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Systematic Review

Epidemiology of Hepatitis B in Iran from 2000 to 2016: A Systematic Review and Meta-Regression Analysis

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Abstract

Background: Hepatitis B infection is the major risk factor for liver cancer in Iran. There is no comprehensive population-based study on the prevalence of hepatitis B by regional distribution. Moreover, systematic reviews of hepatitis B prevalence lack knowledge of some regions. We aimed to estimate the prevalence of hepatitis B and its temporal trends over 17 years by sex, age and geographical distribution.

Methods: We used the Iranian Blood Donors data in addition to systematic reviews on population-based studies at national and provincial levels and statistical methods (A two-stage spatio-temporal model and crosswalk approach) to address the missing points of hepatitis B prevalence among the general population. The direct age-standardized approach was applied using Iran's national population in 2016.

Results: At national level, age-standardized hepatitis B prevalence in Iran decreased from 3.02% (95% uncertainty interval; 2.26 to 3.96) in 2000 to 1.09% (95% uncertainty interval; 0.85 to 1.37) in 2016, with a total -64.84% change. Hepatitis B prevalence was more than 1.3 times greater in males than females in 2016. Overall, the prevalence of hepatitis B increased with increasing age. At provincial level, in 2016, the province with the highest prevalence had a nearly 11-time greater rate compared to the lowest prevalence. The declining annual percent change (APC) of the prevalence trend varied between -11.53% to -0.5% at provincial level from 2000 to 2016. Only one province did not witness a downward trend in which the APC was 0.5% (95% UI:0.47-0.54).

Conclusion: The downward trend in prevalence of hepatitis B infection indicates the effectiveness of strategies and preventive measures adapted in Iran. Nevertheless, we need to eradicate this infection. In this regard, re-evaluating preventive measures, especially in high-risk age groups of the population, is recommended.

Keywords: Hepatitis B, Iran, Prevalence

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Introduction

Hepatitis B virus (HBV) is a public health concern, particularly in developing countries.[1-3] It is estimated that 257 million people live with HBV infection. Hepatitis B is one of the major risk factors for cirrhosis and hepatocellular carcinoma that caused 887 000 deaths in 2015.[4] Since many individuals with chronic hepatitis B are not detected and treated properly, they are at risk of developing cirrhosis, liver failure, and hepatocellular carcinoma.[2]

In the WHO Eastern Mediterranean Region, the estimated prevalence of hepatitis B is nearly 3.3%.[4] The prevalence of hepatitis B varies in Iran's neighboring countries; it is 4.5%, 4.3%, 1.9%, and 1.6% in Turkey,[5] Pakistan,[6] Afghanistan,[7] and Iraq,[4] respectively. In Iran, according to a recent meta-analysis on survey studies, the prevalence of hepatitis B was almost 2%.[8,9] The prevalence of hepatitis B in blood donors in Iran is reported at about 0.58%.[10]

Although viral hepatitis was a major global concern leading to higher mortality rates than serious infectious diseases such as HIV or malaria or tuberculosis in 2015, the issue has yet not been considered by policy makers.[11,12] This situation is even worse in developing countries.[6] It

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is important to screen at-risk provinces for chronic HBV infection to appropriately put the detected individuals under hepatitis care.

Overall, at provincial level, there are no appropriate detailed reports available to evaluate the population-based prevalence of hepatitis B in Iran. There are missing data on the prevalence of hepatitis B in some age groups, genders, and provinces in published systematic reviews. On the other hand, data on the prevalence of hepatitis B in blood donors are available for all provinces in the Iranian Blood Transfusion Organization. To address the missing data and to estimate this lack of information regarding different genders and age groups at population level, we aimed to evaluate the prevalence of hepatitis B at national and provincial levels from 2000 to 2016 by sex and age based on existing population-based reports and available blood donors' records.

Materials and Methods

Data Sources

Systematic Review Data Points

Data were gathered from published national or provincial population-based epidemiological studies on hepatitis B prevalence by sex between January 1, 2000 and January 1, 2016.

Blood Donor Data Points

Independent data of all positive HBV blood donors and the total number of individuals attending blood transfusion centers at national and provincial levels by sex, age, and type of donation were included. The ELISA kit for HBsAg was used to detect HBV.

Covariates

Aggregated covariates were obtained from the Statistical Center of Iran (SCI), demographic and health survey (DHS), including demographic characteristics such as age group, gender, years of schooling, urbanization, and wealth index.[13]

Systematic Search

Medline (PubMed), ISI Web of Science, Scopus, DARE, Iranian Digital databases (SID) (http://www.sid.ir), Barakat Knowledge network system (http://health.barakatkns.com), Irandoc (https://irandoc.ac.ir/) and Magiran (https://www.magiran.com/) were searched without time limitation and were restricted to "Iran". The mesh terms "Hepatitis B", "HBV," and "Iran", "prevalence" and their Persian parallels were searched in the titles and/or abstracts (Supplementary file 1). Duplicates were excluded. Then, titles and abstracts as well as full texts were evaluated by two independent researchers. Disagreements were resolved in group discussions with a third researcher. Finally, the prevalence of hepatitis B was extracted from population-based studies. Inclusion criteria included cross-sectional or population-based cohort studies. Exclusion criteria included case reports, letters to the editor or correspondences, systematic reviews or meta-analyses, overlapping studies, prevalence of high-risk population groups and blood donors, low quality studies, or hospital-based studies and studies before 2000. The data extraction sheet included the author's name, year of study, province or city of the study, participant characteristics such as sex, age, sample size and HBV prevalence. All the studies had measured HBV by the ELISA method.

The quality of the included articles was assessed using the modified STROBE checklist (Supplementary 2). We also compared our results to two recently published systematic reviews and meta-analyses.[8,9]

Statistical Methods to Deal with Data Gap

Spatio-temporal Bayesian Hierarchical Model

There are missing data on the prevalence of hepatitis B in some age groups, genders, and provinces. To address the missing data of blood donors and to estimate the prevalence and uncertainty intervals by sex, age, year, and province, two separate statistical models (the mixed model and spatio-temporal analysis) were developed.[14] A matrix of 10 age-groups, 2 sexes, 31 provinces, and 17 years were included in the models.[15] Using two different models reduces model dependency on the outcomes.

The conditional autoregressive model for the spatial random effects model was used. Measures that were geographically closer were expected to be more relevant than measures that had some distance. This model 'borrows information' from nearby time and provinces to improve estimations for missing values and/or a small number of observations. In addition, we checked the model validity by cross-validation methods and graphical plots.

Crosswalk Approach

Another problem is generalizing the prevalence of hepatitis B in blood donors to the general population. We used regression models to 'crosswalk' between blood donors and the general population's prevalence of hepatitis B.[15] Using this approach, we predicted the correlation between hepatitis B prevalence of blood donors and population-based data by province, year, sex, and age groups.

Age standardization was done using Iran's population in 2016 to facilitate comparison between provinces. All methodological approaches are demonstrated in Figure 1 and Supplementary 3. We also compared the vaccinated group (who were born after 1993 and had hepatitis B on routine vaccination at birth) with other groups on the prevalence of hepatitis B. All programs were written in R statistical package (version 3.0.1) and Stata 14.

Results

This study includes 51 data points from systematic reviews. The characteristics of articles included in the

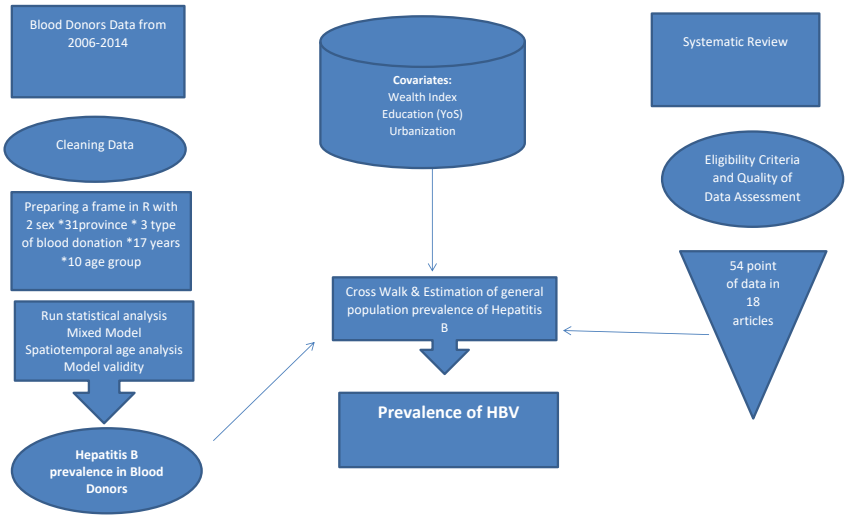

Figure1. Summary of Method and Databases.

systematic reviews are presented in Supplementary 4; the PRISMA Algorithm is presented in Supplementary 5. Five hundred sixty-eight data points were included from blood donors. Other missing points were predicted by statistical modeling discussed earlier; R^2 adjusted for the crosswalk model was 75%.

At national level, age-standardized hepatitis B prevalence in Iran decreased from 3.02% (95% uncertainty interval; 2.26 to 3.96) in 2000 to 1.09% (95% uncertainty interval; 0.85 to 1.37) in 2016 with a total -64.84% change. In 2016, the age standardized hepatitis B prevalence in males was 1.25 (95% uncertainty interval; 0.98 to 1.57) and was more than 1.5 times greater than females at 0.93 (95% uncertainty interval; 0.98 to 1.57). The APC of hepatitis B prevalence was -5.26 in females and -6.82 in males (Figure 2, Table 1). Overall, with increasing age, the mean prevalence of hepatitis B increased at national level from 0.54% (95% uncertainty interval; 0.42 to 0.70) in the 15-20-year-old age group to 4.13% (95% uncertainty interval; 3.2 to 5.27) in the 60-65 year old age group (Figure 3, Table 2).

At provincial level, the highest and lowest age-standardized hepatitis B prevalence rates in 2016 were 4.03 (95% uncertainty interval: 3.07 to 5.20) and 0.34 (95% uncertainty interval: 0.26 to 0.44), respectively. The province with the highest prevalence had a prevalence rate nearly 11 times greater than that of the lowest rate. The hepatitis B prevalence trend has noticeably decreased during the 17 years of the study (Figure 4). At provincial level, in 2016, the province with the highest prevalence had a nearly 11 times greater rate compared to the lowest prevalence. The declining annual percent change (APC) of the prevalence trend varied from -11.53% to -0.5% at provincial level from 2000 to 2016. Only one province did not witness a downward trend in which the APC was 0.5% (95% UI: 0.47–0.54) (Table 1, Figure 2). The age-adjusted prevalence of hepatitis B at provincial level was higher in males than females in 2016. The sex ratio varied between 0.8 and 2.6 at provincial level. Although the sex ratio pattern was the same in 2000, ratios were higher than that in 2016 and varied between 1.17 and 3 (Figure 5). Overall, with increasing age, the mean prevalence of hepatitis B increased in all the provinces.

The prevalence of hepatitis B in the vaccinated group (who were born after 1993 and had routine hepatitis B vaccination at birth) was 0.70 (95% uncertainty interval: 0.63 to 0.77); in the unvaccinated group, it was 2.66 (95% uncertainty interval: 2.40 to 2.93).

Figure 2. Annual Percent Change Map of Prevalence of Hepatitis B by Sex.

Table 1. Prevalence of Hepatitis B at National and Provincial Level in 2000 and 2016 and Average Annual Percent Change

National/Provincial	2000		2016		AAPC	
	Female (UI)	Male (UI)	Female (UI)	Male (UI)	Female (UI)	Male (UI)
Markazi	2.2 (1.64, 2.87)	4.62 (3.45, 6.09)	1.42 (1.11, 1.78)	1.83 (1.43, 2.29)	-2.65 (-2.71, -2.59)	-5.63 (-5.65, -5.6)
Gilan	1.1 (0.81, 1.47)	1.67 (1.24, 2.23)	0.54 (0.41, 0.7)	0.56 (0.44, 0.72)	-4.34 (-4.39, -4.3)	-6.54 (-6.57, -6.51)
Mazandaran	1.37 (1.05, 1.76)	2.4 (1.83, 3.1)	0.54 (0.43, 0.67)	0.7 (0.57, 0.87)	-5.71 (-5.76, -5.66)	-7.4 (-7.43, -7.37)
Azarbaijan East	2.23 (1.69, 2.89)	4.39 (3.3, 5.7)	0.68 (0.53, 0.85)	1.27 (1, 1.58)	-7.16 (-7.21, -7.12)	-7.47 (-7.49, -7.44)
Azarbaijan West	1.53 (1.16, 1.98)	3.63 (2.73, 4.71)	0.31 (0.25, 0.39)	0.7 (0.56, 0.87)	-9.34 (-9.43, -9.26)	-9.64 (-9.73, -9.55)
Kermnshah	2.19 (1.63, 2.87)	5.16 (3.82, 6.78)	0.76 (0.59, 0.96)	1.78 (1.39, 2.25)	-6.32 (-6.37, -6.27)	-6.45 (-6.48, -6.41)
Khuzestan	0.68 (0.51, 0.88)	1.29 (0.97, 1.68)	0.39 (0.31, 0.49)	0.58 (0.46, 0.72)	-3.26 (-3.32, -3.21)	-4.82 (-4.88, -4.76)
Fars	1.06 (0.8, 1.37)	1.92 (1.45, 2.49)	0.69 (0.55, 0.86)	0.82 (0.66, 1.02)	-2.57 (-2.66, -2.49)	-5.12 (-5.16, -5.09)
Kerman	3.22 (2.46, 4.17)	4.44 (3.35, 5.76)	0.88 (0.7, 1.09)	0.81 (0.65, 0.99)	-7.84 (-7.9, -7.78)	-10.14 (-10.17, -10.12)
Khorasan Razavi	1.52 (1.16, 1.96)	2.64 (1.98, 3.4)	0.56 (0.45, 0.69)	0.7 (0.56, 0.86)	-6.05 (-6.08, -6.03)	-7.95 (-7.95, -7.94)
Isfahan	1.47 (1.1, 1.92)	2.23 (1.66, 2.93)	0.44 (0.35, 0.56)	0.49 (0.39, 0.61)	-7.28 (-7.31, -7.25)	-9.03 (-9.05, -9.01)
Sistan and Baluchestan	4.02 (3.08, 5.09)	9.49 (7.23, 12.18)	1.17 (0.93, 1.44)	2.32 (1.85, 2.86)	-7.36 (-7.42, -7.31)	-8.4 (-8.43, -8.36)
Kurdistan	1.97 (1.48, 2.57)	5.4 (4.01, 7.09)	0.43 (0.34, 0.54)	1.01 (0.79, 1.27)	-9.01 (-9.06, -8.96)	-9.94 (-9.95, -9.92)
Hamedan	1.86 (1.39, 2.45)	3.52 (2.61, 4.64)	1.12 (0.87, 1.42)	1.8 (1.41, 2.29)	-3.07 (-3.13, -3.02)	-4.11 (-4.16, -4.06)
Chaharmahal and Bakhtiari	3.27 (2.42, 4.31)	6.88 (5.06, 9.15)	1.54 (1.18, 1.98)	1.92 (1.49, 2.46)	-4.72 (-4.81, -4.64)	-7.71 (-7.75, -7.66)
Lorestn	2.48 (1.87, 3.22)	4.55 (3.42, 5.96)	0.73 (0.58, 0.92)	0.95 (0.75, 1.18)	-7.27 (-7.31, -7.24)	-9.31 (-9.34, -9.28)
Ilam	4.4 (3.21, 5.94)	9.7 (7, 13.09)	2.74 (2.04, 3.59)	3.94 (2.97, 5.17)	-2.98 (-3.03, -2.93)	-5.53 (-5.58, -5.48)
Kohgiluyeh and Boyer Ahmad	2.01 (1.47, 2.68)	6.22 (4.54, 8.36)	0.7 (0.53, 0.91)	1.89 (1.45, 2.45)	-6.39 (-6.45, -6.34)	-7.19 (-7.24, -7.15)
Bushehr	1.87 (1.36, 2.53)	4 (2.9, 5.44)	1.98 (1.5, 2.6)	3.07 (2.34, 3.98)	0.33 (0.27, 0.39)	-1.65 (-1.67, -1.63)
Zanjan	1.69 (1.24, 2.24)	3.28 (2.41, 4.38)	0.25 (0.19, 0.33)	0.44 (0.34, 0.57)	-11.18 (-11.25, -11.11)	-11.74 (-11.83, -11.66)
Semnan	3.74 (2.8, 4.89)	6.42 (4.78, 8.47)	3.04 (2.35, 3.84)	2.43 (1.88, 3.08)	-1.24 (-1.37, -1.12)	-5.84 (-5.9, -5.78)
Yazd	2.13 (1.57, 2.83)	4 (2.95, 5.34)	1.37 (1.04, 1.76)	1.67 (1.29, 2.13)	-2.89 (-3.11, -2.67)	-5.31 (-5.37, -5.26)
Hormozgan	1.92 (1.44, 2.49)	3.81 (2.85, 4.98)	2.84 (2.22, 3.59)	3.32 (2.62, 4.17)	2.54 (2.5, 2.58)	-0.79 (-0.84, -0.73)
Tehran	2.71 (2.07, 3.45)	3.18 (2.42, 4.08)	0.84 (0.68, 1.01)	0.73 (0.59, 0.89)	-7.17 (-7.22, -7.12)	-8.81 (-8.85, -8.77)
Ardabil	2.85 (2.15, 3.67)	7.36 (5.51, 9.56)	1.4 (1.1, 1.76)	2.77 (2.18, 3.48)	-4.21 (-4.32, -4.1)	-5.84 (-5.9, -5.78)
Qom	2.46 (1.82, 3.27)	5.47 (4.01, 7.29)	1.14 (0.88, 1.46)	1.48 (1.14, 1.89)	-4.74 (-4.82, -4.66)	-7.82 (-7.92, -7.72)
Qazvin	2.13 (1.54, 2.87)	3.72 (2.69, 5.05)	0.93 (0.7, 1.22)	1.06 (0.8, 1.38)	-5.07 (-5.11, -5.04)	-7.53 (-7.57, -7.48)
Golestan	4.44 (3.41, 5.65)	9.62 (7.33, 12.33)	2.7 (2.15, 3.31)	4.5 (3.61, 5.54)	-3.11 (-3.15, -3.08)	-4.64 (-4.66, -4.63)
Khorasan North	4.65 (3.51, 6.04)	7.89 (5.9, 10.35)	2.19 (1.7, 2.77)	3.39 (2.65, 4.27)	-4.55 (-4.61, -4.49)	-5.1 (-5.15, -5.05)
Khorasan South	4.71 (3.47, 6.26)	8.92 (6.53, 11.92)	2.87 (2.18, 3.71)	5.2 (3.97, 6.7)	-2.99 (-3.06, -2.91)	-3.35 (-3.38, -3.32)
Alborz	5.1 (3.42, 7.43)	6.31 (4.21, 9.26)	1.89 (1.33, 2.62)	1.76 (1.25, 2.46)	-6.12 (-6.18, -6.06)	-7.62 (-7.66, -7.58)
Iran	2.2 (1.65, 2.88)	3.85 (2.87, 5.05)	0.94 (0.73, 1.18)	1.25 (0.98, 1.58)	-5.26 (-5.33, -5.19)	-6.82 (-6.86, -6.77)

AAPC, average annual percent change; UI, uncertainty interval.

Discussion

Based on our results, age-standardized hepatitis B prevalence decreased over the 17 years of the study at national and provincial levels. Age-standardized hepatitis B prevalence in males was more than 1.5 times greater than in females. Moreover, the APC of hepatitis B prevalence in females was higher than in males. Overall, with increasing age, the prevalence of hepatitis B increased in all the provinces.

The prediction prevalence in this study is very similar to pervious population-based surveys in Iran. The predicted prevalence of hepatitis B in males in 2012 in Chaharmahal and Bakhtiari was 2.9% versus 2.7% in the observed survey report,[16] or 1.7% in Isfahan in 2005 versus 1.3% in the observed survey report.[17]

The World Health Organization's strategy for eliminating viral hepatitis B by 2030 includes global objectives to decrease new viral hepatitis infections by up to 90%. Additionally, the 65% reduction in mortality due to viral hepatitis is another objective, particularly the reduction of HBV and hepatitis C virus related mortalities. Therefore, the declining trend of hepatitis B observed in this study is in line with this strategy.

Iran has a twice lower hepatitis B prevalence than its neighboring countries like Turkey and Pakistan.[5,6,16] However, it has not been eliminated yet and remains the

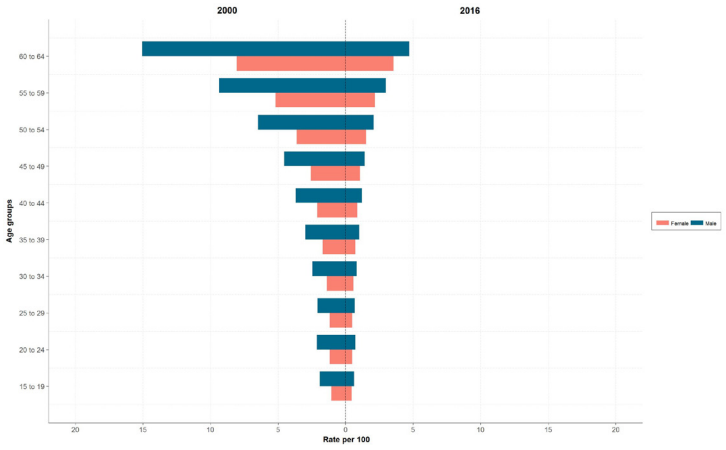

Figure 3. Prevalence of Hepatitis B by Age Categories in 2000 And 2016.

main cause of death due to liver cancer and cirrhosis.[3,17] Therefore, special emphasis should be laid on this objective. Disease prevention is key. This may include reducing the risks of exposure to the viruses, vaccination, and early detection and treatment. As acute hepatitis infections are frequently asymptomatic, detection is a major problem in many countries.[11] Based on the literature, in most Asian and African countries and Iran, hepatitis B infection was found more frequently than hepatitis C infection in liver cancer patients.[3] This situation is reversed in Europe, the United States, Japan, Pakistan, Mongolia, and Saudi Arabia.[18] It is estimated that in Iran, by 2035, the number of newly detected hepatitis B cases will be 2.5 times lower than that in 2016, but the cirrhosis percentage due to hepatitis B will be almost doubled.[16] Vaccination is the key solution in many countries, particularly in Africa and Asia. In Iran, this strategy was established in 1993, and the HBV infection has declined in children and young adults, consistent with the results of this study.[19,20] This could be the reason behind the reduction in prevalence among the 25-30-year-old age group in this study.

The Polaris Observatory estimated that 48 million children lived with HBV in 2016. According to recent documents and this study, due to vaccination, newly detected HBV positivity is on the decline, but hepatitis B infection is still observed in individuals under the age of 25 years according to the present study's results.

Children and childbearing women are still a challenge due to mother-to-child transmission of chronic viral hepatitis.[21] Furthermore, it has been reported that HBV-positive childbearing women had higher viral loads compared to others.[22] Thus, developing comprehensive preventive programs for childbearing women by policymakers is recommended.[16] Studies have shown that preventive strategies for mother-to-child transmission through screening and treatment have led to HBV elimination in sub-Saharan Africa.[23-25] This could be added to Iran's preventive protocol for HBV elimination.[5]

An earlier study showed that females were more likely to produce antibody against hepatitis B than males in reaction to infection, and males became carriers of chronic hepatitis B more frequently.[26-28] This is consistent with our results of the trend in females and the percentage change of hepatitis B prevalence over the 17-year period. The next

Table 2. Prevalence of Hepatitis B at National Level by Age and Sex, in 2000 and 2016

Age Group	2000 (UI)		2016 (UI)	
	Female	Male	Female	Male
15–19	1.05 (0.78, 1.4)	1.92 (1.42, 2.55)	0.45 (0.35, 0.58)	0.64 (0.49, 0.82)
20–24	1.17 (0.87, 1.54)	2.11 (1.56, 2.78)	0.5 (0.39, 0.63)	0.71 (0.56, 0.9)
25–29	1.17 (0.87, 1.53)	2.07 (1.54, 2.73)	0.5 (0.39, 0.63)	0.69 (0.54, 0.87)
30–34	1.38 (1.03, 1.82)	2.44 (1.82, 3.22)	0.59 (0.46, 0.74)	0.81 (0.64, 1.02)
35–39	1.69 (1.26, 2.22)	2.99 (2.22, 3.92)	0.72 (0.56, 0.91)	1.01 (0.79, 1.26)
40–44	2.09 (1.57, 2.72)	3.68 (2.75, 4.83)	0.87 (0.68, 1.09)	1.21 (0.95, 1.52)
45–49	2.56 (1.93, 3.34)	4.53 (3.39, 5.96)	1.07 (0.84, 1.34)	1.42 (1.12, 1.78)
50–54	3.62 (2.73, 4.72)	6.48 (4.85, 8.47)	1.52 (1.2, 1.91)	2.08 (1.64, 2.6)
55–59	5.18 (3.92, 6.72)	9.36 (7.02, 12.2)	2.18 (1.72, 2.73)	2.99 (2.35, 3.75)
60–64	8.06 (6.06, 10.47)	15.04 (11.21, 19.73)	3.56 (2.75, 4.55)	4.72 (3.66, 6.01)

UI, uncertainty interval.

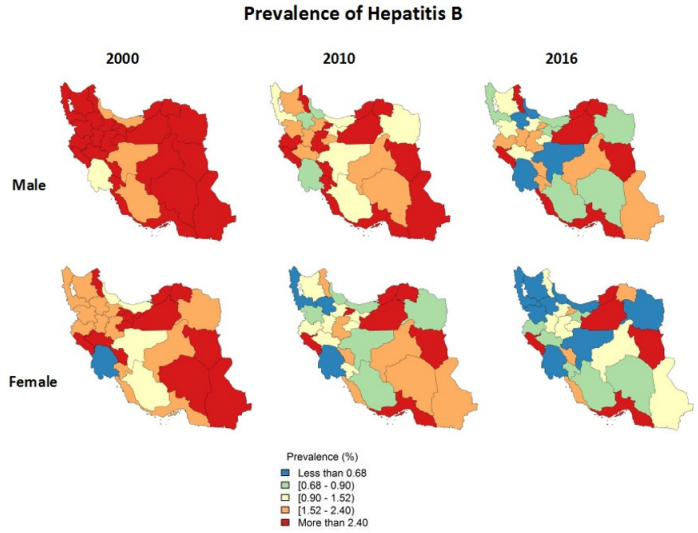

Figure 4. Prevalence of Hepatitis B Map by Province in 2000, 2010 and 2016.

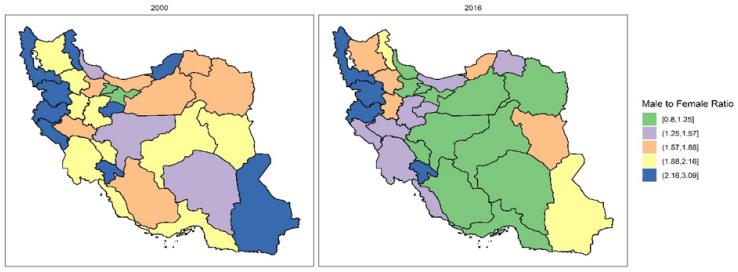

Figure 5. Female to Male Ratio of Hepatitis B Prevalence in 2000 and 2016.

step is to clarify what should be done next.

The role of medical providers in eliminating hepatitis B could be detection of HBV-positive patients, treating them and referring them to psychotherapy if needed, adapting preventive measures to minimize the risk of transmission to others, and referring patients to chronic liver disease specialists to minimize the risk of developing future cirrhosis or hepatocellular carcinoma. Assessment of HBV replication status and severity of liver injury must be also borne in mind.[29] Policymakers and medical providers should establish a lifelong assessment process for all hepatitis B-positive patients to monitor liver disease or cancer progression, and start early treatment and screen responses to treatment.[29] The choice of antiviral therapy for hepatitis B is not curative, but can slow down the progression of the disease and improve survival.[21] However, hepatitis B therapy is a rapidly changing area of clinical practice.[29]

In this respect, establishing a registration system for seropositive chronic viral hepatitis patients is recommended. Formation of a registry enables medical providers and policymakers to provide direct medical management, counseling, notifications, patient follow-up, and to have national, provincial and regional estimates of identified chronic hepatitis B infection rates. Other benefits of these registries are identifying HBV's epidemiologic transitions, treatment success, cancer and liver disease development and monitoring the screening and prevention programs at national, provincial and regional levels. To this end, it is necessary to establish high-quality electronically designed laboratories across the country and methods to prevent duplication of registries. Moreover, for better data gathering and future estimates on the trends and burden of diseases, this registry must be connected to the perinatal screening of women and neonates affected with chronic hepatitis and also to the liver cancer registry and death certificate data.[29] The Iranian Hepatitis Network has been established by Iran's gastroenterologists to achieve the hepatitis elimination strategy.[30]

Nowadays, medical acquiescence is high for testing seropositivity of hepatitis B in certain populations like pregnant women or those who are admitted to hospitals, but it is still necessary for policymakers to facilitate detection and testing of chronic HBV patients in the following: primary care systems, physician's offices, TB health centers, substance abuse centers, refugee offices and health centers, academic or organizational clinics, dialysis, and cancer centers.[29] According to the literature, we do have

the instruments to eliminate viral hepatitis by vaccination (hepatitis B) and through curative treatment (hepatitis C)[11,21]; however, all policymakers and governments should adopt preventive, diagnostic and treatment strategies at a global level.

The strength of this study was its reporting of hepatitis B prevalence over 17 years for all the provinces, both sexes and 10 age groups for the first time using the latest statistical modeling.

As a limitation, our blood donor data was subject to selection bias. Donors have different motivations and attitudes compared to the general population. We checked the trend in weight, as well as systolic and diastolic blood pressure (as independent covariates) of Iranian blood donor data with the national non-communicable diseases risk factors survey (STEPs),[31,32] which is a population-based survey in the country, and found that the patterns were similar. Thus, another strength of this study was that we applied the latest statistical modeling to predict the general population's prevalence from blood donors using population-based covariates[13] and published population-based surveys.

In conclusion, Iran has a low prevalence rate of hepatitis B compared to its neighboring countries and is witnessing a downward trend. Nevertheless, the following steps are recommended to achieve the 2030 Elimination Objective; improving diagnostic strategies, providing better treatment options especially for high-risk groups, discovering and developing functional cures for hepatitis B, knowledge development on the disease, reducing stigma and raising public awareness. Furthermore, establishment of hepatitis B registry networks is useful for clinical management and alleviation of public health concerns. Last but not least, since having knowledge of the disease and fighting stigmas are highly important in preventive strategies, patient education programs should be directed in a culturally sensitive style and easy understanding by any level of education and in the patient's native language.

Authors' Contribution

NR, MP and MM: Writing the original draft. MAL, SKh, SAM, MZ, SAK, FD, ShA and FF: Writing, review and editing. ASh, KG and MP: Methodology, Validation and Software. FF: Supervision.

Conflict of Interest Disclosures

There is no conflict of interest.

Ethical Statement

This study was approved by ethical committee of Iran University of Medical Sciences (IR.IUMS.REC1395.9221128201).

Supplementary Materials

Supplementary file 1. Search strategy in Medline.
Supplementary file 2. Quality assessment of articles by STROBE checklist.
Supplementary file 3. Statistical analysis detail.
Supplementary file 4. Characteristics of included articles in systematic search.
Supplementary file 5. PRISMA algorithm.

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