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Original Article

Incidence, Mortality, and Burden of Hepatitis B and C and Geographical Distribution in Iran during 2008-2015

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Abstract

Background: This study aimed at estimating the incidence, mortality, and burden of Hepatitis B (HBV) and Hepatitis C (HCV) viruses and their trends from 2008 to 2015.

Methods: The Disability Adjusted Life Year (DALYs) index was applied to calculate the burden of the diseases by age, sex, time, and locations. The incidence and demographic data were obtained from HBV and HCV surveillance system, and the data on natural history was extracted from the cohort studies; moreover, the data on the standard life expectancy was obtained from the Iranian life table 2016. The two values of 0.03 and 21.5 yr were set as the discount rate and mean standard duration of the disease for both types of hepatitis.

Results: The burden of HBV decreased from 13735 to 78277.6 yr, but there was an increase in the burden of HCV from 5174 to 14395 yr over the studied period. The burden of both types of hepatitis was higher among males than females. The incidence of HBV increased from 46611 to 22996 cases, and the incidence of HCV increased from 1210 to 3939 cases. The HBV decreased from 1925 to 1394 cases; however, the number of deaths caused by HCV increased from 197 to 583 cases over the studied period. The share of YLLs raised from 5% to 10% for HBV whereas it changed from 23% to 62% for HCV over the studied years. Tehran, Khorasan Razavi, and Golestan had the highest and Chaharmahal and Bakhtiari, Kurdistan, and Kermanshah had the lowest adjusted burden of HBV per 1000 population.

Conclusion: Although the incidence, mortality, and burden of HBV declined over the eight studied years, these values increased dramatically for HCV.

Keywords: Incidence; Mortality; Disability-adjusted life years; Hepatitis; Iran

Introduction

Viral hepatitis is a global threat for public health and one of the leading causes of mortality and disabilities worldwide (1, 2). Despite a decline in the number of deaths caused by most communicable diseases, hepatitis mortality rate had an increasing trend worldwide and changed from 0.89

million in 1990 to 1.45 million in 2013 (1,2). During the same period of time, its Disability Adjusted Life Years (DALYs) raised from 31.7 to 42.5 million, respectively. Viral hepatitis was the 22nd leading cause of DALYs in 1990 and 18th in 2013 (1). Hepatitis B virus (HBV) and Hepatitis C virus (HCV) are the main causes of the high burden of hepatitis worldwide (3-5); they account for 96% of the total hepatitis mortality rate. Although HCV is a global concern, Eastern Mediterranean and European countries are the most contaminated areas in the world. The prevalence of HCV is 2.3% and 1.5% in the mentioned areas, respectively (6). In 2015, the number of people infected by HBV and its mortality, respectively, were 257 million and 887 thousand across the world (7).

Iran, with a prevalence rate of below 1%, is considered as a country with a low HCV infection, as compared with other countries. However, the epidemiological status of HCV is changing in Iran and its infection is increasing due to an increase in the number of injecting drug users. The prevalence of HCV is significantly different in various areas of Iran, ranging from 0.05% to 2.3% (8). In 1979, the prevalence of HBsAg ranged from 2.5% to 7.2% in Iran (9). The number of people infected with HBV before and after 2010 was 2.9% and 1.3%, respectively (10). Over the past two decades, the epidemiological status of HBV has changed and started to decline due to the implementation of a national vaccination plan for infants since 1993. In 2005, the coverage of HBV vaccination reached 94% (11). In 2002, the National Hepatitis Committee expanded the coverage of vaccination to cover people aged 25 yr (12).

With the approval of the Sustainable Development Resolution 2030, more attention has been paid to Hepatitis diseases (6). In 2016, the world health assembly approved the first "Global Health Sector Strategy (GHSS) on Viral Hepatitis, 2016-2021, with a particular focus on HBV and HCV". The main goals of this strategy are to reduce the new cases of infections by 90% and reduce mortality rate by 65% by 2030. This strategy focuses more on HBV and HCV due to their high burdens (13).

HBV and HCV include all cases of liver disorders diagnosed positive by HBV Surface Antigen (HBsAg) and HCV Antibody (Hcv Ab) tests, respectively. The HCV and HBV codes are B18.2 and B19.10, respectively.

Estimating the burden of a disease can be useful for planning, controlling, and monitoring that disease. It helps to observe and judge the success of a country's health system in controlling and managing hepatitis over time. In line with this and in order to depict a comprehensive picture of the disease over the time, we aimed at estimating the burden of HBV and HCV at national and provincial levels to provide evidence-based strategies and policies for the management of hepatitis.

Methods

Data sources

Data on the distributions of HBV and HCV by sex, age, location, and time over 2008-2015 were obtained from the Hepatitis surveillance system. The data had been collected by health centers across the country. Comparing the recorded number of the patients with the prevalence and incidence rates reported in many systematic review studies, there was an underestimation in the available data (14-18); accordingly, the data on HBV and HCV were underestimated by 9.38 and 11.36 times. Therefore, we applied the corrected incidence rates in our calculations and assumed no change in sex and age distributions of the diseases.

Calculation of DALYs

DALYs is calculated through adding Years of Life Lost due to premature death (YLLs) to Years of Life Lost due to disability (YLDs) (19). DALYs index was calculated using the National Burden of Disease formula developed by the WHO (20). We did not include age weights in our calculations; however, a discount rate of 0.03 was applied for discounting health values in future years. YLDs is calculated through multiplying annual incidence rate of the diseases by the related median periods and its disability weights.

HBV and HCV not only have the same natural course of disease lasting 21.5 yr (21) but they also impose the same disease weight on the patients. However, the disease weight varies by age: 0.17 for 0-4 age group, 0.181 for 5-14 age group, 0.209 for 15-44 age group, and 0.212 for >45 age group (22). DALY, YLL, and YLD were calculated and reported by sex, age, time, and place for all the provinces of Iran. For each age group, the mean age of the members in that group was considered as the mortality age for patients died from hepatitis. However, as suggested by the WHO, the mean mortality age for age groups 0-1 and 1-5 was set at 0.1 and 2.6, respectively. The standard life expectancy for each age group was calculated using the life tables of Iranians reported by the WHO (23).

We did not access the incidence rates of HBV and HCV for all years of the study. To overcome this problem, we extracted the prevalence rate of the diseases in the first (2008) and the last (2015) years under the study using the available systematic reviews (14-18) and calculated the related incidence rates through dividing the prevalence rates by 21.5 as the median value for the diseases duration (21). Finally, the rates of incidence in other years were calculated by assuming that the changes during the years of the study were constant and had a linear trend (24-25).

The data on the population of the country and its provinces in 2015 was taken from the Statistical Center of Iran. In order to estimate the population of the country in previous years, the average growth rate of 0.021 was used. The data were analyzed using Excel software (ver. 2010).

Results

Table 1 presents the burden of HBV by sex over the studied period. The disease imposes a higher burden on males than females. Its burden among males decreased from 78343 DALYs in 2005 to 43003 DALYs in 2015. We observed the same trend for females, with a reduction from 59007 DALYs in 2005 to 35275 DALYs in 2015. Overall, the adjusted burden of the disease decreased from 1.9 to 0.99/1000 population over the studied period.

Table 2 presents the burden of HCV by sex over the studied years. In line with an increase in its incidence rate over the studied years, its burden and mortality also increased simultaneously. These values have always been higher in males than in females.

Table 1: Burden of HBV by gender over the study period

Year	*Male mortality (Number)*	*Female mortality (Number)*	*Male *DALYs (Number)*	*Female DALYs (Number)*	*Total DALYs (Number)*	*DALYs per 1000 population (95% CI)*	*Incidence (Number)*
2015	686	279	43002.8	38274.8	78277.6	0.994 (0.89-1.10)	22996
2014	622	274	49312.1	41950.2	91262.3	1.117 (0.99-1.35)	27739
2013	993	392	62206.4	49641.8	111848.2	1.454 (1.28-1.63)	34235
2012	1487	284	70797.6	56520.5	127318.1	1.674 (1.36-1.99)	39807
2011	1484	393	70882.8	58149.5	129032.3	1.717 (1.50-2.10)	41265
2010	1193	467	83333.6	64813.1	148146.7	1.998 (1.76-2.23)	48264
2009	1939	968	74680.5	57268.4	131848.9	1.801 (1.35-2.25)	43840
2008	1257	668	78343.0	59007.0	137350.0	1.901 (1.56-2.224)	46611

* DALYs: Disability Adjusted Life Years, CI: Confidence Interval

Table 2: Burden of HCV by gender over the study period

Year	*Male mortality (Number)*	*Female mortality (Number)*	*Male *DALYs (Number)*	*Female DALYs (Number)*	*Total DALYs (Number)*	*DALYs per 1000 population (95% CI)*	*Incidence (Number)*
2015	480	103	12093	2302	14395	0.196 (0.17-0.22)	3939
2014	478	80	13703	2443	16145	0.238 (0.21-0.27)	3523
2013	389	72	12284	2426	14711	0.198 (0.16-0.23)	3116
2012	480	32	11947	1769	13716	0.249 (0.20-0.28)	2718
2011	486	64	11129	1755	12884	0.222 (0.18-0.26)	2330
2010	353	46	9913	1435	11347	0.216 (0.17-0.26)	1947
2009	440	57	12994	1802	14796	0.298 (0.25-0.35)	1574
2008	177	20	4625	549	5174	0.103 (0.08-0.12)	1210

* DALY: Disability Adjusted Life Years, CI: Confidence Interval

Female and male mortality rates caused by HBV decreased over the studied years. However, HCV mortality rate had an increasing trend. Moreover, male mortality rate did not change significantly after 2009 whereas it had a steady increase among females (Fig. 1).

Fig. 2 shows the changes in the burden of HBV and HCV by adjusted population. The burden of HBV deceased among both males and females over the studied period, whereas the burden of HCV increased among both sexes.

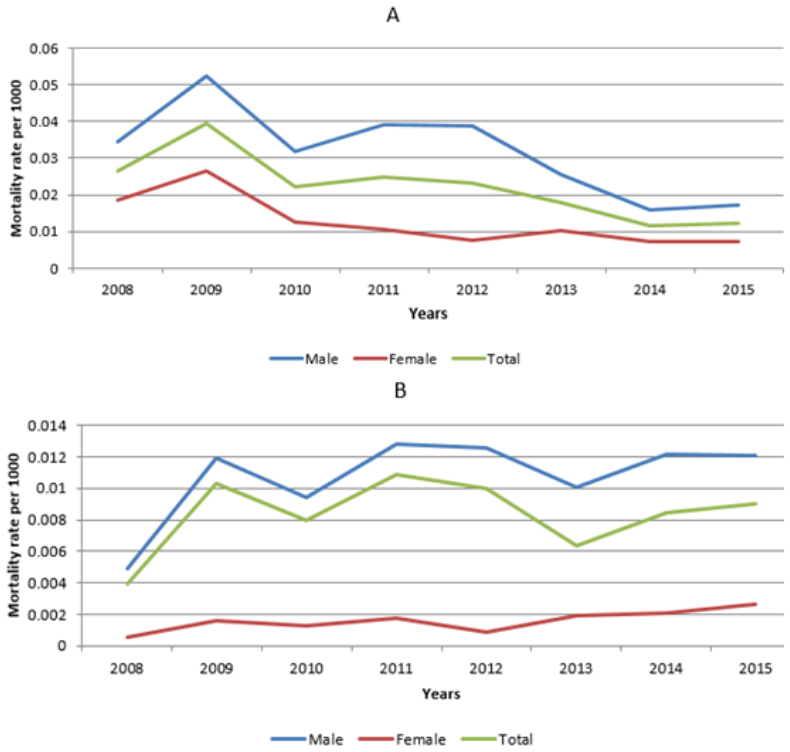

Fig. 1: Trend of HBV (A) and HCV (B) mortality rates; 2005-2015

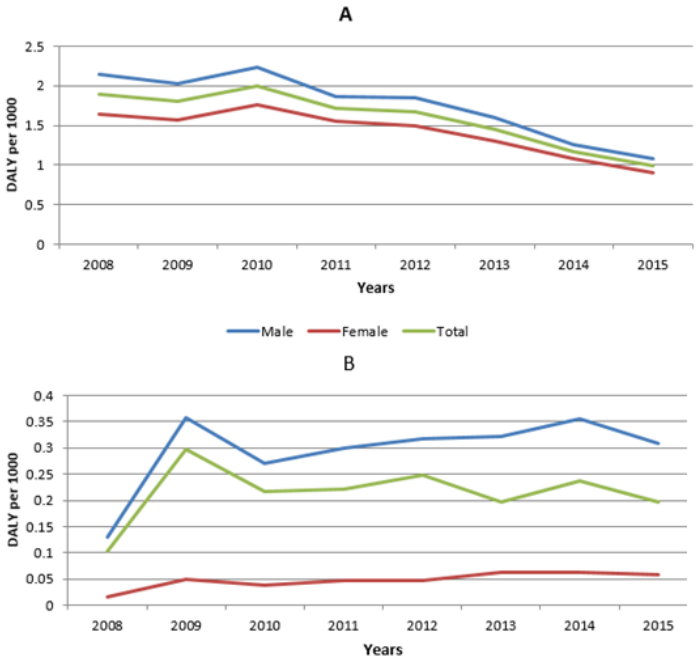

Fig. 2: DALYs attributable to HBV (A) and HCV (B) by sex; 2005-2015

YLLs increased from 5% to 10% for HBV and 23% to 62% for HCV over the studied period (Fig. 3). Figure 4 shows YLLs and YLDs for HBV and HCV by age groups. People in 30-44 and >70 age groups had the highest YLDs and YLLs, respectively. The lowest burden of the disease was observed in <15 and 30-44 age groups. Moreover, 45-59 and 60-69 age groups had the highest burden of HCV. On the other hand, <29 age group had the lowest burden of HCV. The highest YLLs and YLDs were observed in 60-69 and 30-44 age groups, respectively.

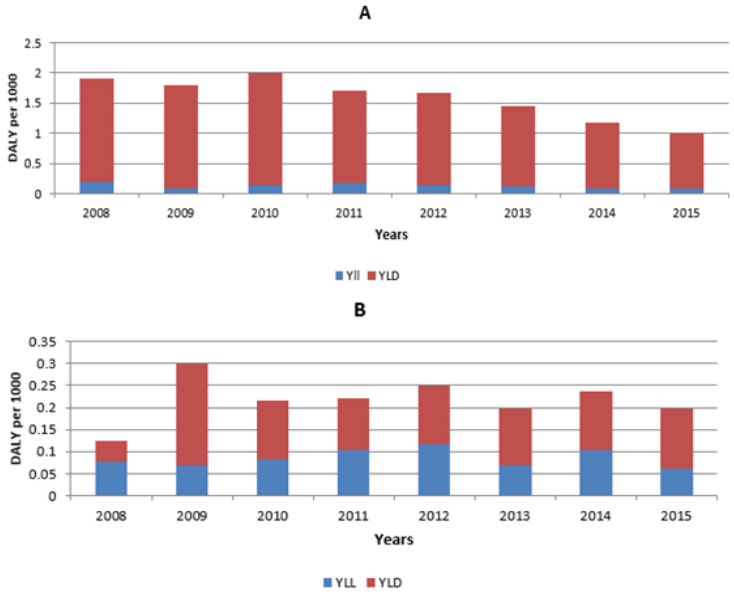

Fig. 3: YLLs, YLDs, and DALYs attributable to HBV (A) and HCV (B); 2005-2017

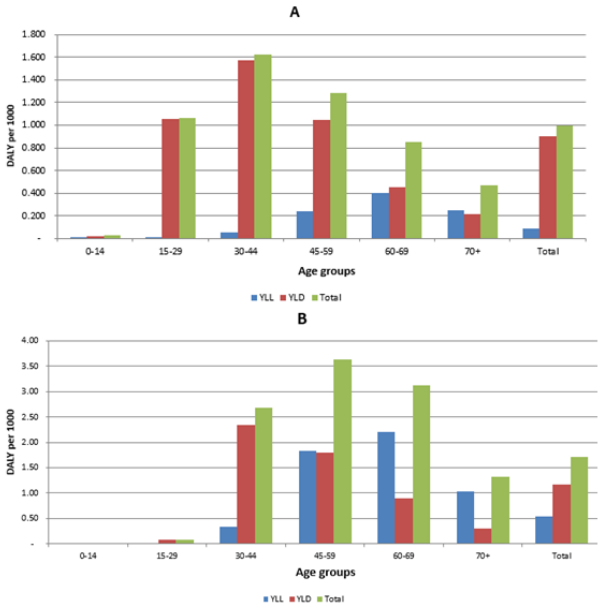

Fig.4: Burden of HBV (A) and HCV (B) by sex and age; 2015

Tehran (0.259), Khorasan Razavi (0.114), and Golestan (0.104) had the highest adjusted burden of HBV per 1000 population. On the other hand, Chaharmahal and Bakhtiari (0.0107), Kurdistan (0.109), and Kermanshah (0.0122) had the lowest burden of HBV. Provinces with invalid data are colored white in the map. Since we did not have access to valid and reliable data on the geographical distribution of HCV (in all the years of the study) and HBV (in all the years of the study, except for 2015), therefore it was not possible to depict the geographical distribution in the mentioned years (Fig. 5).

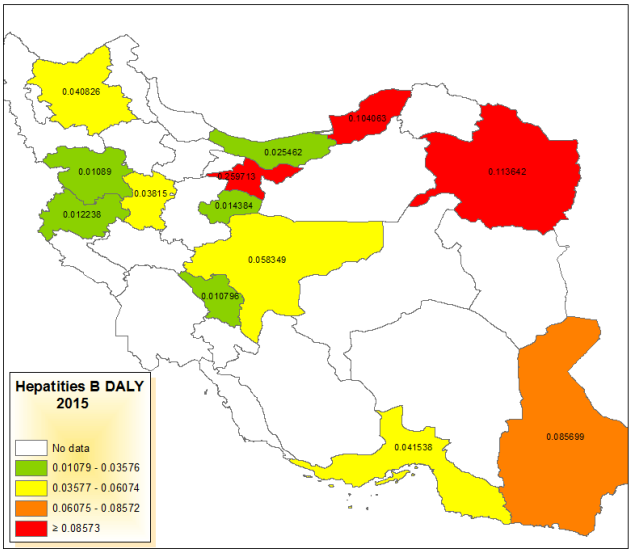

Fig. 5: Geographical distribution of adjusted burden of HBV per 1000 population; 2015

Discussion

According to the results of our study, the incidence, mortality and burden of HBV decreased dramatically in both sexes and all age groups. Adjusted burden of HBV decreased from 1.9 to 0.99 per 1000 population over the studied period. However, the results showed a completely opposite trend for HCV. The incidence, mortality, and burden of HCV increased constantly over the studied period and its adjusted burden raised from 0.1 to 0.19 per 1000 population.

The HBV mortality rate reduced by 45.5% and 58.2% among males and females, respectively. However, the mortality rate among males was still 2.5 times more than that among females. Such positive changes resulted in a reduction in the adjusted and crude burden of the disease by 48% and 43%, respectively over the eight years under the study. However, the burden of HBV among males was higher than that among women, however, the gap between them was reduced. Moreover, the crude burden of HBV among males and females decreased by 45% and 40%, respectively. Such a reduction in the burden of HBV was due to a dramatic decrease in new cases of HBV which in turn reduced the mortality rate after the implementation of the HBV vaccination program for infants and family members of people living with HBV since 1994 (26).

The results of assessing epidemiological indices of HCV and HBV are quite the opposite. The incidence and mortality of HCV increased by 225% over the studied period. It killed more females than males. Its mortality rate among males and females increased by 177% and 415%, respectively. However, the mortality rate among males was 4.7 times higher than that among women. Such epidemiological changes resulted in an increase of 90% in the adjusted burden of the disease and an increase of 278% in the crude burden of the disease over the eight studied years. The disease burden among females and males increased by 319% and 161%, respectively. The observed increase is attributed to an increase in risky behaviors such as injecting drug use and unsafe drug injection (27).

Considering the results obtained for both HBV and HCV, the share of YLLs in the burden of HCV was six times more than that in the burden of HBV. HCV is responsible for a higher rate of mortality among the studied population. However, the share of YLLs in the total burden of both types of hepatitis declined over time. It declined by half and a one-third for HBV and HCV, respectively. It can indicate that the Iranian health system had been successful in diagnosing the disease faster and treating it more effectively (28)

With an increase in the age of the population, the share of YLLs from the total burden of both types of hepatitis increased among both males and females. In >70 age group, the share of YLLs in the total burden of HBV was higher than the share of YLDs; however, in all age groups over 45 yr old the share of YLLs in the total burden of HCV was higher than the share of YLDs, which was due to an increase in the mortality rate with increasing people's age. The highest burden of HBV and HCV was mainly observed among the two age groups of 15-60 and 30-70 yr old, respectively. Therefore, the best approach for controlling and reducing the burden of hepatitis is to prevent the incidence of disease, especially among high-risk groups, diagnose and treat the disease faster, which can reduce the mortality rate and, finally, control the burden of the disease.

The distribution map for the adjusted burden of HBV by population indicates that eastern and northeast provinces, including Khorasan Razavi, Golestan, and Sistan and Baluchestan are the main centers for this disease. Sharing borders with Afghanistan and Tajikistan, as the countries with a high prevalence of HBV, is the main reason for such a difference in the distribution of the disease in the country (29).

According to the results of GBD studies, HBV and HCV, respectively, imposed 24513 and 560 DALYs on Iranian population in 2016, which is far less than what was observed in our study (1). In fact, the number of deaths caused by both types of hepatitis was underestimated by the GBD studies because their results were based on the data published by secondary studies.

DALYs/1000 population attributable to HBV varies across the world. For instance, it was 10.34 in Germany (30), 20.4 in Spain (31), 17 in Santa Catharina state in Brazil (32), 63.4 in Guangdong (33), and 230 in Shandong in China (34). In Brazil, the burden of HBV decreased between yr 2005 to 2010 (32) which is in line with the results of studies in Iran. In all previous studies, the burden of HBV among males was higher than that among females. This finding is in consistent with the results of our study.

There is a limited number of studies estimated the burden of HCV. According to the GBD study in 2016, HCV caused only 560 DALYs, 0.69 DALYs per 100000 population, in Iran, which is far less than what is reported in our study. However, similar to our study, they reported an ascending trend for HCV (1). Other studies have reported 134.5 DALYs per 100000 population in European countries and 90.8 DALYs per 100000 population in Spain (31), both of which are higher than what is reported in our study.

As an important strength, our study used a national and sub-national individual-based panel data collected over eight years to detect age and sex differences between patients with HBV and HCV. However, the main limitation of the present study was the incomplete and weak coverage of hepatitis registration and detection systems.

Health policy implications

In order to control and change the trend of the HCV burden, it is highly recommended to consider the following items: reduce unnecessary injections in health centers, train healthcare staff to ensure safe injections, train and inform drug addicts about the transmission of disease through injections, better manage dialysis patients and people with HIV/AIDS, and increase the coverage of HCV diagnostic tests, especially for vulnerable groups. Obviously, the most efficient way to reduce the burden of disease is to prevent and decrease the incidence of the disease. An important measure for preventing HCV is to reduce its reservoirs in the society which can be best done through treating patients with HCV, especially the vulnerable groups. Our results revealed the success of vaccination program in controlling HBV; therefore, it is necessary to continue current polices; in addition, to increase the effectiveness, health authorities should expand the coverage of the programs across the country.

Conclusion

Although the incidence, mortality, and burden of HBV declined over the eight studied years, these values increased dramatically for HCV. Therefore, it is highly recommended to redistribute the health resources to detect patients, control the transmission of the disease, and treat the affected patients.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interests.

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