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Analysis of inpatients' characteristics and spatio-temporal distribution of liver cancer incidence in Wuwei, Gansu Province, from 1995 to 2016

A long-term span retrospective study

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Abstract

This long-term span retrospective study aimed to determine the incidence and spatial-temporal trends of liver cancer in Wuwei city from 1995 to 2016 to provide scientific knowledge on the prevention and treatment of liver cancer.

Data from the medical records of liver cancer patients treated in 12 sentinel hospitals in Wuwei city were extracted. SAS and Joinpoint software were used for data analysis, ArcGIS 10.2 software was used to make geographical distribution map, and SaTScan 9.4 software was used for clustering area detection.

Of 2271 patients with liver cancer (average age, 58.73 years), 17.7% were 60 to 64 years of age. Majority were males (1680, 74%), with a sex ratio of 2.84. Joinpoint regression analysis from 1995 to 2016 revealed that the standardized liver cancer rate increased [annual average rate of change (AAPC) = 12.80% (95% CI: 9.5%–16.7%)], with a joinpoint in 2009. From 1995 to 2009, the change in overall APC was statistically significant [APC = 16.7 (95% CI: 12.3%–21.3%)]. The average incidence was the highest in Hongshagang Town. After 2005, the incidence gradually increased in each township. Five clusters of liver cancer were noted in Wuwei, including 37 townships.

Males had a higher standardized liver cancer rate. After 2009, increase in the incidence of liver cancer was less rapid. The incidence of liver cancer in townships of Wuwei city was non-random, with certain spatial aggregations, covering 37 townships.

Abbreviations: AAPC = annual average rate of change, APC = annual percentage change, CI = confidence interval, HbsAg = hepatitis B virus surface antigen, HBV = hepatitis B virus, HCC = hepatocellular carcinoma, IL = interleukin, NRCMS = new rural cooperative medical care system, PHC = primary hepatic carcinoma, RR = relative risk, SD = standard deviation.

Keywords: epidemiology, hospitalized patients, liver cancer, spatial trend, spatial-temporal cluster, temporal trend

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1. Introduction

Liver cancer is one of the most common cancers in the world, with unique regional variations in incidence. About 86% of cases occur in developing countries, particularly in East, North, and South Asia, and in sub-Saharan Africa. In contrast, Central and Western Asia, and Northern and Eastern Europe are areas of low incidence.[1] At present, liver cancer accounts for about 5% of all cancers worldwide. The global annual incidence of liver cancer is about 750,000, with a death rate of about 696,000, ranking third among malignant tumors. Nearly 50% of liver cancer cases occur in China. In 2015, liver cancer ranked fourth and third in incidence and cancer-related death rate, respectively, in China.[2] For a long time, studies on the etiology of liver cancer have reported that viral hepatitis, aflatoxin (AFT) intake via food, and contaminated drinking water are the three major risk factors for liver cancer. The risk level of these factors can also vary significantly in different regions with different prevalences. At present, the most common causes of liver cancer in China are hepatitis B virus (HBV) infection, AFT contamination in food, hepatitis C virus (HCV) infection, and blue-green algae toxin contamination in water; other risk factors include family history of liver cancer, drinking, and smoking.[3,4] Therefore, understanding the epidemiological characteristics (such as population distribution, geographical, and temporal changes) of liver cancer is of utmost importance. In this study, data on liver cancer patients treated in 12 sentinel hospitals in Wuwei city from 1995 to 2016 were analyzed to understand the demographic characteristics, morbidity characteristics, and temporal and spatial epidemiological trends in liver cancer patients. Differences in disease characteristics and spatial and temporal trends were compared among liver cancer patients in Liangzhou district, Minqin county, Gulang county, and Tianzhu county, and factors causing the differences in their distribution were explored.

2. Methods

2.1. Data sources

Morbidity data included in this study were extracted from inpatient medical records from 1995 to 2016 in 12 sentinel hospitals (secondary-level or above), in Wuwei city. If the same patient was diagnosed repeatedly in multiple hospitals, simultaneously or sequentially, only one medical record was considered for analysis. Patients who were not from Wuwei city areas were excluded.

2.2. Data quality control methods

Hospitals randomly check 10% of the PDF version of the medical records daily for any omissions and to maintain quality control and consistency of entries in the register. The supervisors perform daily monitoring of the input data in real time, by comparing between a 10% sample of the data and the original PDF for errors. Errors are corrected in a timely manner.

2.3. Statistical methods

SAS (SAS Institute. Cary, NC), Joinpoint software was used for data analysis. A geographical distribution map was made with ArcGIS 10.0 software, and clustered area detection was performed using SaTScan 9.4 software. General data related to demographic characteristics, hospitalization, and treatment were also analyzed by SAS software. Continuous variables were described as mean ± standard deviation (SD), and categorical variables were described as numbers, composition ratio, and frequencies. Comparisons between two groups were performed using the X^2 test or Fisher's exact test, and a $P < .05$ was considered statistically significant.

Standardization of the crude incidence was based on the standard population composition of the sixth national population census in 2010. From 1995 to 2016, the percentage rate, standardized rate, age group rates, and time trends of liver cancer in rural areas of Wuwei city were analyzed using the Joinpoint software developed by the US National Cancer Institute. The annual percentage change (APC) and its 95% confidence (CI) values were calculated. The joinpoint regression model was used in fitting the models. The grid search method was used to determine statistically significant trends, while multiple permutation tests were used to determine the joinpoint points with significant differences in APC and 95% CI values for each trend.[5–7] This approach has two major advantages. First, it estimates the increase or decrease of disease incidence by calculating APC and 95% CI values at each trend stage; second, it determines the year in which the trend direction changed.[8] The overall time trend could be determined by the annual average rate of change (AAPC)—the weighted average APC—which can be directly compared between the different age groups. If there was no change in trend direction (i.e., no joinpoint occurred), then APC was considered equal to AAPC. To describe the trends, the terms "increase" or "decrease" were used when the trend slope (APC) was statistically significant ($P < .05$). For trends that were not statistically significant, the term "stable" was used.[9]

To draw the distribution map, the lower left corner of the Wuwei city map was taken as the origin, and a two-dimensional space Cartesian coordinate system was established. The liver cancer incidence database of 12 sentinel hospitals in Wuwei city from 1995 to 2016 was associated with the map to construct the GIS. To intuitively describe the low and high incidence areas, different colors were used for each region according to the incidence rate; this was based on the average incidence rate of liver cancer in each year. The spatial clustering analysis was performed using SaTScan 9.4 for spatio-temporal scanning, and a series of scanning circles to detect the existence and location of clustering in the study area. The relative risk (RR) of the aggregation area was determined, in addition to any statistically significant difference between the two groups.[10]

2.4. Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Air Force Medical University Ethics Committee and the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

2.5. Informed consent

Informed consent was waived off due to the retrospective design of the study.

3. Results

3.1. Basic information of inpatients with liver cancer in 12 sentinel hospitals from 1995 to 2016

Among the 2271 patients, the mean age (SD) was 58.73 (12.34) years. Most cases were found among those aged 60 to 65 years, shown in Supplemental Digital Content 1 (see Figure, Supplemental Content, which shows the number of inpatients with liver cancer by age group is shown, http://links.lww.com/MD/D648), and Supplemental Digital Content 2 (see Figure, Supplemental Content, which shows the number of patients in different age groups in different regions, http://links.lww.com/MD/D649).

Overall, there were 1,680 males (74%) comprising 1090 (74.4%), 241 (78.5%), 179 (66.1%), and 134 males (71.3%) in Liangzhou District, Minqin County, Gulang County, and Tianzhu County, respectively. There were statistically significant differences in the incidence of liver cancer by sex and by regions in one district and three counties ($P < .05$). Changes in sex distribution and sex ratio from 1995 to 2016 are shown in Table 1.

Among inpatients with liver cancer, 2238 (98.5%), 27 (1.2%), 2 (0.1%), 2 (0.1%), and 2 (0.1%) were Han, Tibetan, Hui, Tu, and Mongolians, respectively. In Liangzhou district, there were 1,461 (99.7%), 2 (0.1%), 2 (0.1%), and 1 (0.1%) Han, Tibetan, Hui, Tu, and Mongolian individuals, respectively. All the 307 people in Minqin county were Han. Gulang County had 270 (99.6%) Han and 1 (0.4%) Mongolian citizens. Tianzhu County had 161 (85.6%), 25 (13.3%), and 2 (1.1%) Han, Tibetan, and Turkish citizens, respectively. There were statistically significant differences in the incidence of liver cancer between different regions and ethnic groups ($P < .001$).

Table 1

The gender distribution and sex ratio of inpatients with liver cancer between 1995 and 2016.

Year	Male	Percent	Female	Percent	Total	Gender ratio
1995	15	1.0	8	1.3	23	1.875
1996	16	1.0	5	0.8	21	3.200
1997	15	0.9	3	0.5	18	5.000
1998	19	1.1	5	0.8	24	3.800
1999	14	0.8	3	0.5	17	4.667
2000	27	1.6	6	1.0	33	4.500
2001	31	1.8	13	2.2	44	2.385
2002	36	2.1	15	2.5	51	2.400
2003	48	2.9	12	2.0	60	4.000
2004	46	2.7	10	1.7	56	4.600
2005	60	3.6	17	2.9	77	3.529
2006	57	3.4	25	4.2	82	2.280
2007	90	5.4	23	3.9	113	3.913
2008	88	5.2	35	5.9	123	2.514
2009	131	7.8	47	8.0	178	2.787
2010	120	7.1	28	4.7	148	4.286
2011	120	7.1	45	7.6	165	2.667
2012	109	6.5	33	5.6	142	3.303
2013	118	7.0	43	7.3	161	2.744
2014	169	10.1	78	13.2	247	2.167
2015	203	12.1	68	11.5	271	2.985
2016	148	8.8	69	11.6	217	2.144
Total	1680	100.0	591	100.0	2271	2.843

By occupation, among liver cancer patients, the majority 1369 (60.3%) were peasants, and students formed the minority at 5 (0.2%). The incidence of liver cancer in patients with different occupations was significantly different on statistical analysis ($P < .001$). Supplemental Digital Content 3 (see Figure, Supplemental Content, which shows the yearly distribution of occupation from 1995 to 2016, http://links.lww.com/MD/D650). By healthcare financing methods for hospitalization settlement, most patients, 1,271 (63%), were paid through the basic social medical insurance system. This medical insurance system includes the new rural cooperative medical care system (NRCMS), basic medical insurance for urban residents and employees, basic social medical insurance (supplementary insurance), and other forms. Overall, 409 (20%), 32 (2%), and 12 (1%) patients were either self-paid, had poverty subsidy, or were treated at public expense. Supplemental Digital Content 4 (see Figure, Supplemental Content, which shows the healthcare financing methods in different regions, http://links.lww.com/MD/D651). Supplemental Digital Content 4 (see Figure, Supplemental Content, which shows the healthcare financing methods for patients from 1995 to 2016, http://links.lww.com/MD/D652).

3.2. Analysis of the temporal trends in incidence of liver cancer in 12 sentinel hospitals in Wuwei city from 1995 to 2016

As shown in Table 2, according to joinpoint regression analysis, from 1995 to 2016, the overall standardized liver cancer rate increased at an average rate of 12.80% per year (95% CI 9.5%–16.7%), with a joinpoint in 2009 (After 2009, the standard incidence of liver cancer increased less rapidly). From 1995 to 2009, the change in APC among males and females during this period was statistically significant (APC = 16.7 [95% CI: 12.3%–21.3%]). From 2009 to 2016, the APC was 5.1 (95% CI: −0.6%–11.1%).

Table 2

The age-standardized rate and APC/AAPC of liver cancer from 1995 to 2016.

	Total		Male		Female	
Year of diagnosis	Age-adjusted rate	APC 95% CI	Age-adjusted rate	APC 95% CI	Age-adjusted rate	APC 95% CI
1995	1.41		1.92		0.90	
1996	1.34		2.07		0.59	
1997	1.18		1.90		0.42	
1998	1.47		2.19		0.73	
1999	1.31		2.15		0.50	
2000	2.07		3.27		0.85	
2001	3.15		4.43		1.88	
2002	3.72		5.23		2.24	
2003	3.98		6.26		1.74	
2004	3.67		5.78		1.44	
2005	5.21		7.94		2.43	
2006	6.00		9.06		3.19	
2007	7.47		11.96		3.16	
2008	8.01		11.36		4.69	
2009	9.82*	16.71† (12.3%–21.3%)	14.36*	16.9† (12.6%–21.4%)	5.39	
2010	8.80		14.09		3.63	
2011	10.96		16.50		5.82	
2012	8.99		13.67		4.42	
2013	9.84		14.59		5.09	
2014	13.94		19.15		8.68	
2015	15.73		23.19		8.05	
2016	9.95	5.1 (-0.6%–11.1%)	13.49	4.0 (-1.6%–9.9%)	6.31	12.3 (9.8%–14.9%)
AAPC 95% CI	12.79† (9.5%–16.7%)		12.4† (9.2%–15.7%)		12.3† (9.8%–14.9%)	

* Indicates there is 1 joinpoint point in the year.

† Indicates that the APC/ AAPC is significantly different from zero at the alpha = 0.05 level.

AAPC = annual average rate of change; APC = annual percentage change; CI = confidence interval.

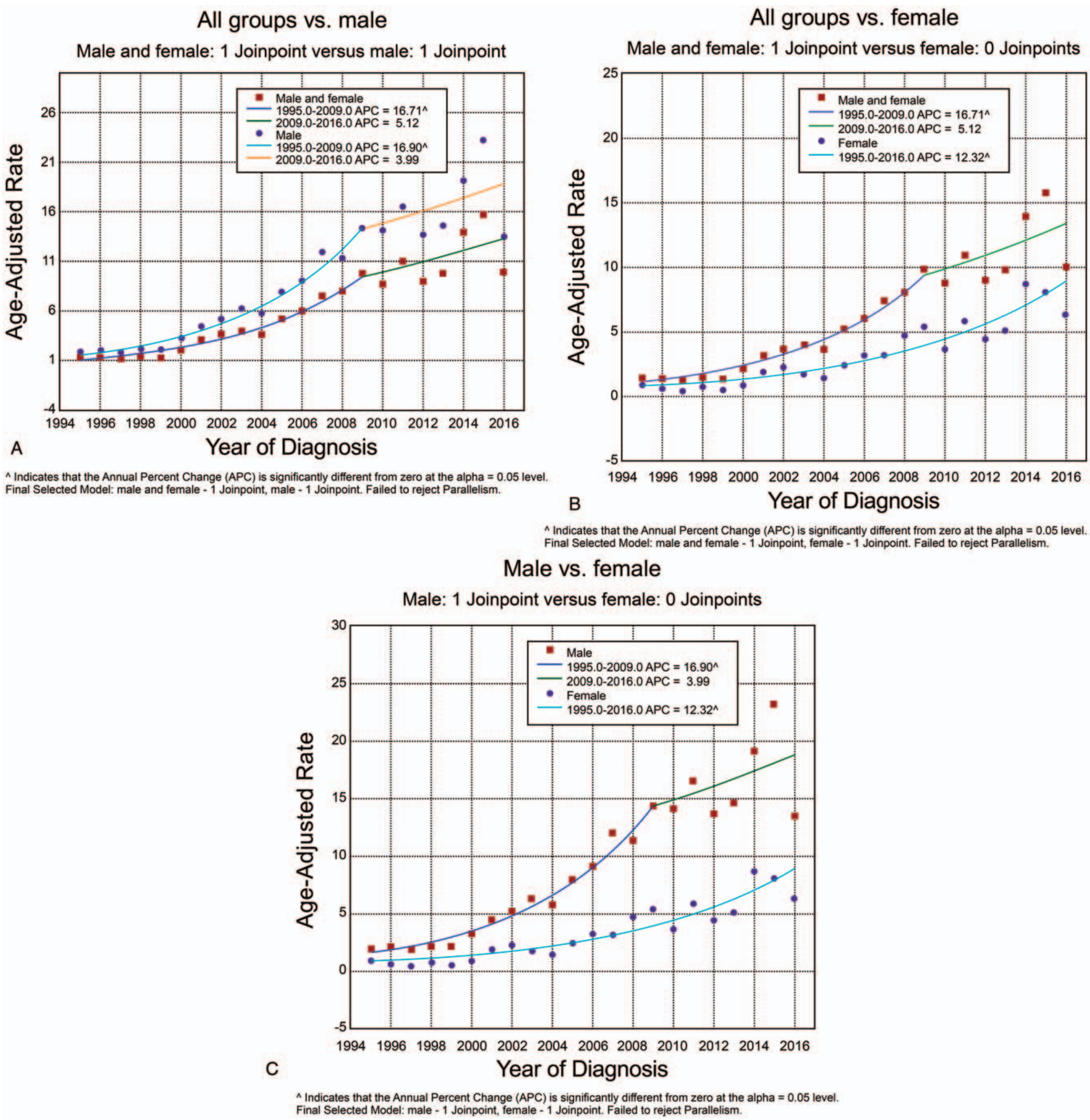

Figure 1. The time trend in liver cancer incidence in all groups and by sex from 1995 to 2016.

The standardized male liver cancer rate increased at an average rate of 12.40% per year (95% CI 9.2%–15.7%). There was a joinpoint in 2009 (a significant turning point in the slowdown). From 1995 to 2009, the change in APC among males during this period was statistically significant (APC=16.9 [95% CI 12.6%–21.4%); the APC from 2009 to 2016 was 4.0 [95% CI: −1.6%–9.9%]. The standardized liver cancer rate in females increased at an average rate of 12.3% per year (95% CI: 9.8%–14.9%), with no change in joinpoint from 1995 to 2016. However, the change in APC in females during this period was statistically significant. From 1995 to 2016, the incidence time trend in liver cancer in all groups and by sex is shown in Figure 1.

3.3. Spatial trend and spatio-temporal clustering analysis of hepatocellular carcinoma at township level in Wuwei City, Gansu Province from 1995 to 2016

In the ArcGIS software, the average annual standardized incidence rate of liver cancer in 102 townships in Wuwei was divided into five grades, and different color shades were used to represent the change in trend from low to high incidence rate, as shown in Figure 2 and Supplemental Digital Content 6 (see Figure, Supplemental Content, which shows the average annual standardized incidence rate of liver cancer, http://links.lww.com/MD/D653). The incidence distribution in each township showed

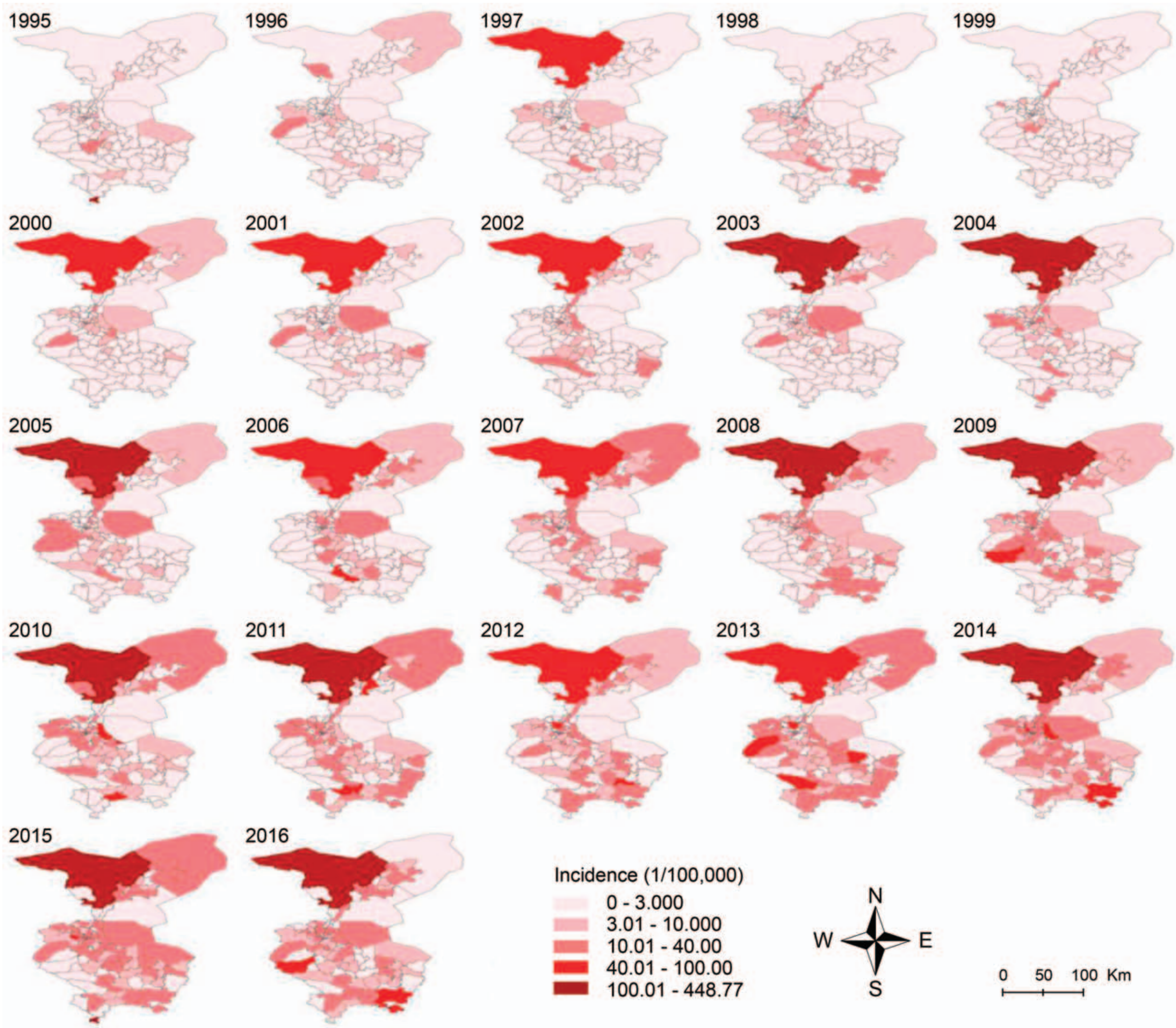

Figure 2. The incidence of liver cancer by township, in Wuwei city, from 1995 to 2016.

that Minqin County, Hongshagang town, had the highest annual incidence rate (129.45/100,000). The average annual incidence rate ranged from 185.78/100,000 (Tianzhu county, Seralon township) to 11.055/100000 in Liangzhou district, Yongchang town. There were no cases in Nanhu township, Minqin county, and Huanghuatan township, Gulang county. However, the average annual incidence was relatively low in Shibabu township, Gulang county, as well as in Dongping township, Tiantian town, and Dongdatan township, all in Tianzhu county, at 0.554, 1.259, 1.500, and 1.551/100,000, respectively. From 1995 to 2016, the incidence of liver cancer by township in Wuwei City is shown in Figure 3.

ArcGis 10.2 and SaTScan software were used to detect the spatio-temporal clustering of liver cancer incidence in Wuwei city, which showed five clusters, from 1995 to 2016. The first cluster covered 14 towns with a maximum scanning radius of 12.13 km. This was mainly distributed in Liangzhou district, subdistrict offices (Dongdajie, Xidajie, Xiguan, railway station, Dizhixincun), and other areas and offices. The clustering of time was from 2009 to 2016 with a log likelihood ratio (LLR) of 192.209749 and RR of 3.16, $P < .0000$. The second-class aggregation area was in Hongshagang town, Minqin county. For the clustering of time from 2001 to 2015, LLR was 78.073084 and RR was 28.14 ($P < .0000$). The third cluster covered two towns (Changurban-rural area and Qingyuan town of Liangzhou district). The maximum scanning radius was 24.08 km, and the agglomeration time was from 2002 to 2016 with LLR of 51.620987 and RR of 3.23, $P < .0000$. The fourth cluster covered nine towns with a maximum scanning radius of 20.28 km and was mainly distributed in the following towns of Gulang county (Sishui, Gulang, Dingning, and other areas and offices.) and of Liangzhou district (Huangyang town, Huangyang river subdistrict office, and other areas and offices.). The clustering of time was from 2014 to 2015 with LLR of 23.884652 and RR of 2.57, $P < .0000$. The fifth cluster area covered 13 towns and villages, with a maximum scanning radius of 39.52 km. It was mainly distributed in the following towns of Tianzhu Tibetan Autonomous county (Huazangsi, Shimen, Dachaigou, Songshan, and other areas and offices.), and in the following towns in Gulang county: Hengliang, Gancheng, and Heisongyi. The clustering of time was from 2011 to 2016, LLR = 19.401583, RR = 1.92, $P < .0000$. Details are shown in Table 3 and Figure 2.

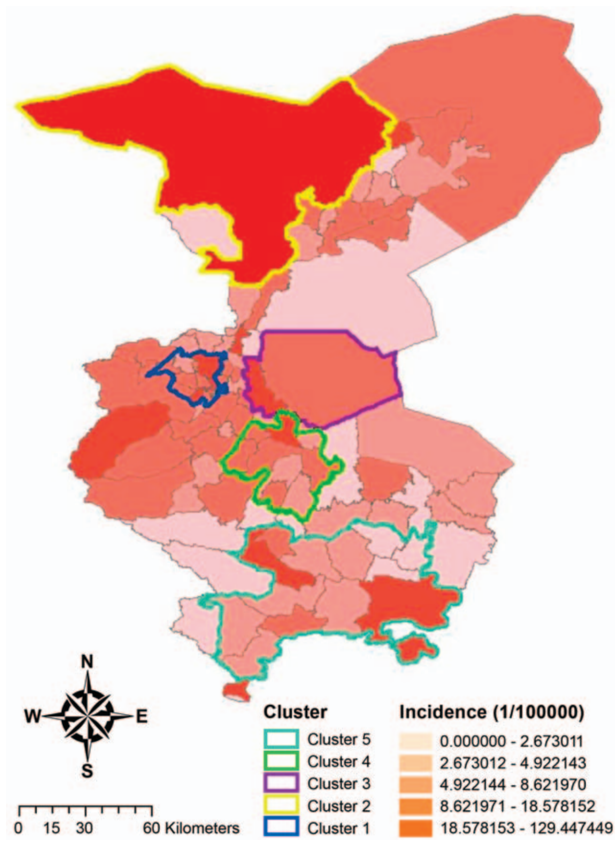

Figure 3. Spatial and temporal clustering of liver cancer incidence at township level in Wuwei city from 1995 to 2016.

4. Discussion

4.1. Basic information of inpatients with liver cancer

The average age of the patients and the age group with the highest liver cancer incidence (60–64 years), in this study were similar to the nationwide high-incidence age group.[11] Similar to the results of studies from other regions, the highest numbers of patients aged 60 to 64 years were noted in Liangzhou district, and Minqin, Gulang, and Tianzhu counties, with the overall age of onset of liver cancer concentrated among those aged 45 to 75 years.[2,12]

The incidence of liver cancer was higher in males than females with a sex ratio of 2.84, which fluctuated from 1995 to 2016, but stabilized after 2012; this was consistent with the incidence of liver cancer in previous studies. The higher incidence in males may be related to smoking, drinking, and other risk factors related to liver cancer in males[13,14] Research suggests that the inhibitory effect of estrogen on interleukin (IL)-6 and IL-Ia may be related to the low incidence of liver cancer in women.[15,16]

Differences in the incidence of liver cancer between various ethnic groups in different regions was statistically significant ($P<.001$), with the majority among those of Han ethnicity (98.5%). This was related to the ethnic composition, geographical location, and ethnic living habits in different regions. In terms of occupation, farmers formed the majority (60.3%), with significant differences in occupation by region ($P<.001$). From 1995 to 2016, the number of workers had increased to a certain extent due to changes in occupation. The increase in the overall proportion of workers may be explained by increased urbanization and industrialization in recent years.

The most common healthcare financing method (63%) among inpatients was basic social medical insurance, which mainly included the new rural cooperative medical care, and basic medical insurance for urban residents and workers. A total of 20% of the patients were fully self-funded, 2% applied for poverty subsidies, 1% paid the fees in the form of full public fees, and only 0.2% of the patients purchased commercial insurance. One district and three counties had similar healthcare financing methods, (basic social medical insurance, with the new rural cooperative medical care accounting for the largest proportion). However, a small number of patients in Liangzhou district and Tianzhu Tibetan Autonomous county had medical insurance while 18% of patients in Tianzhu Tibetan Autonomous county received poverty relief. This may be explained by the fact that the main local economic mode was agriculture and animal husbandry, with considerably slower economic development than the other regions. Owing to differences in values, the purchase rate of commercial insurance differs compared to that of foreign countries; this also increases the economic burden on sick families to some extent. However, with the overall development of China's economy, the basic social medical insurance system has gradually improved.

In December 1998, China established the basic medical insurance system for urban employees. In 2003, China's new rural cooperative medical care system was officially implemented.

Table 3

Spatio-temporal hotspots of liver cancer in Wuwei City, Gansu Province, China, 1995–2016.

Hotspots	1	2	3	4	5
Time period	Jan. 1, 2009 to Dec. 31, 2016	Jan. 1, 2001/1/1 to Dec. 31, 2015	Jan. 1, 2002 to Dec. 31, 2016	2014 to Dec. 31, 2015	2011 to Dec. 31, 2016
No. obs	464	33	110	73	116
No. exp	170.92	1.19	35.29	28.97	61.94
RR	3.16	28.14	3.23	2.57	1.92
LLR	192.209749	78.073084	51.620987	23.884652	19.401583
Annual incidence	15.9	162.3	18.2	14.7	11.0
No of counties	14	1	2	9	13
Population size	333813	1386	39659	215500	180250
Central point/ radius	(37.977600 N, 102.518000 E)/12.13 km	(38.903100 N, 102.707000 E)/0 km	(37.996100 N, 103.085000 E)/24.08 km	(37.601400N, 102.908000 E) /20.28 km	(37.056900N, 103.153000 E) / 39.52 km

LLR = log likelihood ratio; No. counties = number of counties within the hotspot; No. exp = number of expected cases; No. obs = number of observed cases; Population size = population within the hotspot; RR = relative risk for the liver cancer incidence in the hotspot compared to the average incidence at the same time period.

From 1995 to 2016, the payment method of liver cancer inpatients in Wuwei city was the new rural cooperative medical care, which was also related to the largely rural population structure in Wuwei city. With the implementation of the new rural cooperative medical care system in 2003 and improvement in the new rural cooperative medical care financing level, the NRCMS expenditure has been showing a rapid growth in recent years. The number of people benefitting from the new rural cooperative compensation has increased significantly. Moreover, the inpatient costs of cancer patients are higher; reimbursement from the social and primary medical treatment insurance system, which is only a proportion, might have also produced an effect. In January 2016, the state council integrated the basic medical insurance system for urban residents and the new rural cooperative medical care system, to establish a unified basic medical insurance system for the urban and rural residents. This integration unified the safeguard treatment of urban and rural residents. The reimbursement amount is planned to be further increased to accommodate the vast rural population; this will reduce the medical and economic burden to a certain extent.

4.2. Temporal trend

In our cohort, the incidence rate of liver cancer in males had increased gradually, while that in females was relatively stable. However, the overall incidence rate in males was higher than that in females. As the incidence of male liver cancer slows down, it is essential to address the issues of prevention and treatment of liver cancers in either gender. The APC of liver cancer in Wuwei area was significantly higher than that in the United States.[17] The results of two studies conducted in Malaysia and Shanghai show that the incidence of liver cancer is on the decline.[12,18] The higher incidence of liver cancer in Wuwei may be related to the underdeveloped economy of this area, with a gap in the dietary structure and lifestyle between the developed and underdeveloped areas. Alternatively, it may be related to the fact that Wuwei city is located in a dry and rainless area with drinking water problems, and it seriously lacks sanitation and disinfection management.

However, the declining trend in APC of liver cancer incidence was also associated with a slow growth rate. This may be explained by several factors. Etiological factors of liver cancer include hepatitis B virus (HBV) infection, dietary aflatoxins, drinking of alcohol, and smoking.[19,20] Due to the increasing strictness on blood product management, the strengthening of the preventive measures against HBV infection, and implementation of measures for purifying polluted water sources to improve water quality, the risk of HBV and aflatoxin infection has reduced. In recent years, along with the economic development, the local government is paying particular attention to drinking water sanitation, water improvement works, and rainwater collection projects, which also has an impact on the incidence of liver cancer to some extent.[21] HBV infections represent the leading cause of liver cancer and death in China. In order to prevent and control HBV transmission, a comprehensive prevention strategy was initiated in 1992 that included universal vaccination of infants, screening of all pregnant women for HBV, administration of post-exposure prophylaxis to infants born to hepatitis B surface antigen (HBsAg)-positive women, catch-up vaccination of children and adolescents, and vaccination of adults who are at increased risk of infection.[22] Studies have shown that the prevalence of vaccine-induced immunity in Wuwei City is slightly higher than the rates in the United States between 1999 and 2006, suggesting that the comprehensive HBV vaccination was successful.[23] All these measures have led to a change in the incidence of liver cancer.[24,25] Joinpoint analysis revealed that the comprehensive prevention strategy in Wuwei was effective. From the inception of the comprehensive prevention and control strategy in 1992, the standardization rates for liver cancer increased slowly since 2009. In addition, China began the sale and free distribution of HBV vaccine for newborn babies in 1992 and 2002, respectively. In particular, hepatitis B vaccine reseeding was conducted in children under 15 years of age in 2009.[26] Therefore, it is expected that the standardization rates for liver cancer in Wuwei may decrease in the future.

4.3. Spatial trend and spatio-temporal clustering analysis

The incidence distribution in towns and villages showed that the annual incidence was the highest in Hongshagang town, located in the northwest of Wuwei city, a desert geomorphic unit in the north, suffering from drought and water shortage. The average annual incidence of liver cancer in four townships (Shibabu, Dongping, Tiantang, and Dongdatan) was relatively low. Most towns located in the south of Wuwei city and Tianzhu county differ from other towns in their geographical location, dietary structure, and in the local lifestyle. At present, studies have found a relationship between the quality of drinking water in a geological environment and the incidence of liver cancer. In the 1970s, studies showed that the etiology of liver cancer includes the source of drinking water and suggested that the regional high incidences of liver cancer in local residents are related to drinking polluted water. From 1995 to 2016, the incidence of liver cancer in Wuwei city showed a fluctuating but increasing trend. According to Figure 2, before 2004, the incidence of liver cancer was generally low, with only a few towns having a high incidence.

ArcGis 10.2 and SaTScan software were used to detect the spatio-temporal clustering of liver cancer incidence in Wuwei city. The results showed that the incidence of liver cancer in each township was nonrandom and had a certain spatial aggregation. Among the five clusters of liver cancer incidence in Wuwei city, the first covered 14 towns and villages, (clustering of time from 2009 to 2016; log likelihood ratio [LLR] = 192.209749, relative risk [RR] = 3.16, $P < .0000$); the second cluster area covered two townships, with a clustering time from 2001 to 2015 (LLR = 78.073084, RR = 28.14, $P < .0000$); the third cluster area covered two towns, with the maximum aggregation period from 2002 to 2016 (LLR = 51.620987, RR = 3.23, $P < .0000$); the fourth cluster area covered nine towns, and the gathering time was from 2014 to 2015 (LLR = 23.884652, RR = 2.57, $P < .0000$); and the fifth cluster area covered 13 towns, and the clustering time was from 2011 to 2016 (LLR = 19.401583, RR = 1.92). The results from spatial scanning and basic spatial distribution as well as of clustering in time and time trend analysis were consistent. Special attention should have been paid to the high incidence of liver cancer cases in Hongshagang town.[20] It is also suggested that due to the high incidence in aggregation areas in towns and villages, such as in Changcheng and Qingyuan town, residents should carefully select daily food items, particularly fresh fruits and vegetables, as also the drinking water, to avoid organic pollutants in drinking water that can be injurious to human health.[27] Relevant regions should also adopt local control measures and take into account other local environmental factors (viral infections, smoking, alcohol drinking, and other risk factors) to strengthen the comprehensive regional prevention and treatment of liver cancer.

According to the temporal trend analysis, from 1995 to 2016, the overall standardized liver cancer rate increased at an average rate of 12.80% per year. After 2009, the standard incidence of liver cancer demonstrated a less rapid increase. The standardized male liver cancer rate, which was slightly higher than that of females, tended to slow down after 2009. Along with economic development, there is a need to pay more attention to drinking water sanitation, in-depth development of water, and rainwater catchment projects to address these factors. In-depth water improvement works and rainwater catchment projects are factors that may contribute to a decline in liver cancer incidence. The spatial-temporal clustering of liver cancer incidence showed a nonrandom distribution, with a certain spatial clustering pattern. There were five aggregation areas of liver cancer incidence in Wuwei city. The results of spatial scanning and clustering in time and time trend analysis are consistent with the basic spatial distribution results.

According to the spatial trend analysis, the results of the incidence distribution in each township show that the difference in incidence was related to geographical location, dietary structure, lifestyle, drinking water, and sanitation. The incidence of liver cancer was generally low before 2004.

5. Limitations

This study used a retrospective study design with a long-term span. Thus, the available research materials were more restricted, because we were unable to obtain some effective information, especially in the early period of the clinical medical records data collection. Therefore, there might have been some missing data. Furthermore, along with the social economy, science and technology development as well as medical treatment, many of the current common diagnostics, treatments, or drugs were not available previously. Therefore, the factors that were analyzed and discussed in this research, as well as the interpretation of the research content were limited. In a follow-up research, variables with missing data in this study can be further explored. Moreover, morbidity data included in this study were extracted from the inpatients' medical records from 1995 to 2016 in 12 Sentinel hospitals in Wuwei city. This limited the demographic representation of the field of study. In the future, the research field will be further expanded, involving more provinces and even the entire China, to further explore the temporal trend and regional distribution of liver cancer.

6. Conclusions

In conclusion, as a chronic disease with poor prognosis, liver cancer can cause a great burden to the society. Although the results of this study showed that the incidence of liver cancer in Wuwei is different from that in some provinces and regions of China, there was no significant downward trend, but the growth rate of liver cancer in this region was significantly slower. The findings of this study can be used to strengthen the regional prevention and treatment programs on liver cancer in terms of the environmental factors and geographical characteristics in high incidence areas. Regular disease screening, early diagnosis, and treatment should be strengthened for the high-risk population. Strengthen the prevention and control measures of viral hepatitis, carry out measures to purify and pollute water sources and improve water quality in poor mountainous areas, and provide quality education to the public regarding the safety and health of food and drinking water. Especially in areas with a high incidence of liver cancer, measures should be taken according to local conditions, and other local environmental factors (virus infection, smoking, drinking, and other risk factors) should be considered to strengthen the regional comprehensive prevention and treatment of liver cancer.

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