Trends in Global, Regional, and National Burden and Quality of Care Index for Liver Cancer by Cause from Global Burden of Disease 1990-2019

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Despite the tremendous burden of liver cancer and its underlying causes on humankind, there appear to be heterogeneities in coping approaches. The objective of this study was to compare the burden and the quality-of-care of liver cancer by causes among different countries and regions in both sexes and various age groups 1990-2019. Data of liver cancer and underlying causes, including hepatitis B virus (HBV), hepatitis C virus (HCV), alcohol use, nonalcoholic steatohepatitis (NASH), and other causes were obtained from the Global Burden of Diseases 2019. Incidence, prevalence, death, and disability-adjusted life-years (DALYs) were assessed. Principal component analysis was used to combine age-standardized mortality-to-incidence ratio, DALY-to-prevalence ratio, prevalence-to-incidence ratio, and years of life lost–to–years lived with disability into a single proxy named Quality of Care Index (QCI). Globally, the age-standardized incidence, DALYs, and death rates decreased from 1990 to 2019, while the QCI scores increased by 68.5%. The QCI score of liver cancer was from as high as 83.3 in high Sociodemographic Index (SDI) countries to values as low as 26.4 in low SDI countries in 2019. Japan had the highest QCI score (QCI = 100). The age-standardized death rates of liver cancer due to all underlying causes were decreasing during the past 30 years, with the most decrease for HBV. Consistently, the global QCI scores of liver cancer due to HBV, HCV, alcohol use, NASH, and other causes reached 53.5, 61.8, 54.3, 52.9, and 63.7, respectively, in 2019. *Conclusion:* Although the trends in burden are decreasing and the QCI improved from 1990 to 2019 globally, there is a wide gap between countries. Given the inequities in health care quality, there is an urgent need to address discrimination and bridge the gap. (*Hepatology Communications* 2022;6:1764-1775).

Liver cancer is the sixth most common diagnosed cancer and ranked fourth in cancer-related mortality in 2018.[1-3] The World Health Organization (WHO) has reportedly warned that the number of deaths will have exceeded one million by 2030.[4] Globally, there have been 905,677 newly diagnosed and 830,180 deaths due to liver cancer by 2020, which was more than twice the homologous epidemiological measures among men than women.[5]

Abbreviations: DALY, Disability-adjusted life-year; GBD, Global Burden of Disease; HBV, Hepatitis B virus; HCV, Hepatitis C virus; ICD-10, International Classification of Diseases, 10th revision; NASH, Nonalcoholic steatohepatitis; QCI, Quality of Care Index; SDI, Sociodemographic Index; UI, Uncertainty interval; WHO, World Health Organization.

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Current increases in the incidence and the mortality rates of liver cancer are attributable to an increase in liver cirrhosis, which resulted primarily from underlying causes including hepatitis B virus (HBV), hepatitis C virus (HCV), alcohol use, nonalcoholic steatohepatitis (NASH), and other causes.(6-8) Therefore, liver cancer control has been the result of identifying these underlying causes and implementing specific preventive measures in terms of HBV vaccination, antiviral treatment, and reducing exposure to alcohol and other metabolic risk factors.(6)

Despite the tremendous burden of liver cancer and its underlying causes on humankind, there appear to be heterogeneities in coping approaches, and the implementation of current professional knowledge to achieve desired health outcomes has not been fruitful.(9) Less than 20% of the high-risk population undergo screening tests.(10) Diagnostic tools, including ultrasound for the diagnosis of liver cancer, have lower accuracy and sensitivity.(11) Therefore, there is an urgent need to assess the quality of care provided for at-risk and high-risk patients for liver cancer.

The Global Burden of Disease (GBD) 2019 provided detailed data on the epidemiological measures of liver cancer from 1990 to 2019. Although previous GBD studies compared various measures and metrics of liver cancer at global, regional, and national levels, the comprehensive data pointing out the quality of care of liver cancer among various nations and countries were scarce. In addition, the lack of a comprehensive index quantifying the various aspects of quality of care of liver cancer is a cardinal problem.

Herein, we present an index of quality of care for liver cancer, the Quality of Care Index (QCI), which assesses the disparate aspects of quality of care among various age groups, genders, and regions. The objective of this study was to compare the burden and the quality of care of liver cancer and its underlying causes among different nations and regions in both sexes via the QCI from 1990 to 2019, using the data of GBD 2019.

Materials and Methods

DATA COLLECTION

Data were derived from GBD 2019, which provides data on 369 diseases and 87 risk factors by the Institute for Health Metrics and Evaluation, including 204 countries and territories. GBD grouped all countries and territories into 21 regions and seven super-regions. The seven super-regions are high income; Latin America & Caribbean; Sub-Saharan Africa; North Africa & Middle East; Southeast Asia, East Asia & Oceania; South Asia; and Central Europe, Eastern Europe & Central Asia.(12) Regions of GBD studies were presented in Fig. 1. Data included all epidemiological measures and metrics for liver cancer (GBD code: B.1.7) and its underlying causes, including HBV (GBD code: B.1.7.1), HCV (GBD code: B.1.7.2), alcohol use (GBD code: B.1.7.3), NASH (GBD code: B.1.7.4), and a fifth group of "other causes" such as aflatoxin consumption and autoimmune hepatitis (GBD code: B.1.7.5). Defining the underlying causes of liver cancer was based on the International Classification of Diseases, 10th revision (ICD-10), which is generally determined by a physician's decision.(13) Deaths in ICD-10 subgroups C22-C22.8 and D13.4 (malignant neoplasm of liver and intrahepatic bile ducts) were proportionally redistributed into liver cancer due to

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HBV, HCV, alcohol use, NASH, and other causes.[12] ICD-10 codes C22-C22.4, C22.7-C22.9, and Z85.05 were used for mapping new cases.[14]

QCI

Epidemiological measures including incidence, prevalence, mortality, disability-adjusted life years (DALYs), years of life lost (YLLs), and years lived with disability (YLDs) are six current significant variables used in quantifying the epidemiologic status for specific diseases. The secondary indices were as follows: (1) mortality to incidence ratio, (2) DALYs-to-prevalence ratio, (3) prevalence-to-incidence ratio, and (4) YLLs to YLDs ratio. Each of these indices indirectly assesses the particular aspect of the quality of care of liver cancer. Principal component analysis was performed to convert these four newly combined indices to QCI as a summary measure. Principal component analysis is the most widely used technique for interpreting widespread data sets; it drastically reduces the dimensionality of data sets in an interpretable way, while preserving as much variability as possible.[15] In this sense, using principal component analysis, we convert four diverse secondary indices into an interpretable index that highlights the quality of care of liver cancer among different locations, age groups, and genders. Previously, we used the current index for quantifying the quality of care of hematologic, thyroid, brain, central nervous system cancers, and ischemic heart diseases [16-20]. The four secondary indices were calculated as follows:

$$\text{Mortality to incidence ratio} = \frac{\#\text{Age} - \text{standardizaedMortality}}{\#\text{Age} - \text{standardizaedIncidence}}$$

$$\text{DALY to prevalence ratio} = \frac{\#\text{Age} - \text{standardizaedDALY}}{\#\text{Age} - \text{standardizaedPrevalence}}$$

$$\text{Prevalence to incidence ratio} = \frac{\#\text{Age} - \text{standardizaedPrevalence}}{\#\text{Age} - \text{standardizaedIncidence}}$$

$$\text{YLL to YLD ratio} = \frac{\#\text{Age} - \text{standardizaedYLL}}{\#\text{Age} - \text{standardizaedYLD}}$$

DATA VALIDATION

The Healthcare Access and Quality Index, provided by GBD in 2016, assessed individual health care access across the world. This index has been considered for 32 causes.[21,22] To validate the current QCI index, we calculate the correlation between QCI and the Healthcare Access and Quality Index for liver cancer. A mixed-effect regression model of QCI as a dependent variable and inpatient health care utilization, outpatient healthcare utilization, deaths, prevalence, and attributed death rates to all risk factors as independent variables while considering countries as random effects were applied. The Pearson correlation coefficient between predicted values and the Healthcare Access and Quality Index for liver cancer was 0.6.

DATA ANALYSIS

All epidemiological measures used for the calculation of QCI were presented with 95% uncertainty intervals (UIs). Age groups with the intervals of 5 years (i.e., less than 20, 20-24, …, 75-79, and 80+) were used in this survey. The GBD world population standard was used for the calculation of age-standardized rates. QCI ranges from 0 to 100, and the closer to 100, the better quality of care status. The QCI was calculated among both men and women for liver cancer and all of its five significant causes. The gender disparity ratio was obtained based on the following formula, where the ratio closer to 1 implied more equality:

$$\text{Gender Disparity Ratio} = \frac{\text{QCIforfemales}}{\text{QCIformales}}$$

We also used the Sociodemographic Index (SDI), provided by the GBD, to estimate the QCI score based on development status for each country. SDI quintiles were cardinally calculated based on three factors: (1) average income per person, (2) educational attainment, and (3) total fertility rate. SDI scores were categorized into five quintiles including high SDI, high-middle SDI, middle SDI, low-middle SDI, and low SDI. Data analysis and all illustrations were performed using R software version 4.0.2 (http://www.r-project.org, RRID: SCR_001905).

Results

BURDEN OF LIVER CANCER

Globally, the age-standardized incidence of liver cancer in 2019 was 6.5 (95% UI: 6.0-7.2) per 100,000, which indicates a 27.5% (–37.3 to –15.7) decrease between 1990 and 2019. Liver cancer also accounted for an age-standardized death rate of 5.9 (5.5 to 6.4) per 100,000, indicating a decrease since 1990 (−33.4% [−41.9 to −23.2]). Simultaneously, the age-standardized DALYs rate showed a 41.5% (−49.8 to −31.5) decrease. While the high SDI region had the highest incidence rates, the death rates were the lowest (Table 1). Among liver cancer underlying causes, HBV had the highest age-standardized burden rates in 2019; however, the corresponding rates have decreased during the past 30 years. In addition, the age-standardized death rates of liver cancer due to four other underlying causes were decreasing in the same period. For detailed information regarding the burden of liver cancer, see the Appendix (pp. 3-5) and Supporting Figs. S1-S3).

QCI

Liver Cancer

Globally, the age-standardized QCI score of liver cancer was 55.7 by 2019, with 50.8 in females and 56.3 in males. From 1990 to 2019, the QCI score of liver cancer has been increasing constantly, and increased by 68.5% (ΔQCI = 22.7) from 33.1 in 1990. The age-standardized QCI scores were consistently highest and lowest among countries of high income (83.2 in 2019) and Sub-Saharan Africa (27.9 in 2019) super-region across the years, respectively. The difference between the highest and lowest super-regions increased from 30.9 in 1990 to 55.3 in 2019 (Table 2). The high-income Asia-Pacific region (QCI = 97.0) showed the highest QCI scores in regional levels in 2019 (Fig. 1).

Giving the SDI regions, the age-standardized QCI score of liver cancer spanned from as high as 83.3 in high SDI countries to values as low as 26.4 in low SDI countries by 2019 (Table 2). At national levels, Japan (QCI = 100), Finland (QCI = 91.6), and the Republic of Korea (QCI = 91.2) owned the highest age-standardized QCI scores by 2019. Although most countries and regions have shown increasing trends in QCI scores, the QCI score of eight countries deteriorated during the past 30 years (Fig. 2, and Supporting Table S1).

Underlying Causes of Liver Cancer

Among underlying causes of liver cancer, the global QCI scores due to HBV, HCV, alcohol use, NASH, and other causes were 53.5, 61.8, 54.3, 52.9, and 63.7, respectively, in 2019. The QCI score of all causes has increased from 1990 to 2019, with the most increase for HBV (ΔQCI = 22.5), followed by HCV (ΔQCI = 22.0), alcohol use (ΔQCI = 18.4), NASH (ΔQCI = 17.5), and other causes (ΔQCI = 12.7). Among GBD super-regions, the highest and the lowest age-standardized QCI scores due to all underlying causes except for other causes group were for countries belonging in the high income and Sub-Saharan Africa super-regions,

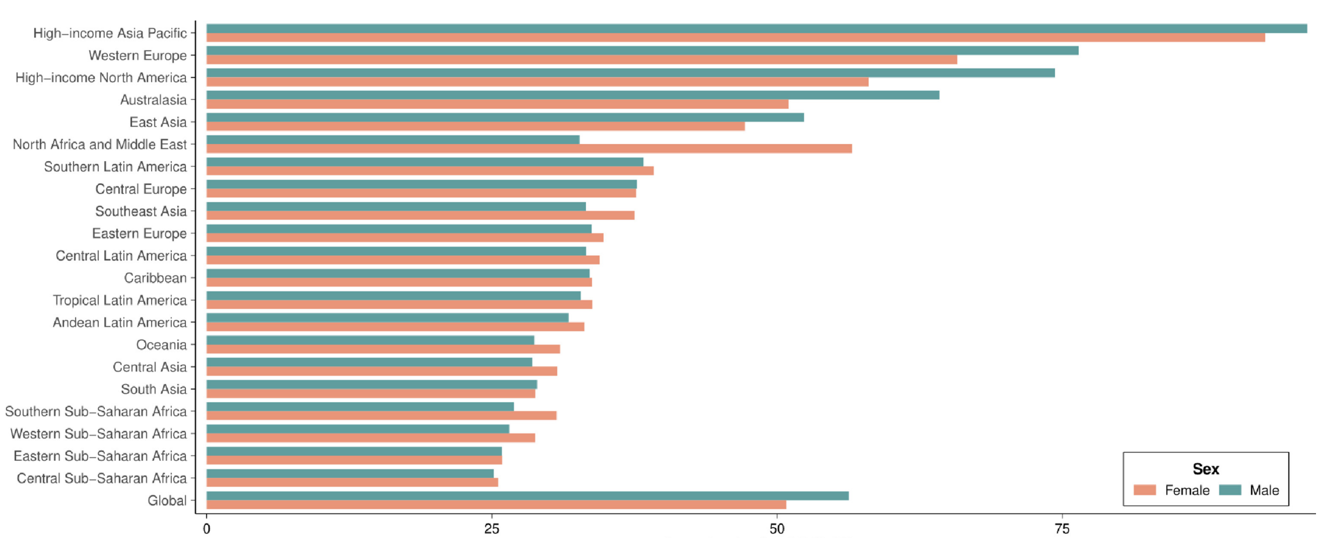

FIG. 1. Age-standardized QCI for liver cancer among various regions in 2019.

TABLE 1. AGE-STANDARDIZED INCIDENCE, DEATHS, AND DALY RATES (95% UIS) FROM 1990 TO 2019

Location		1990			2019		
		ASIR (per 100,000 population)	ASDR (per 100,000 population)	DALYs (per 100,000 population)	ASIR (per 100,000 population)	ASDR (per 100,000 population)	DALYs (per 100,000 population)
Global		9.0 (8.1-10.0)	8.9 (8.1-9.9)	258.4 (230.9-290.1)	6.5 (6.0-7.2)	5.9 (5.5-6.4)	151.1 (137.5-164.8)
Super-regions	High income	4.9 (4.7-5.0)	4.4 (4.2-4.5)	110.4 (107.5-113.0)	7.3 (6.6-8.0)	5.4 (5.2-5.9)	127.0 (119.8-133.0)
	Latin America and Caribbean	3.3 (3.1-3.4)	3.5 (3.3-3.7)	84.9 (81.5-87.9)	2.9 (2.7-3.3)	3.1 (2.8-3.4)	72.1 (65.5-80.2)
	Sub-Saharan Africa	4.4 (3.8-5.5)	4.7 (4.0-5.9)	123.3 (104.7-153.4)	4.2 (3.8-4.7)	4.5 (4.0-5.0)	113.7 (99.2-128.4)
	North Africa and Middle East	6.1 (5.3-6.8)	6.4 (5.6-7.2)	161.1 (141.9-179.7)	6.3 (5.1-7.7)	6.2 (5.1-7.6)	153.3 (121.9-189.8)
	Southeast Asia, East Asia, and Oceania	20.9 (17.9-24.3)	21.1 (18.4-24.4)	619.3 (532.8-723.6)	9.5 (8.2-11.0)	8.8 (7.7-10.1)	239.4 (205.8-276.2)
	South Asia	2.7 (2.2-3.1)	2.8 (2.3-3.3)	72.9 (61.8-83.0)	2.7 (2.3-3.1)	2.8 (2.4-3.2)	71.3 (62.0-81.8)
	Central Europe, Eastern Europe, and Central Asia	2.8 (2.7-2.9)	3.0 (2.9-3.1)	75.2 (72.9-77.5)	3.7 (3.3-4.0)	3.7 (3.4-4.1)	95.7 (86.5-104.8)
SDI regions	High SDI	5.3 (5.1-5.4)	4.7 (4.5-4.8)	122.2 (119.0-125.3)	7.6 (6.9-8.4)	5.9 (5.4-6.2)	133.1 (125.7-139.3)
	High-middle SDI	9.9 (8.7-11.2)	10.0 (8.8-11.3)	289.9 (249.8-332.6)	5.3 (4.7-6.0)	4.8 (4.3-5.4)	127.3 (112.8-144.4)
	Middle SDI	14.7 (17.1-12.8)	15.0 (13.1-17.3)	433.4 (376.3-501.8)	7.3 (6.4-8.3)	7.9 (7.0-8.9)	206.9 (180.2-235.0)
	Low-middle SDI	5.4 (4.9-5.9)	5.6 (5.1-6.1)	154.5 (139.2-170.4)	4.0 (3.6-4.4)	4.2 (3.9-4.7)	109.0 (99.2-120.3)
	Low SDI	4.1 (3.6-4.6)	4.4 (3.8-5.0)	113.1 (98.8-127.7)	3.5 (3.1-3.9)	3.9 (3.5-4.4)	101.2 (88.4-114.3)

Abbreviations: ASDR, age-standardized death rates; and ASIR, age-standardized incidence rates.

TABLE 2. AGE-STANDARDIZED QCI FOR LIVER CANCER AND ITS UNDERLYING CONDITIONS IN 1990 AND 2019

Location		Liver Cancer		Liver Cancer Due to HBV Infection		Liver Cancer Due to HCV Infection		Liver Cancer Due to Alcohol Use		Liver Cancer Due to NASH		Liver Cancer Due to Other Causes	
		1990	2019	1990	2019	1990	2019	1990	2019	1990	2019	1990	2019
Global		33.1	55.7	31.0	53.5	39.9	61.8	36.0	54.3	35.4	52.9	50.9	63.7
Super-regions	High income	57.4	83.2	55.1	86.6	59.6	84.3	52.7	77.5	55.6	77.7	69.4	86.4
	Latin America and Caribbean	30.8	34.3	32.5	36.3	31.2	34.3	30.4	33.7	32.1	35.4	49.4	52.1
	Sub-Saharan Africa	26.5	27.9	29.5	30.1	28.3	29.2	27.1	28.1	29.5	30.1	39.6	43.3
	North Africa and Middle East	30.2	42.6	32.4	44.2	28.8	39.9	30.0	39.2	32.3	48.4	49.6	61.5
	Southeast Asia, East Asia, and Oceania	28.2	49.6	29.6	51.6	29.3	47.3	29.1	45.7	30.8	47.9	50.3	62.7
	South Asia	27.6	29.8	30.7	32.5	28.8	30.3	28.2	30.1	30.2	31.7	37.1	42.0
	Central Europe, Eastern Europe, and Central Asia	30.5	34.7	33.3	35.7	31.1	34.2	30.2	33.8	32.4	35.8	45.0	53.2
SDI regions	High SDI	56.8	83.3	50.7	83.7	61.0	85.8	52.9	77.7	55.0	77.9	68.7	85.9
	High-middle SDI	30.6	55.4	30.7	57.9	33.1	54.3	32.9	50.2	32.8	51.9	51.5	68.5
	Middle SDI	28.1	42.9	29.4	45.1	29.1	40.9	28.9	39.2	30.7	42.7	50.2	60.1
	Low-middle SDI	27.2	30.6	29.1	33.6	29.0	31.1	28.1	29.6	30.1	32.0	44.4	46.2
	Low SDI	26.3	26.4	29.5	29.1	27.8	27.4	27.1	26.5	29.2	29.3	38.8	42.6

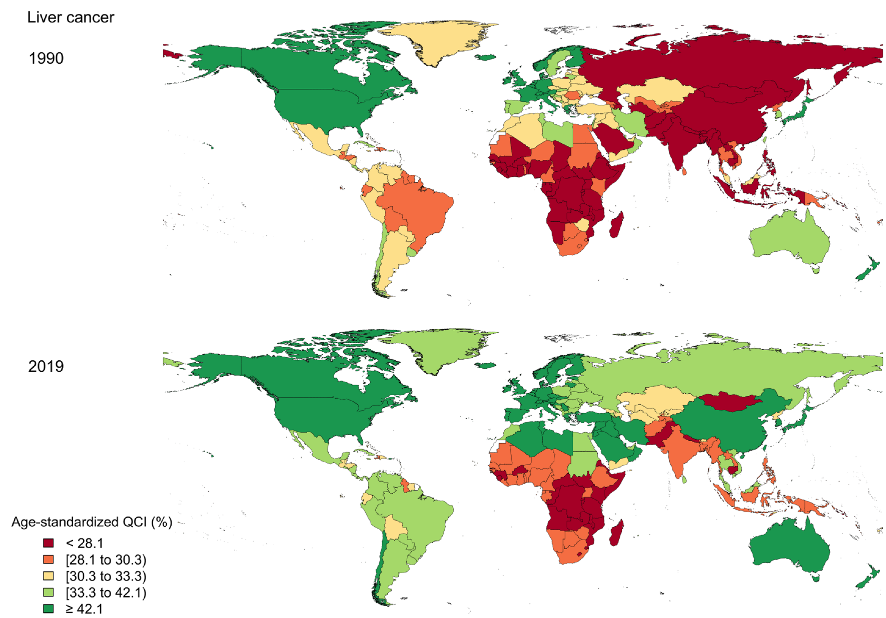

FIG. 2. QCI pattern for liver cancer among various countries in 1990 (A) and 2019 (B).

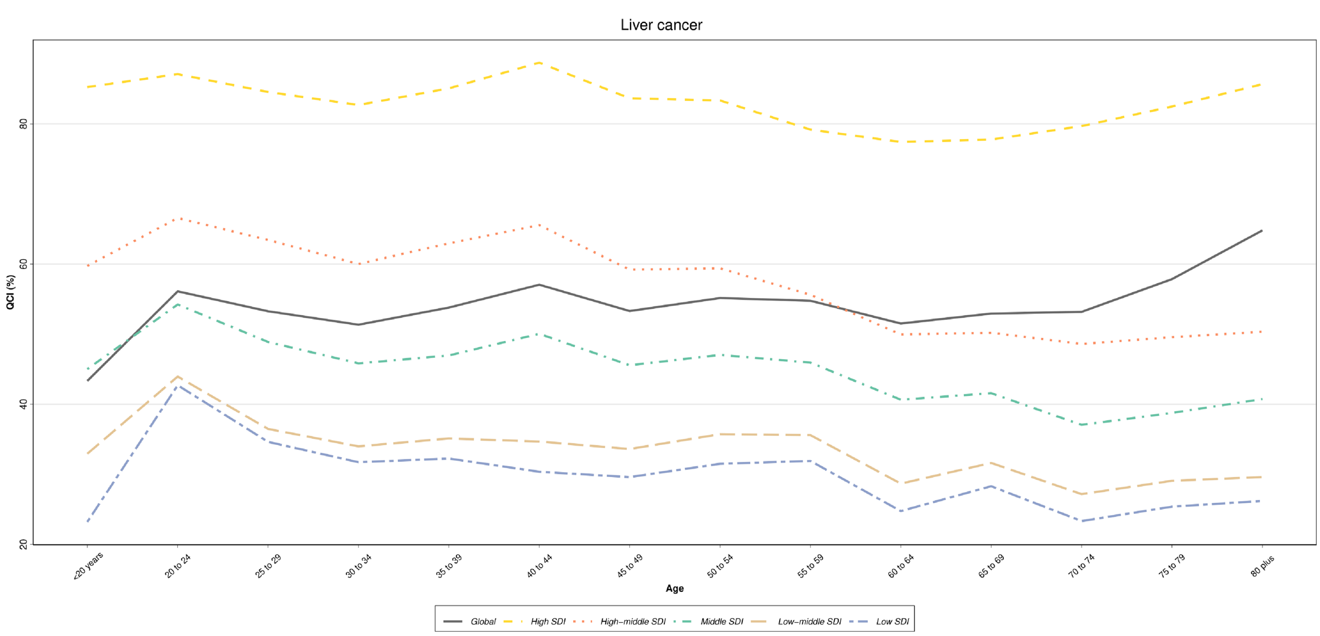

FIG. 3. Age pattern of QCI for liver cancer among various age groups in 2019.

ranging from 30.1 to 86.6 for HBV, 29.2 to 84.3 for HCV, 28.1 to 77.5 for alcohol use, and 30.1 to 77.7 for NASH. The highest and lowest age-standardized QCI score for other causes group was for high income and South Asia, ranging from 42.0 to 86.4, respectively. Similar to liver cancer, the highest age-standardized QCI scores for all causes were among the high-income Asia-Pacific region countries (Supporting Tables S2-S6). The QCI score of liver cancer by causes was highest in high SDI

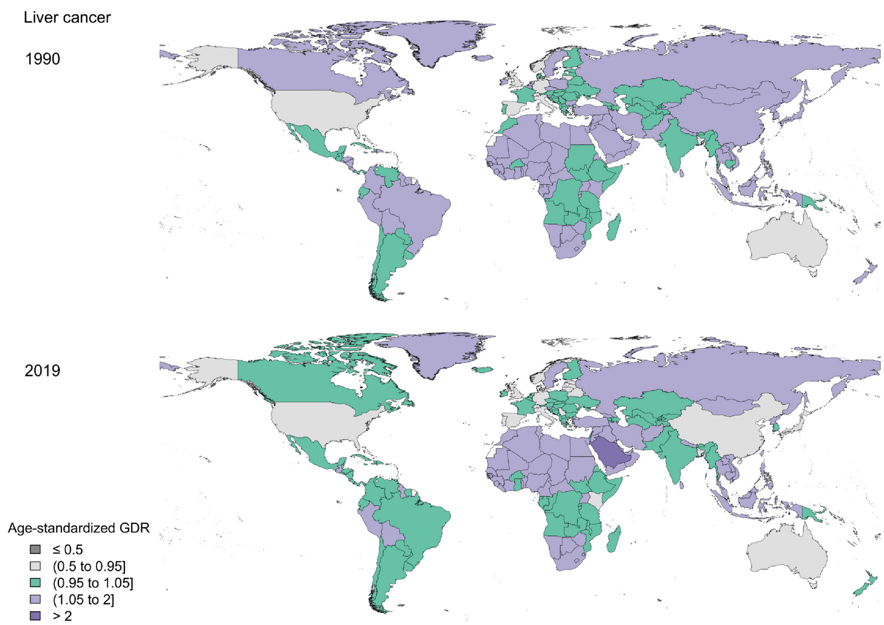

FIG. 4. Gender disparity pattern of quality of care for liver cancer among various countries in 1990 (A) and 2019 (B).

countries, with QCI scores of 83.7 for HBV, 85.8 for HCV, 77.7 for alcohol use, 77.9 for NASH, and 85.9 for other causes. Low SDI countries had the lowest QCI scores for all causes in 2019 (Table 2).

At national levels, Japan ranked first with the QCI score of 100 for all underlying causes of liver cancer. Finland, the Republic of Korea, and Italy were among the three top countries with the highest QCI for underlying causes. The Republic of Korea showed the most improvement in the QCI score for all causes. By 2019, the 31 countries saw decreases in their QCI score for at least one of the underlying causes of liver cancer. QCI scores of countries in categories in 1990 and 2019 are presented in the Appendix, Supporting Fig. S4A-E, and Supporting Tables S2-S6.

Age Pattern

In 2019, inspecting the QCI scores of liver cancer among different age groups revealed diversities at global scales in different age groups, with the highest scores in the age group of more than 80 years. The QCI trend in 2019 fluctuated under the age of 80. Among different SDI regions, low, low-middle, and middle SDI countries were primarily below the global scale across all age groups. On the contrary, QCI scores of liver cancer across all ages in high SDI countries were above global scores (Fig. 3). The age trend of QCI for underlying conditions showed the same pattern of liver cancer on the global and SDI-regional scales, with the higher QCI among patients aged more than 80. The age trend of QCI scores in global and SDI regions is illustrated in the Appendix: Supporting Fig. S5A-E.

Gender Inequity

The overall age-standardized gender disparity ratio was 0.9 by 2019, suggesting a slightly better quality of care for liver cancer among males. The global age-standardized gender disparity in quality of care was 1.1 in 1990. The gender disparity ratio of QCI scores across various age groups ranges from 0.8 for more than 70 years to 1.1 in 15-19 years in 2019, while the ratio was mainly between 0.7 (more than 95 years) to 1.2 (15-19 years) in 1990. Considering the SDI regions, the ratio ranged from 0.9 (for high and high-middle SDI regions) to 1.1 (low SDI region) in 2019. For underlying causes of liver cancer, the ratio for liver cancer due to HBV, HCV, alcohol use, NASH and other causes was 0.9, 0.8, 0.9, 1.0, and 0.9, respectively. The corresponding rates in 1990 were 1.1, 0.9, 1.0, 1.0, and 0.9, respectively (Fig. 4). The gender disparity ratio pattern of QCI scores of underlying causes among various countries is presented in Appendix: Supporting Fig. S6A-E.

Discussion

Globally, the age-standardized incidence, deaths, and DALY rates of liver cancer showed decreasing trends over the past 30 years. In addition, our analysis revealed that the global QCI score of liver cancer was 55.7 in 2019, which increased by 68% from 1990. The quality of care in countries with an established economy and higher SDI countries was markedly better; however, the QCI score among all SDI regions has been increasing since 1990.

Liver cancer is a unique malignancy, as more than 90% of tumors occur in patients with protracted chronic inflammation of the liver, occurring after exposure to various risk factors as follows: HBV, HCV, alcohol use, NASH, and a group of other causes including autoimmune hepatitis and aflatoxin toxicity.[9] Analysis of the underlying risk factor revealed that liver cancer due to HBV had the highest age-standardized incidence, prevalence, and mortality rates in 2019 globally. The trends in mortality of all underlying causes were decreasing during the past 30 years. Consistently, the quality of care for liver cancer due to HBV, HCV, alcohol use, NASH, and other causes have had an increasing pattern since 1990. Lower mortality rates of all underlying causes and better QCI scores could be explained by improved screening methods, suitable treatment options, and enhanced access to cancer care centers worldwide.[23,24] Overall, our study highlights that the most improvements in QCI scores from 1990 to 2019 were for HBV followed by HCV, alcohol use, NASH, and other causes. Better improvements in QCI scores due to HBV imply that HBV vaccination is starting to show success in the prevention.[25] Between 1990 and 2015, HBV vaccine coverage in infants increased to 84%, and aims to reach 90% by 2030.[25] Despite improvements in HBV vaccination coverage and subsequent increase in the QCI score, it is estimated that liver cancer due to HBV will remain a significant cause for two decades due to delayed HBV progression and a long lag between exposure to HBV and cancer occurrence.[26-29]

Unsurprisingly, high-income countries had the highest QCI scores for all causes in 2019. Japan had the highest QCI scores for all causes in 2019. Detailed inspection and precise evaluation of current countries and regions showed that essential factors lead to these achievements. First, an evidence-based guideline is used widely across the countries of the high-income Asia Pacific region. In 2010, a panel of expert hepatologists, hepatobiliary surgeons, radiologists, and oncologists in the Asia-Pacific region gathered to take urgent action regarding liver cancer. Since then, annual guidelines have been published in the Asia-Pacific region, acknowledging the increasing disease burden, and calling for thorough situation assessment. Although the countries in this region have a diversity of medical environments, the evidence-based guideline is generally accepted in the Asia-Pacific region.[30]

Second, established preventive strategies were primarily deployed in the region. These strategies for viral hepatitis–related liver cancer included increased access to clean drinking water and sanitation. All countries in this region have strictly implemented HBV vaccination programs for newborns, and availability of screening tests for blood and tissue, donor recall policies, and harm-reduction strategies are in their initial stages in most countries.[31] As a leading model of liver cancer control, Japan established HBV and HCV screening methods in transfusion products, improved health care facilities, and access to antiviral treatments.[32] For HCV, the *Japan Society of Hepatology* publishes yearly guidelines regarding direct-acting anti-viral therapies for the management of HCV, which fundamentally decreased the burden of liver diseases and cancers due to HCV.[33]

Considering the policies regarding alcohol use restriction, consumption of alcohol per year per adult decreased by about 80% during the past 20 years in Japan.[34] Establishing political action plans regarding the decline in the prevalence of HBV among children 5 years of age and older since 2012 in the Western Pacific Region of the WHO as a super-regional goal led to improvements in liver cancer control in Japan.[35,36]

Third, nationwide strategies for liver cancer surveillance and screening are used widely in the countries of this region; Japan was the first country in the world to develop and implement diagnostic ultrasound systems for liver cancer screening, which was developed in the early 1980s.[32] In addition, national surveillance and screening in Japan has resulted in an early-stage diagnosis of almost 66% of liver cancer.[37] In comparison, more than 60% of liver cancer in Western counties are diagnosed at advanced stages, when they lost the opportunity for curative therapies.[23,37]

Finally, development of insurance coverage and notable investment in liver cancer has resulted in the exemplary increase in the quality of care among high-income countries of the Asia-Pacific region. Established tumor markers for screening, including α-fetoprotein and vitamin K absence or antagonist-II, were included among health insurance–covered screening tests in 1989 and 1994, respectively.[32]

Despite the impressive achievements of liver cancer control among countries of the high-income Asia-Pacific region, the efforts for liver cancer containment were suboptimal in other countries and regions. The QCI scores of the six super-regions (except for the high-income super-region) were lower than the global index. The QCI score of the Sub-Saharan Africa super-region was the lowest. Similarly, the highest number of deaths due to liver cancer was observed in Sub-Saharan Africa.[38,39] Possible explanations for lower quality of care in Sub-Saharan Africa could be suggested by lack of societal awareness and paucity of health care provision, shortage of resources, and absences of preventive measures.[40] Any rudimentary action to overcome the current obstacles in liver cancer control would narrow the gap in this region. Comparing people from Egypt with those from other African countries, Yang et al. showed that HBV was the leading cause of liver cancer for all countries in this region. In contrast, HCV is the leading cause in Egypt.[41] Therefore, comprehensive immunization and birth-dose vaccination against HBV and deployment of any strategy to eliminate HBV are essential to control the burden of liver cancer. People with chronic HBV in this region have a 15%-40% risk of developing cirrhosis, liver failure, or hepatocellular carcinoma, and a 15%-25% risk of dying from HBV-related liver diseases.[42] HBV immunization was broadly implemented in most countries of this region for fewer than 10 years.[41] Therefore, it is anticipated that HBV prevention's success would improve the QCI score of this region in future decades. In addition, it is highly recommended to establish referral systems for patients with HBV and surveillance for high-risk patients.[43]

Another equally compelling strategic plan to control the burden is enhancing general awareness about the disease and health care services. Higher rates of poor outcomes for liver cancer, younger ages of onset, and shorter clinical course among patients of Sub-Saharan Africa could be attributable to the significant chasm between cultural and social beliefs of African people and physicians, which would be eliminated by educating the people.[40] Furthermore, failure or under-ascertainment of cause of death among African regions, particularly in Sub-Saharan Africa, leads to bias in death registration. Many people likely die of liver cancer without being formally diagnosed, as they have no access to care.[44] Thus, the establishment of cancer registry and surveillance systems might empower the policymakers in terms of a better interpretation of the actual situation and allocating resources to contain the burden of liver cancer.

Considering the inequities among various age groups, it has been revealed that the highest QCI scores were in the age group of more than 80. It could be suggested that the delayed referral of patients with liver cancer to cancer centers, delayed diagnosis, and the cohort effect of underlying causes would be the possible explanations of the witnessed trend.[9,45]

Interpretation of the global inequity pattern in gender shows that the quality of care was slightly better among men. In addition, it was also revealed that the gender disparity ratio of quality of care was in favor of men in low SDI regions and women among the higher SDI regions. The suboptimal condition of women with cancer compared with men in developing countries demonstrates the inequality in cancer care.[46] It is worth mentioning that current studies shed light on the higher and faster development of liver cancer among men than women due to genetic and hormonal differences, which would justify the slightly higher quality of care among men.[47]

Strengths and Limitations

The strengths of our study are provided as follows. First, this study quantifies the quality of care for liver cancer and its underlying causes and provides various epidemiological measures and burden in global, regional, and national levels by age and sex. Second, QCI is a robust metric that could be used as a single proxy measure to compare various countries in disease management and empower policymakers by providing a clearer picture of inequities across countries and regions. In addition, the validation of the index was evaluated by the correlation between QCI and the Health Access and Quality Index, which was acceptable on a cause-specific level. We also acknowledge the limitations of the study. We did not investigate QCI on a subnational level due to paucity of data in most countries; however, this could be investigated in future studies in countries where there are subnational data available. In addition, limitations of data availability of GBD and using covariate estimations by GBD in such cases might impose biases on our estimates in the current study. The data of GBD on risk factors were reported separately for HBV, HCV, alcohol use, and NASH. It could be suggested that the entities of the fifth group of other causes be detangled to capture a clearer picture of the status of other causes, including autoimmune hepatitis.

Although the trends in burden of liver cancer are decreasing and the quality of care for the cancer and its underlying causes improved from 1990 to 2019 globally, there is a wide gap among countries, sexes, and age group regarding liver cancer control. Given the inequities, there is an urgent need to address discrimination and bridge the gap. The pioneers in liver cancer containment have to be presented as role models for adapted strategies. There is a need to implement the plans of this distinguished country in line with the Sustainable Development Goals, the Global Health Sector Strategy on Viral Hepatitis 2016 to 2021, and the WHO Global Strategy to Reduce Harmful Use of Alcohol, in order to further reduce the mortality and morbidity of liver cancer worldwide.

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Data Availability Statement: The data that support the findings of this study are available from Non-communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are, however, available from the authors upon reasonable request and with permission of the Institute for Health Metrics and Evaluation.

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