

# Prevalence of Hepatitis B Surface Antigen Among People Attending Medical Diagnostic Laboratories in Neyshabur, Northeast of Iran, During Years 2011 to 2015

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## Abstract

**Background:** Hepatitis B Virus (HBV) infection remains a public health and health care issue in Iran. Since the data on its outbreak is required for effectual policies, this epidemiological study was performed on population from Neyshabur, where there has been no former epidemiological information.

**Objectives:** This study aimed at investigating the epidemiology of hepatitis B surface antigen among subjects from Neyshabur, from year 2011 to 2015.

**Methods:** The researchers established this study from data collected from a surveillance system. Screening tests were carried out by the Chemiluminescence method. Age, gender, referral year and month were the investigated variables. Data were analyzed by the SPSS-20 software.

**Results:** The prevalence of HBsAg in Neyshabur was 4.11%. In the age group of more than 40 years (1.87%) and females (2.2%) had significantly ( $P < 0.0001$ ) higher rates of HBV seropositivity. Also the year 2011 (5.26%) and the month of July (0.48%) had the highest prevalence.

**Conclusions:** Hepatitis B Virus (HBV) infection rate was seemingly high in Neyshabur, even higher than other parts of Iran. An immunization program should be continued progressively for high-risk areas, especially the Neyshabur city of Iran.

**Keywords:** Epidemiology, Hepatitis, HBV, Iran

## 1. Background

One of the major causes of liver disease in the world is Hepatitis B virus (HBV) infection (1). The prevalence of hepatitis B worldwide is 5%, with 80% living in Asia (2, 3). Middle Eastern countries are mesoendemic with an infection rate of 2% to 7% (4).

According to the world health organization (WHO) report, currently 2 billion people have HBV infection and acute infection has turned to chronic infection in more than 350 million people. Annually, it has been estimated that more than 500000 deaths occur due to hepatocellular carcinoma (HCC) and cirrhosis caused by chronic HBV infection (1, 5). In Iran, almost 46% of HCC and 51% of cirrhosis are related to HBV (6). Also, 70% to 80% of chronic hepatitis in Iran is related to HBV (7). For HBV transmission, blood and blood products are the principal route (6).

In a comprehensive epidemiological study from Iran, HBV prevalence was reported as 1.07% in Shiraz to 8.96% in Toicerkan. The province's outbreak ranged from 1.7% to 5% in Fars and Sistan and Baluchestan, respectively. In Tehran,

HBV prevalence was 3.6% and 1.6% for males and females, respectively (8).

In a systematic review of the literature, Alavian et al. (2008) indicated the seroepidemiology of HBV infection in the general population of Iran by extraction from the surveillance system. Based on their findings, the prevalence was estimated as 2.14% for only 7 provinces (9). Also, the prevalence of Hepatitis B surface antigen (HBsAg) in Sistan and Baluchistan was 3.38%, and the same went for Kermanshah 0.77%, Ravansar 1.66%, Sanghar 1%, Kangavar 3.79%, Dalahou 1.66%, Islam Abad 0.62%, Baneh 2.06%, Saghez 1.4%, Sar Abad 2.13%, Sanandaj 0.67%, and Ghorveh 2.13% (10-12). In a study from the great Khorasan province (including North, South and Razavi Khorasan), hepatitis B prevalence was 3.6% (13).

Neyshabur (coordinates: 36°12'48''N 58°47'45''E) is a city in the Razavi Khorasan province, located in the north east of Iran, and has an area of 6753.95 km<sup>2</sup> and a population of 433105 with elevation of 1250 m (4,100 ft) (14).

Monitoring seroepidemiology is vital because it may facilitate the final eradication of HBV infection (15). Since

the data on its outbreak in the general population is required for the formulation of effectual policies, this epidemiological study was performed on a population from Neyshabur, where there has been no former data on the prevalence of HBV. Also, Razavi Khorasan province is of great importance because of a common border with Afghanistan (where the prevalence is 6.5%), which is hyper-endemic area for HBV infection (16).

## 2. Objectives

The current study aimed at investigating the epidemiology of HBsAg among people in Neyshabur from year 2011 to 2015.

## 3. Methods

### 3.1. Patients and Collection of Specimens

An epidemiological survey was carried out in Neyshabur between years 2011 and 2015 to determine the prevalence of HBsAg infection. The researchers established the prevalence of HBV infection from data extracted from a surveillance system, during years 2011 to 2015. Thus, there was no sample selection and questionnaire and the variables were age, gender, and year and month of referral. The sample of the study was a biased sample and laboratories were selected for inclusion in the study. Overall, participants were referred due to pregnancy screening, checkup, personal or family history of HBV, check-up for visa applications, operation and having high-risk behavior like tattooing or needling. The personal data of participants were confidential.

### 3.2. Identification Procedures

Serological samples were tested with a HBsAg Kit (Disorin) and by a Chemiluminescence method (Germany) that had a diagnostic sensitivity of 100% (95% confidence level of 99.3% to 100%) and diagnostic specificity of 99.55% (95% confidence level of 99.32% to 99.71%). Any titer above 10 units was considered positive for HBsAg and reported as qualitative values.

### 3.3. Data Analysis

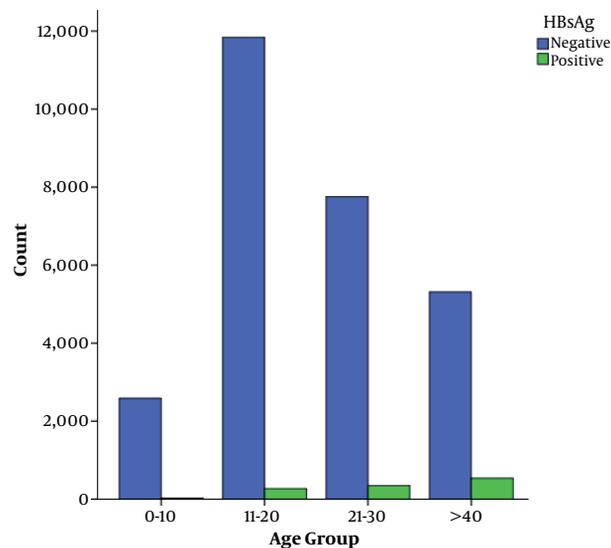
The SPSS version 20 software was used for data analysis (IBM SPSS statistics for windows, version 20, Armonk, NY, IBM Corp.) by chi-square test and P values of < 0.05 were considered significant.

### 3.4. Ethical Approval

Approval for this study was obtained from the research and technology deputy of ACECR, Mashhad branch.

## 4. Results

The number of subjects during the 5 years of this study was 28685. According to gender, from 28685 subjects, 6213 (21.7%) were male and 22472 (78.3%) were female. subjects mean age (mean age  $\pm$  standard deviation) was  $32.2 \pm 12.86$  years, which ranged from < 1 to 95 years. Overall, according to Chemiluminescence results, 1181 (4.11%) cases had evidence of HBsAg. The demographic characteristics of the subjects are displayed in Table 1. As indicated, 20 to 29 years was the most frequent age group and age of more than 40 years was the major risk factor for infection with odds ratio of 10.901 (95% CL: 7.223 to 16.453) followed by the age of 30 to 39 years (OR: 4.853, 95% CL: 3.202 to 7.357), gender (OR: 3.34, 95% CL: 2.966 to 3.756) and the age of 20 to 29 (OR: 2.468, CL: 1.622 to 3.755). Regarding age frequency distribution in the present study, it was shown that the frequency of hepatitis B increased with age so that older than 40-year-olds and the 30 to 39-year-olds had the highest rates of hepatitis B. The lowest prevalence was observed in 0 to 19-year-old subjects (0.08%). The year of 2011 (5.26%) had the highest prevalence followed by 2012 (4.23%), 2015 (4.14%), 2014 (3.77%), and 2013 (3.51%) (Table 2). Also, the month of July (0.48%) had the highest prevalence yet there was no relationship between HBV infection and the month of the year ( $P = 0.132$ ) (Table 3).



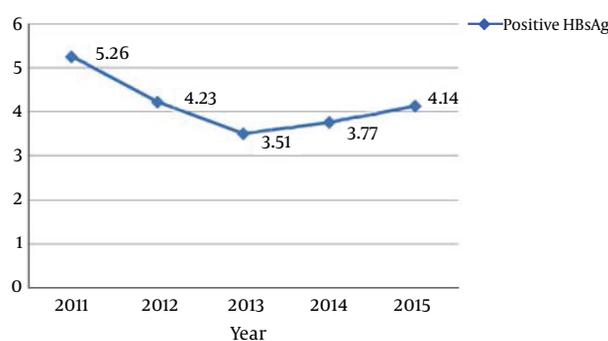
**Figure 1.** The Schematic Representation of Age Groups Infected and Not Infected With HBV

**Table 1.** Age- and Gender-based Distribution of Individuals and Overall HBsAg-Positive and HBsAg-Negative Cases

Variable	No. (%)	Positive Cases (%)	Odds Ratio (OR)	CI (95%CI)	P Value
<b>Age (year)</b>					
0 -19	2613 (9.1)	24 (0.08)	Baseline		
20 -29	12115 (42.2)	271 (0.94)	2.468	1.622 - 3.755	< 0.0001
30 -39	8106 (28.3)	349 (1.22)	4.853	3.202 - 7.357	< 0.0001
≥ 40	5851 (20.4)	537 (1.87)	10.901	7.223 - 16.453	< 0.0001
<b>Gender</b>					
Male	6213 (21.7)	548 (1.91)	3.34	2.966 - 3.756	< 0.0001
Female	22472 (78.3)	633 (2.2)			
Total	28685 (100)	1181 (4.11)			

**Table 2.** The Annual Prevalence of HBsAg-Positivity and HBsAg-Negativity Investigated in this Study

Year	Number	Total Percentage
2015	Positive: 246	Positive: 4.14
	Total: 5942	Total: 20.71
2014	Positive: 243	Positive: 3.77
	Total: 6452	Total: 22.49
2013	Positive: 214	Positive: 3.51
	Total: 6099	Total: 21.26
2012	Positive: 238	Positive: 4.23
	Total: 5630	Total: 19.62
2011	Positive: 240	Positive: 5.26
	Total: 4562	Total: 15.9
Total	Positive: 1181	Positive: 4.11
	Total: 28685	Total: 100

**Figure 2.** The Frequency of HBsAg-Positivity and HBsAg-Negativity According to Year

## 5. Discussion

According to the results, the seroepidemiology of HBV infection in Neyshabur was 4.11% (1181 out of 28685), which *Arch Pediatr Infect Dis.* 2017; 5(4):e61633.

was higher in comparison with the published literature performed in other areas of Iran, even in comparison with great Khorasan province (3.6%) and Mashhad (1%), which are nearly the size of Neyshabur city (10, 13, 17-20). According to WHO and results of the present study, Neyshabur is considered as a mesoendemic region (21).

In this study, the correlation between demographic features including age, gender, and HBsAg infection was significant. The high prevalence of HBsAg infection that was found in this study might be due to a possible higher risk of infection in these samples, because most the cases were referred for evaluation of HBsAg by physicians. Also, most citizens of Neyshabur have migrated from the surrounding villages and countries, especially Afghanistan, which has encountered less attention culturally. Neyshabur has 175 villages and is the second over-crowded city in Razavi Khorasan.

According to statistical analysis, both age and gender play an important role in HBV infection, so that older and female subjects had higher probability of HBV seropositivity. The incidences of risk factors, such as the frequency of sexual relations in people who have different sexual partners, hospitalization, tattoo, and blood transfusion increase with age and subsequently the likelihood of infection will also increase.

As it was shown in [Table 1](#), according to age, the age group of more than 40 years (1.87%) showed significantly higher rate of HBV seropositivity, which is similar to other reports (20). Despite the high prevalence of HBV in males in some reports, the current findings revealed that females (2.2%) had significantly higher rates of HBV seropositivity (18, 22, 23). The higher positive incidence in females may relate to the sample size that was over three times more than that of the male sample (6213 vs. 22472) and, as the participants were referred by physicians, they were at a high risk for infection. Thus, a greater sample size would re-

**Table 3.** The Frequency of HBsAg-Positivity and HBsAg-Negativity According to Month<sup>a</sup>

Month	Year					Positive (%)	Total
	2011	2012	2013	2014	2015		
April	367	469	531	545	577	110 (0.38)	2489
August	456	474	395	570	505	91 (0.32)	2400
December	365	432	465	456	462	91 (0.32)	2180
February	30	566	943	496	403	102 (0.35)	2438
January	417	484	589	496	492	109 (0.38)	2478
July	509	565	588	730	628	138 (0.48)	3020
June	348	374	392	418	419	90 (0.31)	1951
March	330	386	390	451	382	68 (0.24)	1939
May	547	553	592	655	604	136 (0.47)	2951
November	468	549	496	589	605	107 (0.37)	2707
October	321	384	318	513	428	75 (0.26)	1964
September	404	394	400	533	437	64 (0.22)	2168
<b>Total</b>	4562	5630	6099	6452	5942	1181(4.11)	28685

<sup>a</sup> P value is considered as 0.132.

sult in a higher infection prevalence. On the other hand, females pay attention to their wellbeing more than males and more commonly refer to the laboratory for pregnancy screening. According to Mohebbi et al., 0.7% of pregnant females in Lorestan were positive for HBs-Ag (24).

The lowest prevalence according to age was related to younger age; reduced HBsAg prevalence in this group was strongly associated with vaccination among younger people. In Iran, vaccination of newborns from 1993 onwards has been the most significant between all measures for controlling HBV and through the national immunization program, people less than 24 years old must have received HBV vaccine.

The prevalence surveyed in the present study was similar to studies carried out in cities and countries, so that, HBV prevalence in the study of Merat et al. regarding province of Golestan was 5.1% (25). Ziaee et al. determined the prevalence of HDV infection among chronic hepatitis B in Birjand and there was an HDV infection rate of 3.1% (26). A long-term protection against HBV for more than 20 years was illustrated by Saffar et al. among neonates, who were immunized against HBV and it was very effective in decreasing chronic HBV infection prevalence in young adults, who were vaccinated in Iran. However, the continuity of protection presented by preliminary vaccination remained unknown (27). The adjusted seroprevalence of HBsAg in South Korea in 2009 was 4%, which was in agreement with the current study (15). The prevalence of HBsAg in

young adults in Banjarmasin, Indonesia was 4.6% (28). Recently a report indicated that a low dose of RPB5-mediating protein (RMP) could inhibit HBV transcription and replication (29). A comprehensive study in Singapore showed that the prevalence of hepatitis B surface antigen (HBsAg) was 3.6% in 2010 (30). Mahabadi et al. screened chronic HBV patients, who did not receive any antiviral treatments and then attempted to determine hepatitis B virus reverse transcriptase (RT) protein variations among them. Their results showed that in comparison with other studies, the mutations related to drug resistance in Iranian treatment-naïve chronic HBV patients were higher. Hence, in order to attain an excellent regimen option, they suggested that chronic HBV patients should be monitored closely before the start of therapy (31).

The year 2011 (5.26%) had the highest prevalence. However, the rate of HBsAg seropositivity has gradually decreased during other years. It seems that the reduction in HBsAg rate was mainly due to increased awareness among people and the national vaccination program.

Also the month of July (0.48%) had the highest prevalence yet there was no relationship between HBV infection and the month of the year ( $P = 0.132$ ). However, this is the first report, which considered the month variable and its relationship with HBV infection.

Because of the absence of data on risk factors of HBV among the general population of Neyshabur, authors of this work suggest that the next study should be performed

based on risk factors. In order to manage this disease and attain additional measures, more accurate epidemiological data is necessary.

In conclusion, the current results confirm that the prevalence of HBsAg in Neyshabur is high, even higher than some other parts of the county. Lack of management by authorities and those, who categorize regions for hygiene policy may be the main causes of HBV infection in Neyshabur. Therefore, immunization programs should be continued progressively and further strengthened for high-risk areas, especially Neyshabur.

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### Footnotes

**Authors' Contribution:** Somaye Najafi and Mohammad Salehi performed the study and managed the manuscript preparation; Mohammad Salehi was the advisors of this research.

**Conflict of Interest:** None declared.

### Implication for Health Policy/Practice/Research/Medical Education:

The study results provide valuable information for policy makers and health system workers with regards to hepatitis B vaccine in high-risk areas, such as Neyshabur.

### References

- Farzadegan H, Shamszad M, Noori-Arya K. Epidemiology of viral hepatitis among Iranian population—a viral marker study. *Ann Acad Med Singapore*. 1980;**9**(2):144–8. [PubMed: 7425524].
- Perz JF, Armstrong GL, Farrington LA, Hutin YJ, Bell BP. The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide. *J Hepatol*. 2006;**45**(4):529–38. doi: 10.1016/j.jhep.2006.05.013. [PubMed: 16879891].
- Andre F. Hepatitis B epidemiology in Asia, the Middle East and Africa. *Vaccine*. 2000;**18 Suppl 1**:S20–2. [PubMed: 10683538].
- Gust ID. Epidemiology of hepatitis B infection in the Western Pacific and South East Asia. *Gut*. 1996;**38 Suppl 2**:S18–23. [PubMed: 8786047].
- Alavian SM, Fallahian F, Lankarani KB. The changing epidemiology of viral hepatitis B in Iran. *J Gastrointest Liver Dis*. 2007;**16**(4):403–6. [PubMed: 18193122].
- Joshi N, Yr NK, Kumar A. Age related seroprevalence of antibodies to hepatitis A virus in Hyderabad, India. *Trop Gastroenterol*. 2000;**21**(2):63–5. [PubMed: 10881625].
- Iran's health and disease surveillance report (in Persian). Tehran: National Medical Research Centre; 2001.
- Zali MR. Epidemiology of hepatitis B in the Islamic Republic of Iran. *East Mediterr Health J*. 1996;**2**(2):290–8.
- Alavian SM, Hajarizadeh B, Ahmadzad-Asl M, Kabir A, Bagheri-Lankarani K. Hepatitis B Virus infection in Iran: A systematic review. *Hepat Mon*. 2008;**8**(4):281–94.
- Salehi M, Alavian SM, Tabatabaei SV, Izadi S, Sanei Moghaddam E, Amini Kafi-Abad S, et al. Seroepidemiology of HBV infection in South-East of Iran; a population based study. *Iran Red Crescent Med J*. 2012;**14**(5):283–8. [PubMed: 22829987].
- Alavian SM, Tabatabaei SV, Nourizad S, Mansouri F, Khademi N, Amini Kafi-abad S, et al. Seroepidemiology of hbv infection in kermanshah-west of Iran; a population based study. *Jundishapur J Microbiol*. 2012;**5**(4):564–9. doi: 10.5812/jjm.4156.
- Alavian SM, Tabatabaei SV, Ghadimi T, Beedrapour F, Kafi-Abad SA, Gharehbaghian A, et al. Seroprevalence of Hepatitis B Virus Infection and Its Risk Factors in the West of Iran: A Population-based Study. *Int J Prev Med*. 2012;**3**(11):770–5. [PubMed: 23189228].
- Farhat A, Khademi G, Mazlouman SJ. The prevalence of hepatitis B carrier state in Khorassan province of Iran. *Saudi Med J*. 2003;**24**(5):549–51. [PubMed: 12847639].
- Honigsmann EBCE. Encyclopaedia of Islam. second ed. Brill Online; 2013.
- Lee BS, Cho YK, Jeong SH, Lee JH, Lee D, Park NH, et al. Nationwide seroepidemiology of hepatitis B virus infection in South Korea in 2009 emphasizes the coexistence of HBsAg and anti-HBs. *J Med Virol*. 2013;**85**(8):1327–33. doi: 10.1002/jmv.23594. [PubMed: 23723057].
- Todd CS, Abed AM, Strathdee SA, Scott PT, Botros BA, Safi N, et al. HIV, hepatitis C, and hepatitis B infections and associated risk behavior in injection drug users, Kabul, Afghanistan. *Emerg Infect Dis*. 2007;**13**(9):1327–31. doi: 10.3201/eid1309.070036. [PubMed: 18252103].
- Amini S, Mahmoodi MF, Andalibi S, Solati AA. Seroepidemiology of hepatitis B, delta and human immunodeficiency virus infections in Hamadan province, Iran: a population based study. *J Trop Med Hyg*. 1993;**96**(5):277–87. [PubMed: 8411302].
- Alizadeh AH, Ranjbar M, Ansari S, MirArab A, Alavian SM, Mohammad K, et al. Seroprevalence of hepatitis B in Nahavand, Islamic Republic of Iran. *East Mediterr Health J*. 2006;**12**(5):528–37. [PubMed: 17333790].
- Nazila K, Behrooz A, AbbasAli J, Ziba F, Peyman A. Hepatitis B Markers in Isfahan, central Iran: A population-based study. *Hepat Mon*. 2009;**9**(1):12–6.
- Shakeri MT, Foghanian B, Nomani H, Ghayour-Mobarhan M, Nabavinia MS, Rostami S, et al. The prevalence of hepatitis B virus infection in mashhad, Iran: a population-based study. *Iran Red Crescent Med J*. 2013;**15**(3):245–8. doi: 10.5812/ircmj.8200. [PubMed: 23984006].
- World Health Organization. Introduction of hepatitis B vaccine into childhood immunization services: Management guidelines, including information for health workers and parents. ; 2001.
- Moosazadeh M, Amiresmaili MR, Nezammahalleh A. The epidemiology of HBsAg positive cases reported to the health deputy of Mazandaran University of Medical Sciences, Iran. *J Health Dev*. 2012;**1**(2):130–7.
- Eskandar H, SayedJalal H, AbuulRahim M. Seroepidemiology of hepatitis B virus infection in Khuzestan province, southwest of Iran. *Hepat Mon*. 2009;**9**(1):34–8.
- Mohebbi SR, Sanati A, Cheraghipour K, Rostami Nejad M, Shalmani HM, Zali MR. Hepatitis C and hepatitis B virus infection: epidemiology and risk factors in a large cohort of pregnant women in Lorestan, West of Iran. *Hepat Mon*. 2011;**11**(9):736–9. doi: 10.5812/kowsar.1735143X.749. [PubMed: 22235217].
- Merat S, Rezvan H, Nouraie 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. [PubMed: 19400598].
- Ziaee M, Azarkar G. Prevalence of hepatitis d virus infection among patients with chronic hepatitis B attending birjand hepatitis clinic (East of Iran) in 2012. *Hepat Mon*. 2013;**13**(8):e11168. doi: 10.5812/hepatmon.11168. [PubMed: 24171009].

27. Saffar H, Ajami A, Saffar MJ, Shojaei J, Sotudeh-Anvari M, Shams-Esfandabad K, et al. Prevalence of hepatitis B virus seromarkers in young adults vaccinated at birth; impact on the epidemiology of hepatitis B infection in Iran. *Hepat Mon.* 2014;**14**(5):e17263. doi: [10.5812/hepatmon.17263](https://doi.org/10.5812/hepatmon.17263). [PubMed: [24829589](https://pubmed.ncbi.nlm.nih.gov/24829589/)].
28. Darmawan E, El-Khobar KE, Nursanty NK, Thedja MD, Muljono DH. Seroepidemiology and occult hepatitis B virus infection in young adults in Banjarmasin, Indonesia. *J Med Virol.* 2015;**87**(2):199–207. doi: [10.1002/jmv.24045](https://doi.org/10.1002/jmv.24045). [PubMed: [25521058](https://pubmed.ncbi.nlm.nih.gov/25521058/)].
29. Zhou Q, Huang F, Chen L, Chen E, Bai L, Cheng X, et al. RPB5-Mediating Protein Suppresses Hepatitis B Virus (HBV) Transcription and Replication by Counteracting the Transcriptional Activation of Hepatitis B virus X Protein in HBV Replication Mouse Model. *Jundishapur J Microbiol.* 2015;**8**(9):e21936. doi: [10.5812/jjm.21936](https://doi.org/10.5812/jjm.21936). [PubMed: [26495109](https://pubmed.ncbi.nlm.nih.gov/26495109/)].
30. Ang LW, Cutter J, James L, Goh KT. Seroepidemiology of hepatitis B virus infection among adults in Singapore: a 12-year review. *Vaccine.* 2013;**32**(1):103–10. doi: [10.1016/j.vaccine.2013.10.057](https://doi.org/10.1016/j.vaccine.2013.10.057). [PubMed: [24200974](https://pubmed.ncbi.nlm.nih.gov/24200974/)].
31. Mahabadi M, Norouzi M, Alavian SM, Samimirad K, Azad TM, Saberfar E, et al. Drug-related mutational patterns in hepatitis B virus (HBV) reverse transcriptase proteins from Iranian treatment-naive chronic HBV patients. *Hepat Mon.* 2013;**13**(1):e6712. doi: [10.5812/hepatmon.6712](https://doi.org/10.5812/hepatmon.6712). [PubMed: [23596461](https://pubmed.ncbi.nlm.nih.gov/23596461/)].