

HOSTED BY



Contents lists available at ScienceDirect

Asian Pacific Journal of Tropical Disease

journal homepage: www.elsevier.com/locate/apjtd



Epidemiology investigation doi: 10.1016/S2222-1808(15)60828-3 ©2015 by the Asian Pacific Journal of Tropical Disease. All rights reserved.

The epidemiological aspects of hepatitis B virus in Iran

Majid Afzali¹, Hamidreza Naderi², Masoud Mirzaei^{3*}¹North Khorasan University of Medical Sciences, Bojnurd, Iran²Department of Infectious Diseases, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran³Research Centre for Epidemiology and Prevention of Chronic Diseases, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

ARTICLE INFO

Article history:

Received 15 Dec 2014

Received in revised form 29 Dec

2014, 2nd revised form 15 Jan 2015

Accepted 5 Mar 2015

Available online 20 May 2015

Keywords:

Hepatitis B

Virus

Epidemiology

Vaccination

ABSTRACT

Objective: To investigate the epidemiological features and demographic characteristics of hepatitis B virus (HBV)-infected patients and the accurate incidence rates of HBV infection in Iran.

Methods: This retrospective study was conducted using the data from Iranian National Hepatitis Registry Database. Based on the registered records of HBV patients during 2010-2012, the sample size of this study was 28227. Data were analyzed to calculate the incidence of hepatitis B infection according to age, sex and region of residence in Iranian population during the period.

Results: The average age of infected people was (39.7 ± 16.0) years and the mean annual incidence rate of the infection was 55.37 per 10^5 population. The highest incidence and frequency rates were in the 60-69 ($23.0/10^5$) and 20-29 (28.7%) age groups, respectively. The lowest incidence and frequency rates, regardless of age and sex, were in the age group under 10 years old. The incidence rate was almost the same in urban ($18.7/10^5$) and rural areas ($17.5/10^5$).

Conclusions: Hepatitis B prevention programs should focus more on people aged 20-40 years. Vaccination of people who are at risk of exposure to the virus should also be emphasized.

1. Introduction

More than two billion people have been infected with hepatitis B worldwide[1], and among these individuals, more than 350 million individuals are hepatitis B virus (HBV) carriers[1,2]. In all Eastern Mediterranean countries, hepatitis B infection is endemic[3].

By 2009, the World Health Organization Regional Office for the Eastern Mediterranean Region estimated that 170 million people had chronic HBV infection in the region; each year, around 4.3 million new HBV infections occur in the region[4,5].

The risk of infection with hepatitis B is high in five countries (Afghanistan, Pakistan, Yemen, Sudan and Somalia), accounting for

more than 55% of the total population of the region, and moderate in the remaining 17 countries, including Iran[6].

Prevalence of hepatitis B surface antigen (HBsAg) in countries in the Mediterranean region ranges from 0.8% in Algeria[7] and 1.69% in Lebanon to 9.9% in Jordan[8]. The percentage of prevalence of HBsAg positive cases in Iran varies from 1.5% to 6.5%. Accordingly, Iran is in the intermediate group of the world in the prevalence of HBsAg positive[9,10]. It is estimated that over 35% of Iranians have been exposed to the HBV and 2%-3% are chronic carriers[10].

Based on the Iranian National Population and Housing Census conducted in 2011, Iran had 31 provinces and the population of the country was 75 149 669 with 21 446 783 people living in rural areas, 53 646 661 residing in urban areas and 22 556 non-resident[11]. Since 1993, the Ministry of Health and Medical Education of Iran established the HBV infection registry system and all medical universities participated in this national program[12,13]. The aim of this surveillance system is to eliminate hepatitis B. However, no

*Corresponding author: A. Professor Masoud Mirzaei, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

Tel: +983538239970

E-mail: mmirzaei@ssu.ac.ir

Foundation Project: Supported by School of Public Health, Shahid Sadoughi University of Medical Sciences and Health Services, Yazd, Iran.

specific time has been set to achieve this goal[14].

Although many epidemiological studies of hepatitis B infection have been conducted in Iran, so far as we know, except for the study by Zali in 1996[15], the epidemiology of HBV infection in Iran has not been investigated thoroughly. Eighteen years after Zali *et al.* paper, it seems that a comprehensive look at the epidemiology of hepatitis B in Iran is necessary. The present study is the first in the country with these large set of data. The aim of this study was to investigate the epidemiological features and demographic characteristics of infected patients and the accurate incidence rates of HBV infection in Iran, according to the data provided by the Iranian National Hepatitis Registry during 2010-2012.

2. Materials and methods

This retrospective study was conducted based on the data provided by the National Hepatitis Registry Database (NHRD). According to this surveillance system recommendation, each case of confirmed HBV infection had to be reported and all of the demographic data on infected cases should be recorded systematically throughout the country[12]. Under these regulations, blood transfusion organization, all public and private laboratories, hospitals and medical centers should report the diagnosed cases to their City Health Department. To ensure the accuracy of the records, in the urban or rural health centers a registered physician justifies the collected data[13]. The information is recorded in a questionnaire provided by the Hepatitis Prevention and Control Office at the Communicable Diseases Management Center of the Ministry of Health and Medical Education.

Based on the data registered at the Iranian National Hepatitis Database (INHD) during 2010-2012, the sample size of this research was 28 227 with confirmed positive test results. All identified patients with HBV infection during the period whose recorded demographic characteristics were complete and accessible were included.

Given that it was to analyze the data provided by the national database, the approval from Ethics Committee was not necessary. Data were analyzed by SPSS 18 software using descriptive statistics to calculate the province-specific incidence of hepatitis B infection regarding the age, sex and region of residence of each infected case.

To estimate the "population at risk" for calculating the incidence rate, all vaccinated individuals under twenty years old were subtracted. The infected persons were ignored, because they comprised a relatively small percentage of the general population.

3. Results

In the present study, the data on all diagnosed HBV infected cases were analyzed provided by NHRD during 2010-2012, approximately 28 227 people.

The average age of infected people was (39.7 ± 16.0) years old and the mean annual incidence rate of the infection was 55.37 per 10^5

population.

The frequency and the annual incidence rate of HBV infection were slightly higher in men than those in women (Table 1). Nevertheless, the total incidence rate had a gradual decline within three years of the study.

Table 1

Demographic characteristics of HBV infected people in IR Iran 2010-2012.

Parameters	Domain	%
Age groups	1-9	0.7
	10-19	3.8
	20-29	28.7
	30-39	23.8
	40-49	15.9
	50-59	13.0
	60-69	8.0
	Over 70	6.1
Sex	Male	51.6
	Female	48.4
Marital status	Dead spouse	1.3
	Single	10.5
	Divorced	0.4
	Married	87.8
Residential status	Urban	73.8
	Rural	25.6
	Nomadic	0.6
Source of report	Laboratory	24.5
	Hospital	24.2
	Private office	5.0
	Blood transfusion organization	7.8
	Clinic	1.4
	Health center	37.1

There was an apparent difference in the highest incidence and frequency rates according to sex, and between the age groups. The highest incidence and frequency rates were in the 60-69 and 20-29 age groups, respectively. These rates for men were in the 60-69 and 30-39 age groups, and for women in age groups 60-69 and 20-29, respectively (Table 1 and Figure 1). The lowest incidence and frequency rates, regardless of age and sex, were in the age group under 10 years old. The difference between the highest and the lowest incidence rates in various age groups were 40 folds, and more than 60 folds in men and more than 35 folds in women were observed.

The incidence rate of HBV infection in men increased with aging until the age of 70 and declined thereafter. However, in females, the incidence rate increased until the age of 40 and declined thereafter. There was a slight increase between the age of 60 to 70 in females (Figure 1).

The incidence rate in different age groups had a gradual decline within three years of the study.

The highest frequency rate of hepatitis B infection was among the married and the lowest rate was among the divorced cases (Table 1). In Table 2, incidence according to sex and area of residence was calculated and the average of three years was reported. Regarding the distribution of infected people by residential status, the incidence rate was nearly the same in urban and rural areas (Table 2). Health centers reported most cases of the infection (37.1%) while the lowest

number of reports came from the clinics (1.4%).

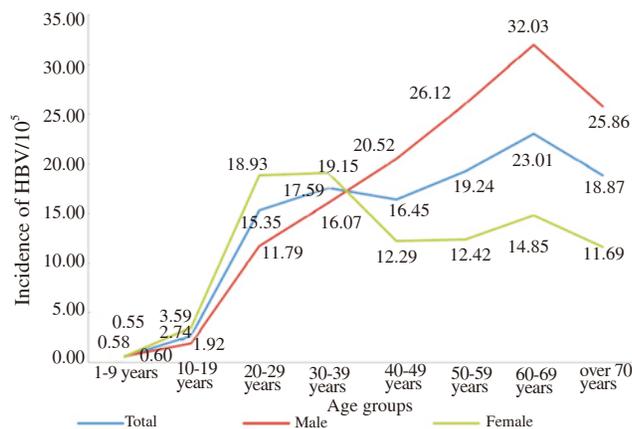


Figure 1. Annual incidence rate of HBV infection according to age groups and sex in IR Iran during 2010-2012.

Table 2

The mean annual incidence rate* of hepatitis B infection in IR Iran during 2010-2012.

Parameter	Incidence rate*	
Sex	Male	19.16
	Female	17.77
Region	Urban	18.71
	Nomadic	0.27
	Rural	17.50
Total incidence rate	55.37	

*: per 10⁵ population.

4. Discussion

The results of the present study showed a slightly higher incidence of HBV infection in men than women, and this difference increased with aging. The highest incidence and frequency rates were noted in 20-29 age group, married cases and residents of urban areas. Health centers diagnosed and reported the majority of patients recorded in NHRD.

To our knowledge, the present study is the first big data analytics that calculated the incidence of hepatitis B infection using all documented cases in NHRD. So far, most published research papers that studied the epidemiology of HBV in Iran estimated the prevalence rate of infection using much smaller data set, and their results cannot be compared with the results of the present study. The mean age of hepatitis B infected cases in Iran was (39.7 ± 16.3) years old while in Iran, this rate was lower in Pakistan [(29.8 ± 12.5) years old] and higher in China [(41.7 ± 12.2) years old] and USA [(43.0 ± 1.0) years old][16-18]. These differences might be attributable to cultural and behavioral differences.

In the present study, the average annual incidence rate of the infection between 2010 and 2012 was 55.37 per 10⁵ population. This rate is 24.5 in Singapore, 10.7 in China, 4.8 in Malaysia and 14.4 per 10⁵ population in India[19]. The estimated annual incidence rate of hepatitis B infection was 7.4 per 10⁵ population in England

and Wales[20] and 2.1 per 10⁵ in the United States[21]. The lower incidence rate reported in countries such as England and the United States is probably due to the vaccination programs, preventive measures and screening programs. However, considering that these studies did not report how the incidence rate was calculated, these differences might be due to different methods of determining the incidence rate of the infection.

In the present study, the number of patients in each age group was compared with the total population in all age group, and it was found that the highest number of infected people belonged to the 20-29 age group (28.7%). Given that 20-29 age group comprises 23% of Iran's population, it is clear that this age group is more vulnerable to hepatitis B infection in the age pyramid of Iran. The lowest number of infected people was in the age group under 10 years old. Iranian population aged over 60 years old has the lowest number in age pyramid and less than 10 years old people comprise almost 25% of the general population. But hepatitis B frequency in older age groups is almost 20 times the age group under 10 years. This considerable difference is probably due to the lack of immunization and more exposure to the virus among the older. The hepatitis B infected cases were divided into eight groups, and the highest frequency and incidence rates were in age groups 20-29 and 60-69, respectively. The lowest rates were noted in the age group less than ten years old.

These results are consistent with the findings of studies in Bahrain[22], China[23], Libya[24], Pakistan[16] and USA[21] where the lowest rates were reported in age group less than 10 years and the highest frequency rates were noted in age group 20-30. In Spain[25] and Libya[26], the lowest frequency and incidence rates were in age group less than ten years while the highest incidence rate was noted in age group above 65 years old.

As noted in these studies, the high incidence and frequency rate in older age groups are possibly due to lack of immunization in older population, and their broader range of high risk activities and more situations of exposure to the virus than the youngsters. In this study, the highest frequency rate of HBV infection in men and women was in people aged 30-39 years and 20-29 years old, respectively, and the lowest frequency was noted in the age group under 10 years old. In a study from India, a similar result has been reported[27].

In the present study, the frequency and incidence rate of hepatitis B were higher in men than women. Consistent with these results, in the studies done in Iraq[28], Singapore[19], Turkey[29], China[30], Canada[31], and the National Health and Nutrition Study conducted in USA[32], the prevalence rate of hepatitis B is reported to be higher in men than in women[33]. This study found that the incidence rate increased with aging in men. Similar results have been reported from France[34] and Libya[35].

Overall, the incidence of infection is higher in men, possibly because men are more active in the community and more exposed to the virus. Estrogen may play an important role in the natural resistance of hepatocytes against virus and the consequence of chronic liver disease[36]. Married people comprised the highest

number of HBV infected cases (87.8%) while the divorced population showed the lowest number (0.4%). As almost 60.5% of Iranian population are married and only 10.5% are divorced, these results justify the high frequency of the infection in the married and the very low frequency in the divorced. These findings have also been reported in other Islamic countries[24,35].

In Bahrain, the majority of patients were married and the divorced and widows had much lower frequency of HBV[22]. However, results of the studies conducted in non-Muslim countries such as China[30] and USA[37] have shown a higher incidence of cases among widows.

Based on the results of this study, the highest percentage of hepatitis B infection was noted in the urban areas (73.8%) and the lowest in the nomadic regions (0.6%). The urban population of Iran comprises 71.4% of general population and the nomads comprises 0.1%, indicating a greater risk of infection in urban areas and lower risk, in relation to their population, among nomads.

In the present study, the incidence rate of hepatitis B infection was roughly the same in urban and rural areas, but Mehmet from Turkey reported a much higher incidence rate of the infection in rural regions[29]. This difference might be the results of differences in transmission routes of the infection in different areas. Most HBV cases were reported by health centers and clinics. While, in Norway, the least cases were reported by the laboratory units[38]. However, this could be due to the compliance of more co-operative laboratories in Norway, or due to the firm structure of health care networks in the remotest and the most deprived rural areas in Iran.

The major limitation of this study was the inadequacy of the data reported to the NHRD. Despite being mandatory[13], the report of identified HBV infected cases by the health organizations, especially in the private sector, is far from ideal. Therefore, the findings should be interpreted cautiously. Further, we included the recently diagnosed cases as the new cases to calculate the incidence rate. So, the results may be a little bit overestimated.

Due to the inclusion of hepatitis B vaccination in the national immunization program, the incidence of the infection in people under 20 years old became very low. Most infected individuals in this study had no history of vaccination which shows the effect of introducing HBV vaccination to the newborns since year 2000.

In conclusion, hepatitis B infection prevention programs might focus on people aged 20–40 years, with emphasis on health education programs about the prevention of exposure to hepatitis B infection as well as the vaccination of the people who are most exposed to the virus.

Given that the current status of reporting newly detected HBV infected cases is less than adequate by the private sector, national policies must address this pitfall and encourage the private sector to report the new cases correctly.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgments

This article is in part, based on a MSc thesis on Epidemiology, School of Public Health, Shahid Sadoughi University of Medical Sciences and Health Services. The sincere effort of the director and staff from the Centre for Communicable Diseases, Ministry of Health and Medical Education is appreciated. Thanks for Dr. Mohammad Mehdi Gouya, Dr. Abbas Nouruznejad, Dr. Mohammad Nabavi and Ms. Maryam Mashlool for providing access to the data of NHRD.

References

- [1] Thabit AM, Al-Moyed KA, Al-Balushi MS, Hasson SS, Sallam TA. Occult hepatitis B virus among chronic liver disease patients in Yemen. *Asian Pac J Trop Dis* 2012; **2**(1): 4-6.
- [2] Azarbahra M, Tajbakhsh E, Momtaz H. Phylogenetic analysis of hepatitis delta virus isolated from HBsAg positive patients in Shahrekord, Iran. *Asian Pac J Trop Dis* 2014; **4**(5): 391-7.
- [3] Qureshi H. Hepatitis B infection in Eastern Mediterranean Region: challenges and the way forward. *East Mediterr Health J* 2013; **19**(7): 585-6.
- [4] Hatzakis A, Van Damme P, Alcorn K, Gore C, Benazzouz M, Berkane S, et al. The state of hepatitis B and C in the Mediterranean and Balkan countries: report from a summit conference. *J Viral Hepat* 2013; **20**: 1-20.
- [5] Esmat G. Hepatitis C in the Eastern Mediterranean Region. *East Mediterr Health J* 2013; **19**(7): 587-8.
- [6] World Health Organization. Prevention and control of viral hepatitis infection: framework for global action. Geneva: World Health Organization; 2012. [Online] Available from: http://www.who.int/csr/disease/hepatitis/GHP_framework.pdf [Accessed on 21st November, 2014]
- [7] Romanò L, Velati C, Cambiè G, Fomiatti L, Galli C, Zanetti AR, et al. Hepatitis B virus infection among first-time blood donors in Italy: prevalence and correlates between serological patterns and occult infection. *Blood Transfus* 2013; **11**(2): 281-8.
- [8] Hepatitis B and C Public Policy Association. Conference on hepatitis B and C in Mediterranean and Balkan Countries, Nicosia, Cyprus 5-7 December 2012. Luxembourg: Hepatitis B and C Public Policy Association; 2012. [Online] Available from: <http://www.hepsummit2012.org/sites/default/files/pdfs/CyprusConfEXECUTIVE SUMMARY26.02.2013-1.pdf> [Accessed on 21st November, 2014]
- [9] World Health Organization. Introduction of hepatitis B vaccine into childhood immunization services: management guidelines, including information for health workers and parents. Geneva: World Health Organization; 2001. [Online] Available from: http://whqlibdoc.who.int/hq/2001/WHO_V&B_01.31.pdf [Accessed on 21st November, 2014]
- [10] Merat S, Rezvan H, Nouraei M, Jamali A, Assari S, Abolghasemi H, et al. The prevalence of hepatitis B surface antigen and anti-hepatitis

- B core antibody in Iran: a population-based study. *Arch Iran Med* 2009; **12**(3): 225-31.
- [11] Presidency of the I.R.I Management and Planning Organization. Implementation of the 2011 Iranian population and housing census in autumn (24 October – 13 November 2011). Iran: Presidency of the I.R.I Management and Planning Organization. [Online] Available from: <http://www.amar.org.ir/Default.aspx?tabid=765> [Accessed on 21st November, 2014]
- [12] Mirzaei M, Afzali M, Lotfi MH, Alavinia SM, Fallahzadeh MH, Ayatollahi J. Hepatitis B infection in North Khorasan province during March 2010 - February 2012. *J North Khorasan Univ Med Sci* 2014; **6**(2): 432-9.
- [13] Asgari F, Haghazali M, Esteghamati A, Haj Rasoliha H. [*Hepatitis B surveillance guideline*]. Iran: MOHME Publishing; 2007. [Persian]
- [14] World Health Organization. Global policy report on the prevention and control of viral hepatitis in WHO Member States. Geneva: World Health Organization; 2013. [Online] Available from: http://apps.who.int/iris/bitstream/10665/85397/1/9789241564632_eng.pdf [Accessed on 21st November, 2014]
- [15] Zali MR, Mohammad K, Farhadi A, Masjedi MR, Zargar A, Nowroozi A. Epidemiology of hepatitis B in the Islamic Republic of Iran. *East Mediterr Health J* 1996; **2**(2): 290-8.
- [16] Zafar A, Khan E, Khan MS, Moiz B, Jafri W. Changing trends of hepatitis B seromarkers amongst Pakistani population: a laboratory-based review. *J Pak Med Assoc* 2013; **63**(7): 826-30.
- [17] Zhang HW, Yin JH, Li YT, Li CZ, Ren H, Gu CY, et al. Risk factors for acute hepatitis B and its progression to chronic hepatitis in Shanghai, China. *Gut* 2008; **57**(12): 1713-20.
- [18] Wai CT, Fontana RJ, Polson J, Hussain M, Shakil AO, Han SH, et al. Clinical outcome and virological characteristics of hepatitis B-related acute liver failure in the United States. *J Viral Hepat* 2005; **12**(2): 192-8.
- [19] Chan SH, Oon CJ. Epidemiology of HBV infection in Singapore. *Asian Pac J Allergy Immunol* 1984; **2**(1): 139-43.
- [20] Hahné S, Ramsay M, Balogun K, Edmunds WJ, Mortimer P. Incidence and routes of transmission of hepatitis B virus in England and Wales, 1995–2000: implications for immunisation policy. *J Clin Virol* 2004; **29**(4): 211-20.
- [21] Kim WR. Epidemiology of hepatitis B in the United States. *Hepatology* 2009; **49**(5 Suppl): S28-34.
- [22] Janahi EM. Prevalence and risk factors of hepatitis B virus infection in Bahrain, 2000 through 2010. *PloS One* 2014; **9**(2): e87599.
- [23] Lu FM, Li T, Liu S, Zhuang H. Epidemiology and prevention of hepatitis B virus infection in China. *J Viral Hepat* 2010; **17**(Suppl 1): 4-9.
- [24] Elzouki AN, Smeo MN, Samud M, Elahmer O, Daw M, Furarah A, et al. Prevalence of hepatitis B and C virus infections and their related risk factors in Libya: a national seroepidemiological survey. *East Mediterr Health J* 2013; **19**(7): 589-99.
- [25] Salleras L, Domínguez A, Bruguera M, Plans P, Costa J, Cardeñosa N, et al. Declining prevalence of hepatitis B virus infection in Catalonia (Spain) 12 years after the introduction of universal vaccination. *Vaccine* 2007; **25**(52): 8726-31.
- [26] Zenebe Y, Mulu W, Yimer M, Abera B. Sero-prevalence and risk factors of hepatitis B virus and human immunodeficiency virus infection among pregnant women in Bahir Dar city, Northwest Ethiopia: a cross sectional study. *BMC Infect Dis* 2014; **14**(1): 118-25.
- [27] Sandhu R, Sharma G. Prevalence of hepatitis B surface antigen as a serological marker in HBV infection. *Int J Pharm Biol Sci* 2014; **4**(1): 19-24.
- [28] Hamied L, Mujahid Abdullah R, Mujahid Abdullah A. Seroprevalence of hepatitis B and hepatitis C virus infection in Iraq. *N Iraqi J Med* 2010; **6**(3): 69-73.
- [29] Mehmet D, Meliksah E, Serif Y, Gunay S, Tuncer O, Zeynep S. Prevalence of hepatitis B infection in the southeastern region of Turkey: comparison of risk factors for HBV infection in rural and urban areas. *Jpn J Infect Dis* 2005; **58**(1): 15-9.
- [30] Li XQ, Zheng YJ, Liau A, Cai B, Ye DQ, Huang F, et al. Hepatitis B virus infections and risk factors among the general population in Anhui Province, China: an epidemiological study. *BMC Public Health* 2012; **12**(1): 272-9.
- [31] Public Health Agency of Canada. *Reported cases and rates of hepatitis C, by province/territory and sex, 2005 to 2009*. Ottawa: Public Health Agency of Canada; 2011. [Online] Available from: <http://www.catie.ca/sites/default/files/Reported-Cases-and-Rates-HBV-HCV-2010.pdf> [Accessed on 21st November, 2014]
- [32] Wasley A, Kruszon-Moran D, Kuhnert W, Simard EP, Finelli L, McQuillan G, et al. The prevalence of hepatitis B virus infection in the United States in the era of vaccination. *J Infect Dis* 2010; **202**(2): 192-201.
- [33] Ioannou GN. Hepatitis B virus in the United States: infection, exposure, and immunity rates in a nationally representative survey. *Ann Intern Med* 2011; **154**(5): 319-28.
- [34] Meffre C, Le Strat Y, Delarocque-Astagneau E, Dubois F, Antona D, Lemasson JM, et al. Prevalence of hepatitis B and hepatitis C virus infections in France in 2004: social factors are important predictors after adjusting for known risk factors. *J Med Virol* 2010; **82**(4): 546-55.
- [35] Daw MA, El-Bouzedi A; In association with Libyan Study Group of Hepatitis & HIV. Prevalence of hepatitis B and hepatitis C infection in Libya: results from a national population based survey. *BMC Infect Dis* 2014; **14**: 17.
- [36] Baig S. Gender disparity in infections of Hepatitis B virus. *J Coll Physicians Surg Pak* 2009; **19**(9): 598-600.
- [37] McQuillan GM, Coleman PJ, Kruszon-Moran D, Moyer LA, Lambert SB, Margolis HS. Prevalence of hepatitis B virus infection in the United States: the National Health and Nutrition Examination Surveys, 1976 through 1994. *Am J Public Health* 1999; **89**(1): 14-8.
- [38] Rimseliene G, Nilsen Ø, Klovstad H, Blystad H, Aavisland P. Epidemiology of acute and chronic hepatitis B virus infection in Norway, 1992-2009. *BMC Infect Dis* 2011; **11**: 153.