographical regions such as countries or states, but is unreliable for small areas such as counties.

$$\text{If } SMR \begin{cases} > 1 \text{ (is very Larg) } & \text{the expected numbers of cases are small} \\ = 0 & \text{no observed count data or cases} \\ < 1 \text{ (is very small) } & \text{the expected numbers of cases are larg} \end{cases} \quad (2)$$

However, to be able to overcome these problems which are resulting from the use of SMR method, many researchers have led to produce other alternative methods to estimate the relative risk of the disease. One of these methods was the use of Bayesian methods. In this research, we suggested very common method to estimate the relative risk of a disease, as will discuss in next section.

2.2. Poisson-gamma Model

As earlier mentioned, disadvantages of SMR in disease mapping such as in areas where there are no observed count data or cases, so necessarily the SMR will be zero, have been encouraged several researchers to provide a set of methods to estimate the relative risk of a particular disease. These methods include the employ of Bayesian methods. A study by Clayton and Kaldor (1987), were the first to suggest the Poisson-Gamma model, which supposed that the relative risk has the Gamma distribution. However, Lawson et al., (2003) confirmed that the Poisson - Gamma model is one of the earliest examples of Bayesian mapping. In this model, for $i=1, 2, \dots, H$ study areas and $j=1, 2, \dots, C$ disease sites, Let $O_{ij}, E_{ij}, \theta_{ij}$ be the observed count, expected count and relative risk parameter in the i th area, respectively. Then the numbers of new cases O_{ij} are assumed to follow a Poisson distribution with period time, as follows:

$$O_{ij} \mid E_{ij}, \theta_{ij} \sim \text{Poisson}(E_{ij} \theta_{ij}) \quad (3)$$

Then the relative risks θ_{ij} have a gamma distribution with parameters α and β

$$\theta_{ij} \sim \text{Gamma}(\alpha, \beta) \quad (4)$$

There was a comparison between Poisson-Gamma model and SMR method which has been done by Lawson et al. (2003). This study showed that the use of the Poisson-gamma model gives a smoother map with less extreme values for relative risk estimates. However, adjustment in this model is difficult and there is no possibility for allowing spatial correlation between risks in the neighbouring areas. In other words, among the advantages of the Poisson-Gamma model that is simple and easy to use, but it is unable to deal with spatial correlation between neighbouring areas and relative risks. Therefore, the problems of this model have motivated many researchers to propose other alternative models to estimate the risk.

3. THE APPLICATION: RELATIVE RISK OF DISEASE USING SMR METHOD AND POISSON-GAMMA MODEL TO LIVER CANCER MAPPING

This section explains and displays the outcome of the applications of existing relative risk estimation methods, corresponding to the classical model based on the standardized morbidity ratio and one of earliest examples of Bayesian mapping methods based on the Poisson-gamma model using observed liver cancer in Libya. Models were fitted to data using WinBUGS software, which is a package designed to carry out wide variety Bayesian Models, EXCEL to get

relative risks and standard error for SMR. Then, all of these outcomes are compared and displayed in the table and maps, to reveal the best-fitted model for relative risk estimation for liver cancer disease mapping in Libya.

3.1. Cancer Data

In this applied, ecological research, information of the Libyan regions for one-year 2020 was analyzed, which is obtained from Africa Oncology Institute (AOI) These administrative regions are Alnikat, Zawia, Aljafara, Tripoli, Almergaib, Musrata, Sirt, Benghazi, Almarg, Aljabal Alakhader, Darna, Albatnan, Nalut, Aljabal Algarbi, Wadi Shatee, Aljufra, Ejdabiya, Ghat, Wadi Alhiya, Sabha, Morzuk and Alkufra. A geographical system of Libya's regions is explained in Figure 1, where ID, name and population for each region in the map are shown. Liver cancer disease data is used to illustrate the SMR model and Poisson-gamma model to estimate the relative risk of disease (Libyan National Statistics Figures, 2011; Alhdiri et al., 2016; Abusaa, 2008).

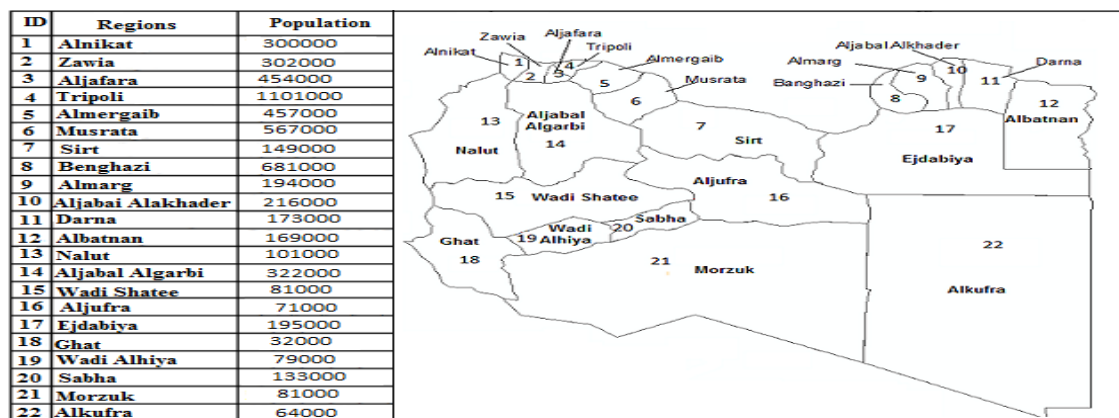


Figure 1. Names of 22 Geographic boundaries, Code on the map and population of all regions in Libya (Source: Alhdiri et al., 2016).

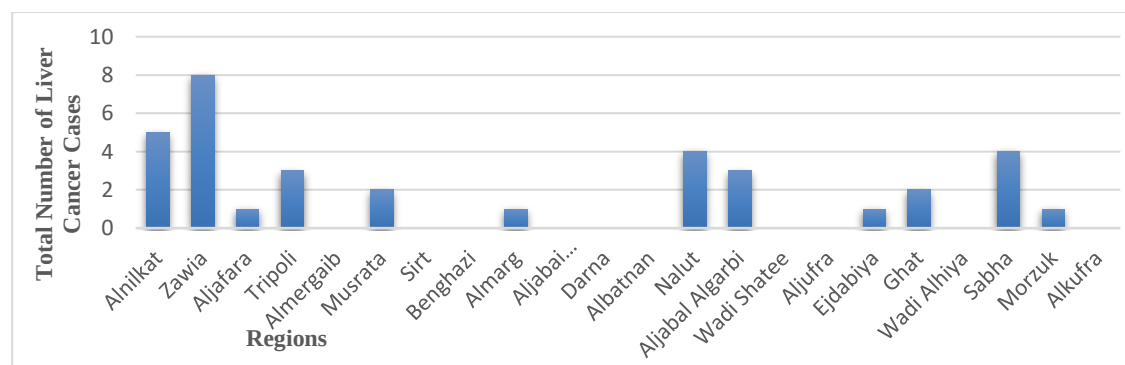


Figure 2. Total number of Liver cancer cases reported for each region in Libya, 2020

In this study, from 1 January 2020 to 31 December 2020, the total number of liver cancer disease involving all regions in Libya is 35 cases. Fig. 2 present the total number of liver cancer cases reported for each area in Libya in the year of 2020. Obviously, we can see that Zawia region shows the highest number of cases which is 8 cases. The second highest case is at Alnikat which reported 5 cases of liver cancer. There are ten regions which are free from liver cancer disease which are Almergaib, Sirt, Benghazi, Aljabal Alakhader, Darna, Albatnan, Wadi Shatee, Aljufra, Wadi Alhiya and Alkufra.

3.2. The Results

The outcomes for the relative risk estimation using the Poisson-gamma mode and the SMR for 2020 are displayed in table 1. Table 1 presents two obvious differences in terms of the value of relative risk. Ten regions have value of relative risk equal to zero, in the absence of cases of observed liver cancer based on analysis using the SMR method. These regions are Aljafara, Sirt, Benghazi, Aljabal Alakhader, Darna, Albatnan, Wadi Shatee, Aljufra, Wadi Alhiya, and Alkufra. Based on SMR method, susceptible people within the region of Nalut have the highest risk of contracting liver cancer, while susceptible people within the above regions have the lowest risk of liver cancer when compared with people in the overall population. The corresponding values of relative risk are between 10.575 and 0, respectively. Conversely, by using Poisson-gamma model, the finding shows opposite results where the value of relative risk is not zero although there are regions with no observed counts of liver cancer cases, which can be a disadvantage of the SMR approach. However, the Poisson-gamma model does not suffer from this drawback and generates positive estimates of relative risk in regions that have no observed case.

The latter model can overcome the drawback of SMR, which is when there are no observed cases in particular areas. In addition, from table 1, Zawia, Nalut and Alnikat have a high value of relative risk during 2020. Estimation using the Poisson-gamma model shows that susceptible people within the region of Nalut have the highest risk of about 3.668, while susceptible people within the regions of Benghazi have the lowest risk of about 0.216.

In addition, the results in table 1 displayed that a small population (small number of people in the i^{th} region) has low expected counts, but SMR and standard error are high (see 18th region, Ghat). Conversely, region with high population (high number of people in the i^{th} region) has high expected counts,

but SMR and standard error are low (see 4th region, Tripoli). Generally, SMRs have the greatest uncertainty because they have small population then standard error are high. Therefore, we can say that the relative risks based on Poisson-gamma model provide a more stable risk estimate such as yielding low standard error than using the classical method (SMR).

Table 1. Observed, Expected and Relative risk of liver Cancer Disease based on SMR Method and Poisson-gamma Model for the year 2020

No.	Region	O _i	E _i	Relative Risk based on SMR Method		Relative Risk based on Poisson-Gamma Model	
				RR	SD	RR	SD
1	Alnikat	5	1.773	2.82	1.261	2.314	0.023
2	Zawia	8	1.785	4.482	1.585	3.429	0.039
3	Aljafara	1	2.683	0.373	0.373	0.582	0.009
4	Tripoli	3	6.507	0.461	0.266	0.556	0.005
5	Almergaib	0	2.701	0	0	0.289	0.009
6	Musrata	2	3.351	0.597	0.422	0.726	0.007
7	Sirt	0	0.881	0	0	0.589	0.013
8	Benghazi	0	4.025	0	0	0.216	0.008
9	Almarg	1	1.147	0.872	0.872	1.034	0.012
10	Aljabal Alakhader	0	1.277	0	0	0.486	0.011
11	Darna	0	1.023	0	0	0.528	0.0122
12	Albatnan	0	0.999	0	0	0.551	0.014
13	Nalut	4	0.597	6.701	3.3505	3.668	0.0602
14	Aljabal Algarbi	3	1.903	1.576	0.9101	1.468	0.012
15	Wadi Shatee	0	0.479	0	0	0.762	0.013
16	Aljufra	0	0.419	0	0	0.805	0.016
17	Ejdabiya	1	1.152	0.868	0.868	1.025	0.0102
18	Ghat	2	0.189	10.575	7.478	3.323	0.078
19	Wadi Alhiya	0	0.467	0	0	0.756	0.014
20	Sabha	4	0.786	5.089	2.544	3.166	0.0502
21	Morzuk	1	0.479	2.089	2.089	1.602	0.019
22	Alkufra	0	0.378	0	0	0.838	0.023

“RR” denotes Relative Risk, “SD” denotes standard deviation, and values highlighted in bold denotes highest or lowest relative risk or expected cases

Fig. 3 shows the relationship between the relative risk and standard error based on SMR method and Poisson-gamma model. From this Fig. 3a, it can be seen that the relative risk increases as standard error increases. While in Fig. 3b shows that the relative risk of disease using Poisson-gamma model produced higher precision of estimate than classical method.

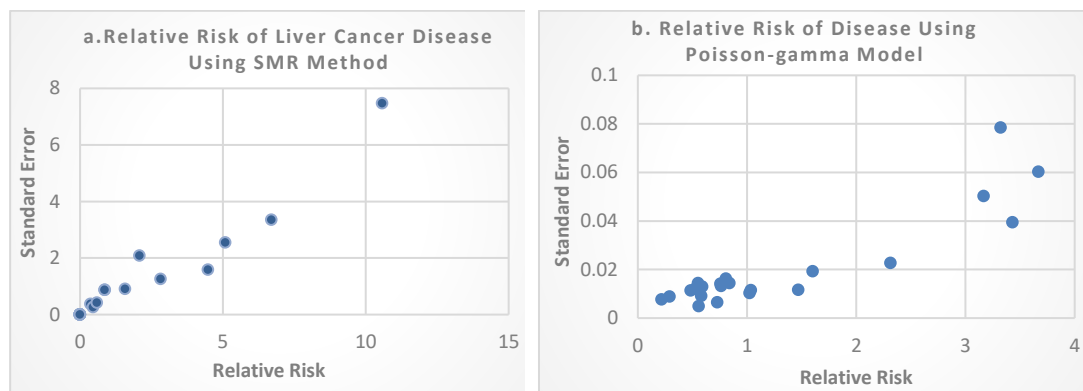


Figure 3. a) Relative risk based on SMR method vs standard error; b) Relative risk based on Poisson-gamma model vs standard error

For the purpose of this study, a comparison of the bar graphs using these two methods is also made in Fig. 4 in order to help ascertain which method produces a better relative risk estimation for liver cancer data in Libya.

Fig. 4 shows the estimated relative risk based on the SMR method and Poisson-gamma model for each region in Libya in the year of 2020. From Fig. 4, it can be seen that majority of the regions in Libya have SMR less than one. Hence, it can be concluding that those regions have smaller observed number of liver cancer cases compared to expected number of liver cancer cases. From Fig. 4a, there are seven regions with SMR greater than one which is the region of Alnikat, Zawia, Nalut, Aljabal Algarbi, Ghat, Sabha and Morzuk, while in Fig. 4b using Poisson-gamma model, nine regions with relative risk greater than one, which are Alnikat, Zawia, Almarg, Nalut, Aljabal Algarbi, Ejdabiya, Ghat, Sabha and Morzuk. Most these regions are located at the North, south and Northwest of the country. The highest relative risks are at the regions of Ghat and Nalut with recorded the value of 10.575 and 3.668 using SMR and Poisson-gamma respectively. These regions can be said having an excess death in the study population because the ratio of the observed divided by the expected deaths is greater than one. Among all regions in Libya, there are ten regions with zero relative risk using SMR method, which are the regions of Almergaib, Sirt, Benghazi, Aljabal Alakhader, Darna, Albatnan, Wadi Shatee, Aljufra, Wadi Alhiya and Alkufra. Likewise, the Poisson-gamma model does not suffer from this drawback and generates positive estimates of relative risk in regions that have no observed cases.

Moreover, the results of relative risk estimation based on the methods presented in table 1 and Fig. 4 show that the susceptible people within these regions are more likely to contract liver cancer compared to people within the overall population of the country, whilst susceptible people within the other regions are less likely to contract liver cancer compared to people within the overall population

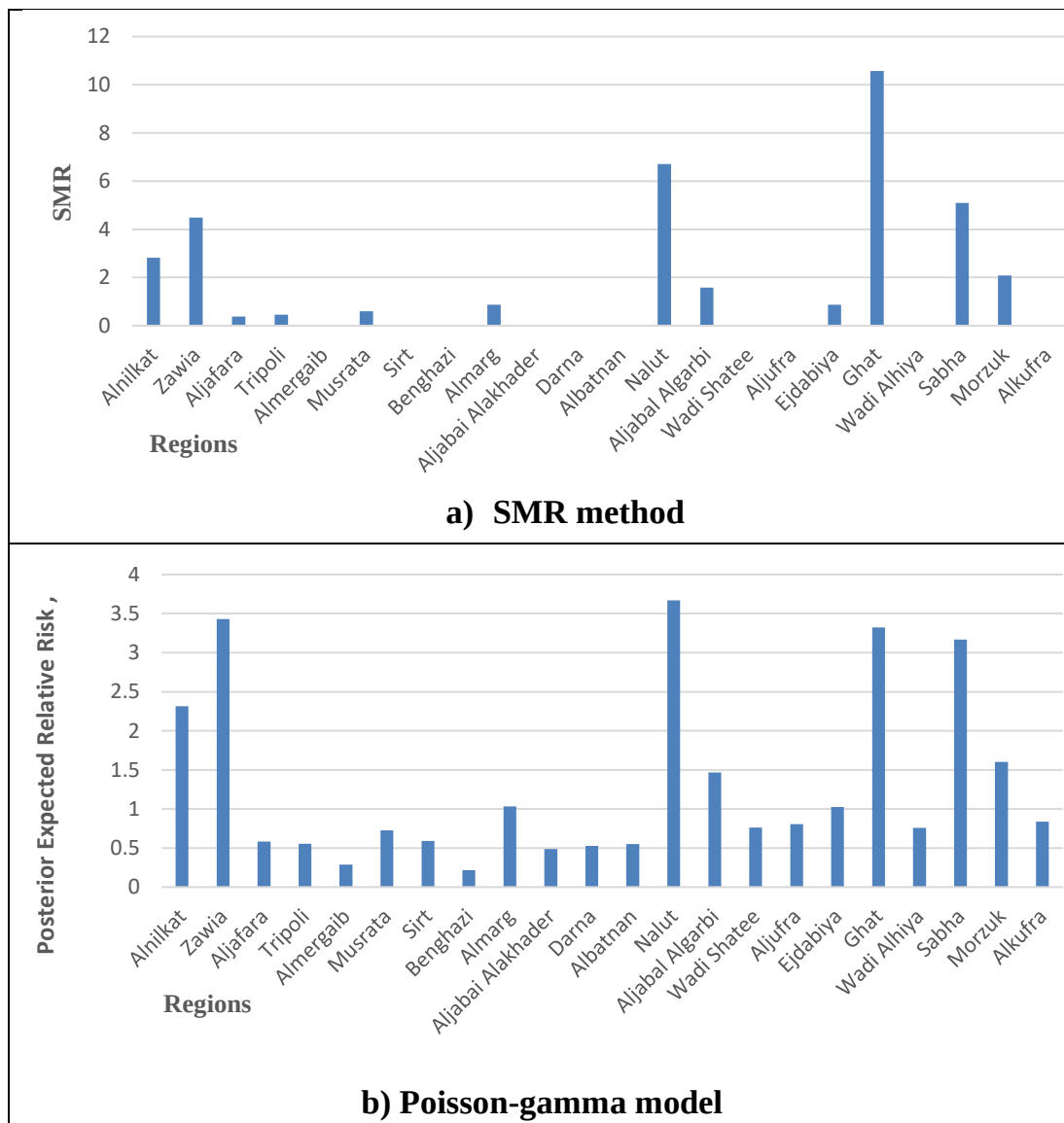


Figure 4. a) Bar graph of the estimated relative risk based on the SMR method for each region in Libya; b) Bar graph of the estimated relative risk based on Poisson-gamma model for each region in Libya

3.3. Disease Maps of Relative Risk Estimates for Liver Cancer in Libya

Disease maps are used to represent the different levels of risk for liver cancer, which covered all 22 regions in Libya. Diseases maps graphically display statistical outcomes for relative risk estimation and are an inferential and fundamental decision-making tool. In this study, multiple colors are applied in the maps to identify and display among the hot areas which have high or low risk of liver cancer incidents for all regions in Libya. The results represent the hot points of liver cancer incidents. Fig. 5 shows the risk maps for liver cancer based on the SMR method and the Poisson-gamma model. All these maps show the results for each region in Libya during the year 2020.

Mapping issues related to aggregated data are discussed in (Lawson, 2006) and also other issues related to the interpretation and representation of disease risk in a map were presented by other researchers (Pickle et al., 1999; Lewandowsky et al., 1993; Pickle & Herrmann, 1995; Mungiole et al., 1999). For the interpretation of thematic maps, this study applied multiple colors to illustrate and differentiate among the high and low risk regions for liver cancer incidents that are considered in this study for each region in Libya. Therefore, each region will be categories into five different levels of hazard. These levels are very high, high, medium, low and very low with their intervals of $[(<0.5)$, $[0.5,1)$, $[1,1.5)$, $[1.5,2)$ and $[2, \infty)]$ respectively. In our application, depending on the concept, and definition of relative risk that is given in several studies, we choose these intervals to cover the range of observed values. In addition, we mean by the dark shade in the map the highest risk (very high) and by the lightest shade the very lowest risk (very low).

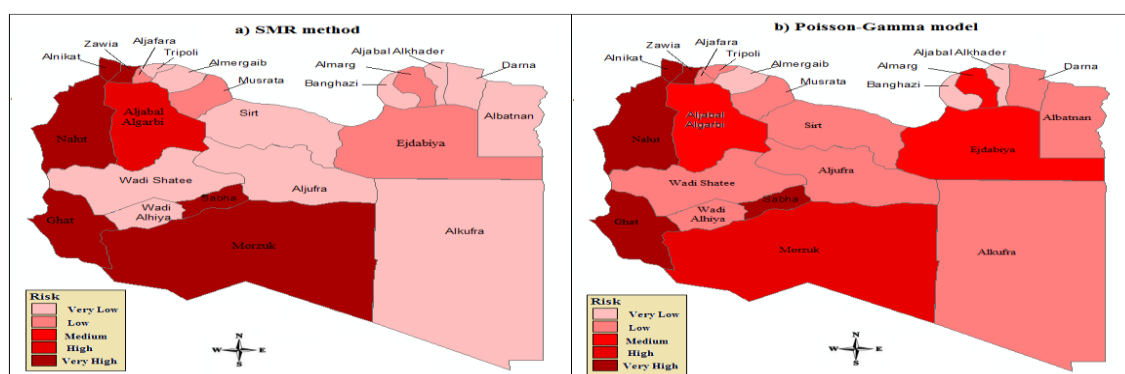


Figure 5. (a) Disease Map of estimated relative risk of liver cancer in Libya based on SMR method, 2020; (b) Disease Map of estimated relative risk of liver cancer in Libya based on Poisson-gamma model, 2020

Fig. 5a for the SMR map shows that there are six regions with very high risk of liver cancer, which are Alnikat, Zawia, Nalut, Ghat, Sabha and Morzuk. There was only one region with high risk, Aljabal Algarbi. This is followed by one region with high risk, which was Aljabal Algarbi and no regions have medium risk. The regions of Musrata, Almarg and Ejdabiya with low risk and the regions of Aljafara, Tripoli, Almergaib, Sirt, Benghazi, Aljabal Alakhader, Darna, Albatnan, Wadi Shatee, Aljufra, Wadi Alhiya and Alkufra with very low risk. The Poisson-gamma model map in Fig. 5b shows that the regions of Alnikat, Zawia, Nalut, Ghat, and Sabha have very high risk of liver cancer occurrences, while the region of Morzuk has high risk. The regions with medium risk are Almarg, Aljabal Algarbi, and Ejdabiya. The regions Aljafara, Tripoli, Musrata, Sirt, Darna, Albatnan, Wadi Shatee, Aljufra, Wadi Alhiya, Alkufra have low risk, while the other three regions with very low risk include the regions of Almergaib, Benghazi and Aljabal Alakhader.

Here, comparisons between the SMR method and Poisson-gamma model for only one-year 2020 show no evident differences in terms of the estimated risks based on both maps considered. Therefore, disease maps are mostly meant to be a better presentation tool for identifying areas, which have very high, or high risk of liver cancer disease, so that further interest could be provided to these priority regions.

4. DISCUSSION AND CONCLUSION

The study findings for relative risk estimation using Poisson-gamma model that is suggested in this study provides an important approach to assessing future risk compared to the SMR method. Some previous interpretations which had been explained are expected to be used as a reference in order to control and prevent liver cancer disease before it occurs.

These findings also showed that the Poisson-gamma model can overcome the drawback of SMR especially when there is no observed liver cancer case in certain regions. The maps show that the high risks are concentrated in the north-west part of the study area (the country) and least as we head south and east. It is identical in terms of population concentration congestion in the north and the least concentration of population as we head south and east. The regions with the highest risks are located in the west probably due to oil installations in this area such as Mellitah Oil and gas B.V, the Zawia Oil Refining Company and Bouri Oil Field, as well as the electrical power stations (Alsaker, 2013). The

higher risk of these areas, the more serious attention of government policy and financial support are needed. Susceptible people within regions located in the eastern part of the country have the lowest risk based on both methods when compared to the people in the overall population.

In this manner, individuals at hazard will be more mindful and comprehend through logical clarification that likelihood of contracting liver growth later on. For further advancement, it is relied upon to utilize other better techniques or models recommended or proposed in the writing to improve estimation of relative hazard.

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