Gastrointestinal Cancer

Incidence and Patterns of Liver Cancers in Sri Lanka from 2001 to 2010: Analysis of National Cancer Registry Data

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Abstract

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Objectives Varying trends in the incidence of liver cancer have been observed in many Asian countries. We conducted this study to examine trends in liver cancer incidence and histological patterns in Sri Lanka.

Materials and Methods All newly diagnosed patients with liver cancer included in Sri Lanka National Cancer Registry during 2001 to 2010 were analyzed.

Statistical Analysis Joinpoint regression analysis was performed. A *p*-value of less than 0.05 was considered statistically significant.

Results Overall, 1,482 (male:female = 2.7:1; mean age = 57.5 years) liver cancers were analyzed. Majority were hepatocellular carcinomas (*n* = 1,169; 78.9%), followed by intrahepatic cholangiocarcinomas (*n* = 100; 6.75%). Highest incidence of liver cancer was observed in 70–74-year age group (5.1/100,000). Overall, the World Health Organization age-standardized rate (ASR) has increased during 2001 to 2004, from 0.6/100,000 (95% confidence interval [CI] = 0.48–0.72) to 1.0/100,000 (95% CI = 0.85–1.15), with an estimated annual percentage change (EAPC) of 17.8 (95% CI = 5.0–46.2); $p > 0.05$. From 2004 to 2010, a gradual decline in the incidence was observed. ASR in 2010 was 0.96 (95% CI = 0.81–1.1), with an EAPC of −0.9 (95% CI = −6.7 to 5.4); $p > 0.05$. Similar patterns of incidence change were observed in both genders.

Conclusions Overall, the incidence of liver cancer appears to be steadily declining in Sri Lanka. Similar patterns of incidence change were observed in both genders. The actual decline is likely to be greater as it is likely that diagnostic scrutiny and reporting would have improved during the study period.

Keywords
- incidence
- age-standardized rate
- liver cancer
- Sri Lanka
- National Cancer Registry

Introduction

Globally, liver cancer is the fifth most common malignancy in males (554,000 cases; 7.5% of the total) and the ninth in females (228,000 cases; 3.4%).[1] Liver cancer is a major burden in developing countries where 83% of the approximately 800,000 new cancer cases were reported in 2012.[1] Furthermore in 2012, liver cancer was the second leading cause of cancer-related deaths worldwide (approximately 745,000; 9.1% of the total). The ratio of mortality to incidence

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is high for liver cancer (0.95) due to the general poor prognosis. As a result, the geographical patterns of incidence and mortality remain quite similar.[1] In males, high incidences were seen in Eastern and South-Eastern Asia (age-standardized rates [ASRs]: 31.9 and 22.2, respectively) and the lowest rates in Northern Europe and South-Central Asia (ASRs: 4.6 and 3.7, respectively). The rates were much lower in females, with the highest reported rates in Eastern Asia and Western Africa (ASRs: 10.2 and 8.1, respectively).[1] In Sri Lanka, according to the 2010 cancer registry data, the estimated age-standardized mortality rate per 100,000 population for males and females were 4.2 and 2.3, respectively.[2]

Varying patterns were shown with regard to the incidence of liver cancers in Asia. Countries such as China and Japan have shown a reduction in the incidence in both men and women with corresponding reductions in mortality rates. Thailand reported an increase in the incidence in both men and women while a substantial rise in mortality is reported from Singapore, especially among women.[1,3]

In Sri Lanka, liver cancer incidence is less common compared to other parts of Asia and the trend in the incidence has not been previously studied.[2] The National Cancer Control Programme (NCCP) in Sri Lanka has been collecting nationwide cancer data since 1985. Over the last three decades, the coverage has gradually increased and as of 2014, it is estimated to include at least 80% of all cancers diagnosed in Sri Lanka.[2,4] The data include all cancers treated at the national cancer institutions and other major government and private hospitals and pathology laboratories. This study was aimed to describe the incidence of liver cancers in Sri Lanka based on data from the NCCP. Furthermore, the age- and gender-specific liver cancer incidence rates have also been assessed.

Subjects and Methods

Data of all patients with liver cancer diagnosed during the period between January 1, 2001, and December 31, 2010, were obtained from the NCCP, Sri Lanka.[2] The classification of liver cancer was based on ICD-10—*International Classification of Diseases, Tenth Revision*—system (CD22). The data on age, gender, and histology type were pooled and analyzed. ASRs of liver cancer per 100,000 population were calculated for each year by gender, using the World Health Organization (WHO) age-standardized populations.[5] Moreover, gender- and age-specific rates were also calculated for each year under consideration. Age in years was categorized into 0–44, 45–59, 60–74, and 75 and more.

Joinpoint regression analysis was used to identify trends in the incidence of liver cancer over the study period.[6] This study followed the same methodology that analyzed the incidence of common cancers in Sri Lanka.[7–12] Joinpoint analysis creates minimum number of joinpoints, and tests whether the change between one and more joinpoints are statistically significant. Joinpoint tests of significance use a Monte Carlo permutation method.[13] In the final model, each joinpoint indicates a statistically significant change in the trend. An estimated annual percentage change (EAPC) was computed for each of those trends by means of generalized linear models assuming a Poisson distribution. Changes in direction or in the rate of increase or decrease were calculated with p-values, and p-values <0.05 were considered as statistically significant. Joinpoint software version 4.3 was used for Joinpoint regression analysis.

Results

A total of 1,482 liver cancers diagnosed over the 10-year study period was analyzed. There were 1,086 (73.3%) males and 396 (26.7%) females with a male to female ratio of 2.7:1. The overall mean age of study patients was 57.5 years; the mean age in males was 60.0 and in females was 50.6 years. Highest incidence of liver cancers was observed in 70–74-year age group overall (5.1 per 100,000 population), as well as for female and male groups (8.5 and 2.1 per 100,000 population, respectively; ►Fig. 1). Of those, 1,169 (78.9%) were hepatocellular carcinomas (HCCs), and 100 (6.75%) were intrahepatic cholangiocarcinomas (ICCs). Other histological types included hepatoblastoma (n = 67; 4.5%), adenocarcinoma (n = 43; 2.9%), and other histology types (n = 37; 2.5%). Around 4.5% (n = 66) were classified as malignant neoplasm, not otherwise specified.

Results of liver cancer incidence in Sri Lanka with Joinpoint analysis of trends by gender and age group according to the WHO ASRs are shown in ►Table 1. The incidence of liver cancer in Sri Lanka was observed to have increased from 0.6 per 100,000 in 2001 (95% confidence interval [CI] = 0.48–0.72) to 1.0 per 100,000 in 2004 (95% CI = 0.85–1.15): a 1.7-fold increase ($p > 0.05$ for trend), with an EAPC of 17.8 (95% CI = –5.0 to 46.2). This is followed by a slightly declining trend from 2004 to 2010 to an ASR of 0.96 in 2010 (95% CI = 0.81–1.1) with an EAPC of –0.9 (95% CI = –6.7 to 5.4; ►Fig. 2, ►Table 1). The proportional increase in incidence was greater for males with a similar pattern compared with females (►Fig. 2, ►Table 1). The overall cancer incidence in both genders is shown in ►Fig. 3.

Analysis of the overall cohort in terms of the age-related incidence of liver cancer showed variations in the trend of incidence depending on the age category. The <45-year age category showed an increasing trend with an EAPC of 5.8 (95% CI = –1 to 12.9; $p > 0.05$). Similarly, the 60–74-year category showed an increasing trend with an EAPC of 6.4 (95% CI = 1.9–11; $p < 0.05$). However, 45 to 59 and 75+ age

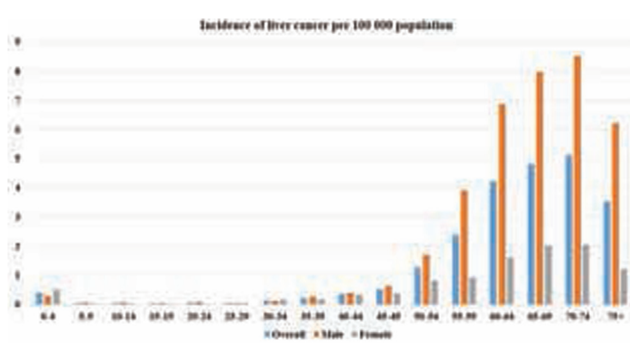

Fig. 1 Incidence of liver cancer with age (per 100,000 population).

Table 1 Liver cancer incidence in Sri Lanka by gender and age group with Joinpoint analysis 2001–2010

2001		2010		EAPC 2001–2010 (95% CI)		
n	Rate (95% CI)	*n*	Rate (95% CI)			
Age group (y): Male						
0–44	7	0.10	15	0.19	–	
45–59	31	2.18	27	1.73	–	
60–74	32	5.03	76	10.92	–	
75+	7	3.74	12	5.85	–	
Age standardized	77	1.0 (0.78–1.23)	130	1.59 (1.32–1.86)	Segment 1: 2001–2004	16.2 (−1.8 to 37.5)
					Segment 2: 2004–2010	0.8 (−4 to 5.8)
Age group (y): Female						
0–44	6	0.09	18	0.23	–	
45–59	2	0.13	8	0.49	–	
60–74	8	1.15	10	1.30	–	
75+	3	1.38	2	0.84	–	
Age standardized	19	0.2 (0.1–0.3)	38	0.4 (0.3–0.5)	1.2 (−7 to 10.2)	
Overall age-standardized rate	96	0.6 (0.48–0.72)	168	0.96 (0.81–1.1)	Segment 1: 2001–2004	17.8 (−5 to 46.2)
					Segment 2: 2004–2010	−0.9 (−6.7 to 5.4)

Abbreviations: CI, confidence interval; EAPC, estimated annual percentage change.

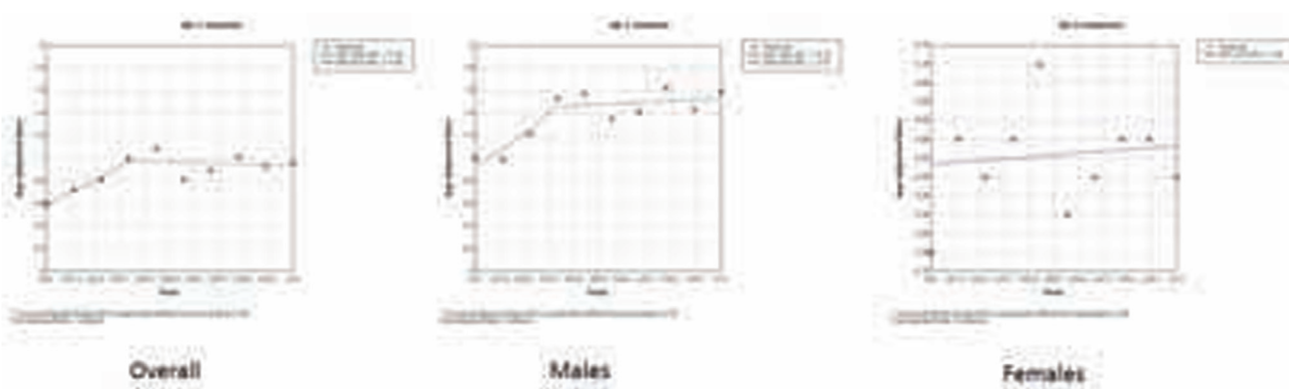

Fig. 2 Joinpoint regression analysis of trends of age-standardized rate in liver cancer incidence including all histology types.

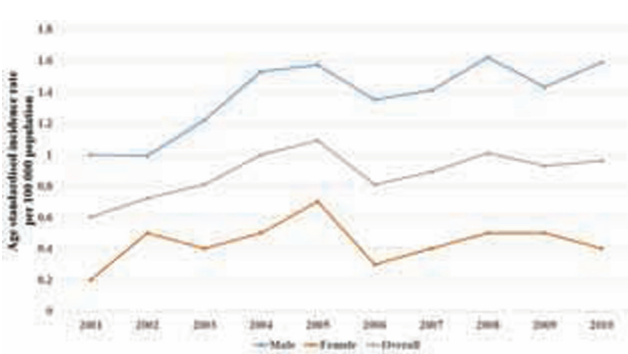

Fig. 3 Age-standardized rate of liver cancer from 2001 to 2010.

groups showed an early increasing trend followed by a sharp decreasing trend (►Fig. 4). A similar trend was seen in males where an increasing trend was noted in the age categories of <45 years and 60 to 74 years, with an EAPC of 3.3 (95% CI = −3.3 to 10.4; $p > 0.05$) and 8 (95% CI = 4.2–11.9; $p < 0.05$), respectively; whereas, the 45 to 59 and 75+ age categories showed a mild decreasing trend with an EAPC of −0.5 (95% CI = −6.9 to 6.3; $p > 0.05$) and −1.4 (95% CI = −9.2 to 7.2; $p > 0.05$; ►Fig. 5), respectively. Similar trends were also noted in females; however, highest magnitude of the increasing trend was observed in 0–44-year age category with an EAPC of 8.3 (95% CI = 0.7–16.5), which was statistically significant ($p < 0.05$; ►Fig. 6).

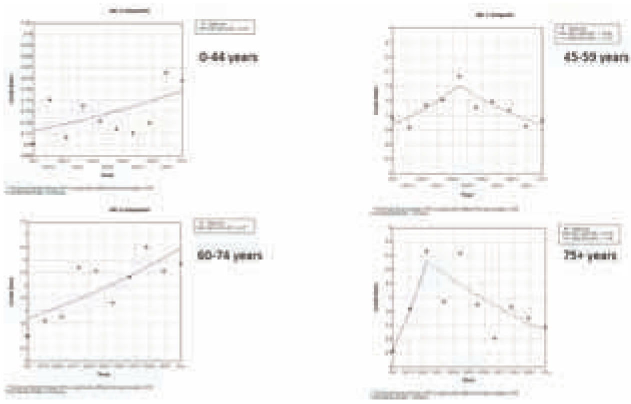

Fig. 4 Joinpoint regression analysis of overall age-categorized trends in incidence of liver cancer.

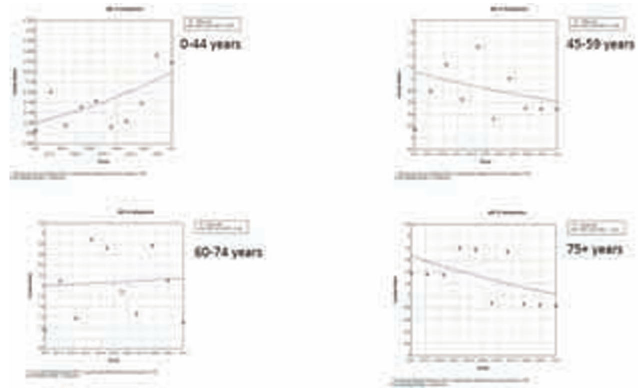

Fig. 6 Joinpoint regression analysis of age-categorized trends in incidence of liver cancer in females.

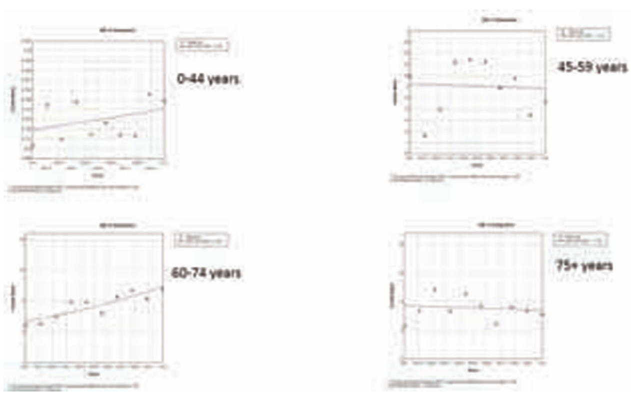

Fig. 5 Joinpoint regression analysis of age-categorized trends in incidence of liver cancer in males.

Discussion

In our study, we used the data obtained from the NCCP during the period 2001–2010 to identify the trends in the incidence of liver cancer in Sri Lanka. Overall, the incidence of liver cancer appears to be steadily declining in Sri Lanka since 2004. The actual decline is likely to be greater as it is likely that diagnostic scrutiny and reporting would have improved during the study period.

Globally, liver cancer is widely regarded as one of the cancers with highest mortality rates, though it is relatively uncommon when compared to other common malignancies including breast or colorectal malignancies.[1] The patterns of incidence of liver cancer are mainly studied in the developed world and the data from developing countries are relatively sparse.[14] A wide variation in the trends in incidence has been noted during the past decade among these different countries. For instance, generally increasing incidences are seen in developed countries, including countries of North America, Western Europe, and Oceania.[14] However, these countries reported the lowest incidence of liver cancer worldwide. In contrast, decreasing trends in the incidence of liver cancer was observed in Europe and some countries in Asia, where the incidence rates are relatively greater. The countries with highest reported incidence of liver cancer include China, Philippines, and Japan.[14] Even among the Asian countries, a wide variation in the incidence of liver cancer is observed. For instance, the incidence in Eastern and South-Eastern Asia is far greater compared with South-Central Asia, which include India, Pakistan, and Sri Lanka.[14] However, recent analysis has shown that the liver cancer incidence rates continue to increase in some of the traditionally low-risk regions while a decreasing trend has been observed in highest-risk countries in Asia.[14]

HCCs are the commonest primary liver cancer, followed by ICC.[14] In Sri Lanka, a variety of risk factors may have given rise to the observed trends in the patterns of liver cancer. The identified risk factors for HCC include chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, exposure to dietary aflatoxin, fatty liver disease, alcohol-induced cirrhosis, obesity, diabetes, smoking, and iron overload,[3,14] while the identified risk factors for ICC include chronic liver fluke infestation and cirrhosis.[3,14]

Although chronic HBV and HCV infections are well-recognized risk factors for liver cancer, their contribution to liver cancer in Sri Lanka is not well understood. No reliable data are available on the national prevalence or the trends of HBV and HCV infections in Sri Lanka. However, the regional estimates show a very low prevalence of HBV and HCV infections in Sri Lanka.[15] Therefore, their contribution is likely to be minimal. Studies have shown a high prevalence of fatty liver disease in Sri Lanka, which is a major risk factor for cirrhosis and subsequent HCC.[16] Although nonalcoholic fatty liver disease has been common in the Western countries such North America and Europe, a rapidly rising nonalcoholic fatty liver disease is observed in Asian countries including Sri Lanka.[16,17] Furthermore, metabolic risk factors for liver cancer such as central or overall obesity, type 2 diabetes mellitus, hypertension, dyslipidemia, and metabolic syndrome have also become increasingly prevalent in Sri Lanka.[16,18,19]

Heavy alcohol consumption and cigarette smoking are among the risk factors for liver cancer and may play a vital role in the increased incidence especially among males. In Sri Lanka, the consumption of alcohol has shown an increase over the recent years, which may have contributed to chronic liver disease associated with HCC.[20] On the other hand, a decreasing trend in the prevalence of smoking is observed in

Sri Lanka since the late 1970s.[21] Therefore, the role of smoking and alcohol in the incidence of HCC is not clear. Other risk factors such as exposure to dietary aflatoxin are unlikely to be important factors in the etiology of liver cancer in Sri Lanka.[18]

Although an increasing trend in the incidence was expected due to better diagnostic scrutiny and improvements in cancer recording and reporting in the country similar to other malignancies including breast, thyroid, and colorectal, a decreasing trend was observed for liver cancers since 2004. In Sri Lanka, the HBV vaccine was introduced into the national immunization program in 2003, and therefore it is unlikely to have caused the decreasing trend. Further prospective studies including risk factor analysis will be helpful to identify the cause of the decreasing incidence.

Limitations

Proper documentation of liver cancer-related data was not available during the civil war (i.e., 1983–2009) in the northern and eastern parts of the country. We were unable to analyze outcomes of liver cancers or its association with tumor stage as staging and outcomes were not implemented in the NCCP till 2007. Furthermore, NCCP data did not include many other important information that would have helped to identify possible reasons for the observed trends in incidence. For instance, tumor biological characteristics, body mass index, chronic liver disease, HBV status, method of detection, and other established risk factors were not available in the NCCP database. Collection of such information in the future may help better understand the reasons for observed trends in incidence.

Conclusion

Overall, the incidence of liver cancer appears to be steadily declining in Sri Lanka. The actual decline is likely to be greater as it is likely that diagnostic scrutiny and reporting would have improved during the study period. The reasons for the observed trends are not clearly understood. Further prospective studies including risk factor analysis will be helpful to identify the cause of the observed trends in liver cancer incidence in Sri Lanka.

Ethical Approval Statement

Ethical approval for th is study was obtained from the ethical review committee of Faculty of Medicine, University of Colombo.

Authors' Contributions

UJ, VU, and AF analyzed the data and wrote the first version of the manuscript. AF, SS, and DNS provided the data, advised on analysis, and provided comments on the manuscript. UJ, VU, SS, and DNS conceived the idea, supervised the data analysis, and wrote the final version of the manuscript. All authors read and approved the final manuscript.

Declaration

The abstract of this study was presented at the Asian-Pacific Digestive Week 2019 held in Kolkata, India.[22]

List of Abbreviations

WHO: World Health Organization
EAPC: Estimated annual percentage change
CI: Confidence interval
ASR: Age-standardized rate
HCC: Hepatocellular carcinoma
ICC: Intrahepatic cholangiocarcinoma
HBV: Hepatitis B Virus
HCV: Hepatitis C Virus

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None.

Conflict of Interest

None declared.

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None.

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