Original Article

Where we are in the Fight against Hepatitis B Infection; Trends in Hepatitis B Virus Seroprevalence in Black Sea Region of Turkey

FA Igde, H Taskin[1], M Igde[2], Z Yazici[3], A Atilla[4]

Department of Family Medicine, Faculty of Medicine, Ondokuz Mayıs University, [1]Department of Microbiology, [2]Department of Pediatric Allergy, Pediatric Allergy Clinic, [4]Infectious Diseases, Samsun Education and Research Hospital, [3]Department of Virology, Faculty Veterinary, Ondokuz Mayıs University, Turkey

Abstract

Context: To determine new strategies for complete coverage of hepatitis B virus (HBV) vaccination, every country needs to take into concern factors of infection transmission in its own region. **Aims:** The aim of this study was to investigate the seroprevalence of hepatitis B among all age groups in northern Turkey using HBsAg and anti-HBs serological markers. **Materials and Methods:** The laboratory records of a total of 101648 patients of all ages attending a tertiary level hospital in Samsun, a Black Sea coastal city, between January 2014 and May 2016 were evaluated retrospectively. **Results:** HBsAg and anti-HBs seropositivity was found to be 4% and 38.3%, respectively. There was a significant difference between HBsAg ($\chi 2$ = 209.08; P = 0.00), anti-HBs ($\chi 2$ = 124.12; P = 0.00) seropositivity, and immunization status. Although we found a statically difference between men and women ($\chi 2$ = 32.2 P = 0.00) for HBsAg seropositivity, there was no significant difference for anti-HBs (P = 0.22). In 1998, the universal infant immunization program changed the HBV epidemiology in Turkey, and resulted in an apparent trend towards reduced disease levels. However, prevalence of HBV infection is still high in adolescent and young adults. **Conclusions:** Therefore, a catch-up immunization program, education, and follow-up policy for these groups, in addition to routine infant immunization, will decrease the HBV infection rate, reducing morbidity and mortality rates, and will help to reduce hepatitis B transmission in Turkey.

Key Messages: A catch-up immunization program, education, and follow-up policy for adolescents and young adult groups could help reduce hepatitis B transmission in many countries.

Keywords: *Hepatitits B, seroepidemiologic studies, Turkey*

Date of Acceptance:
25-Jan-2017

Introduction

Hepatitis B virus (HBV) infection is one of the most common infections in the world. Among the entire world population of seven billion people, one-third (2 billion) have been infected with HBV.[1] Approximately 240 million people worldwide are estimated to have chronic HBV infection.[2] Hepatitis B may cause hepatocellular carcinoma, cirrhosis, or both in infected persons. The natural course of the disease is complex; during their lifetimes, various phases of the disease in infected individuals can be seen. Liver disease caused by the virus can worsen or corrects itself without prediction.[3,4]

The endemicity of HBV infection is classified into three categories as low (seroprevalence < 2%), intermediate (seroprevalence between 2% and 8%), and high (seroprevalence > 8%) according to surface antigen (HBsAg).[5] In highly endemic areas, HBV is most commonly transmitted from mother to child at birth, or from person to person during early childhood. The prevalence of overall HBV infections varies markedly

Address for correspondence: Assoc. Prof. Fusun Artiran Igde, Department of Family Medicine, Faculty of Medicine, Ondokuz Mayıs University, Turkey.
E-mail: fartiran@yahoo.com

Access this article online

Quick Response Code:

Website: www.njcponline.com

DOI: 10.4103/njcp.njcp_368_16

How to cite this article: Igde FA, Taskin H, Igde M, Yazici Z, Atilla A. Where we are in the fight against Hepatitis B Infection; Trends in Hepatitis B virus seroprevalence in Black Sea Region of Turkey. Niger J Clin Pract 2018;21:87-92.

according to age and regions within a country. South Asia, China, Indonesia, Nigeria, and sub-Saharan Africa are reported to be highly endemic regions because HBsAg can be more than 8% of the population, whereas developed countries such as North America, Western Europe, and Australia are considered to have low endemicity (HBsAg less than 2%).[6] Eastern and Southern Europe and Middle Eastern countries showed intermediate endemicity.[6] Turkey is an intermediate endemic country, however, HBV dynamics vary within each region of the country.[5]

Antiviral therapy to chronic hepatitis B infection can result in accelerating clearance of HBsAg and HBeAg in some carriers. However, the long-term benefit of antiviral therapy is unclear.[7] In the fight against the disease, vaccination programs are more effective strategy than antiviral therapy along with the added benefit of being cost effective.

There are two important serological markers for the diagnoses of HBV. These are known as HBsAg and the antibody against surface antigen anti-HBs. HBsAg is the first serological marker that indicates active infection, and anti-HBs is a neutralizing antibody whose presence indicates immunity.[6]

To determine new strategies for complete coverage of HBV vaccination, every country needs to account factors of infection transmission in their own region. For developing preventive strategies against Hepatitis B infection, epidemiologic data should be known. In Turkey, despite universal infant HBV immunization program for the prevention of perinatal transmission, which began in 1998, the effect of vaccination on the prevalence of hepatitis B infection as well as the condition of the unvaccinated age groups is unclear. The aim of this study was to investigate the seroprevalence of hepatitis B for all age groups in the northern side of Turkey using HBsAg and anti-HBs serological markers.

Materials and Methods

Study area and patients

The laboratory records of a total of 101648 patients of all ages attending a tertiary level hospital in Samsun, which is a Black Sea coastal city, between January 2014 and May 2016 were evaluated retrospectively. Patients up to the age 18 were considered as children and 19 years and above as adults. Adulthood was divided in a 10-year period as a routine. Attention was paid to two important dates when evaluating age groups. First was year was 1998 when the universal infant immunization program started for the prevention of HBV perinatal transmission in Turkey. Thus, all 18-year-old and young patients were considered to be immunized. The second year was 1986 when a recombinant hepatitis B vaccine was licensed in the United States. Thus, patients between 19 and 28 years old were considered as possible immunized patients. Patients older than 29 years old were considered as nonimmunized; these patients were divided as 29–38, 39-48, 49-58, 59-68, and ≥ 69 years' age groups. Records were analyzed and grouped according to gender, age, and date of application. HBsAg and anti-HBs parameters in the laboratory records of the patients were included in the study. For HBsAg, there were 113096 records and 43000 records for anti-HBsAg at the beginning of the study. After elimination of repeated measures for the same person, data were decreased to 101648 and 41434 records, respectively. According to the hospital laboratory records, anti-HBs parameter could be viewed only when HBsAg was positive. Therefore, less numbers of anti-HBs records were evaluated.

Serological assays

Two serological markers of HBV, HBsAg, and anti-HBs in serum samples were investigated by using Elecsys HBsAg II and Anti-HBs II enzyme-linked immunosorbent assay (ELISA) (Roche Diagnostics, Mannheim, Germany) kits with fully automatic systems according to the manufacturer's instructions.

Hepatitis B surface antigen test

Elecsys HBsAg is an electrochemiluminescence immunoassay "ECLIA" for the *in-vitro* qualitative determination of HBsAg in human serum and plasma. The Elecsys HBsAg II assay uses monoclonal and polyclonal anti-HBs antibodies (mouse and sheep) for HBsAg determination. Elecsys HBsAg is a two-step sandwich assay for the qualitative detection of HBsAg in human serum or plasma, with a total incubation time of 18 min. All the reactions are performed automatically by the Elecsys 2010 system. Samples with a cutoff index < 0.90 are nonreactive in the Elecsys HBsAg II assay. These samples are considered negative for HBsAg. Samples with a cutoff index ≥1.0 are considered reactive.

Antibody to Hepatitis B surface antigen test

Elecsys antibody to HBsAg test is an electrochemiluminescence immunoassay "ECLIA" for the *in-vitro* quantitative determination of human antibodies to the HBsAg in human serum and plasma. Anti-HBs is a specific (generally IgG) antibody that is directed against the hepatitis B surface antigen. The Elecsys Anti-HBs test uses a mixture of purified antigens of the HBsAg subtypes ad and ay from human serum. Total incubation time is 18 min. All the reactions are performed automatically by the Elecsys 2010 system. Results are determined via a calibration curve, which is an instrument specifically generated by two-point calibration and a master curve provided via the reagent barcode. The analyzer automatically calculates the analyte concentration of each sample in IU/L. Values below the

detection limit are reported as < 2.00 IU/L. Samples with concentrations < 10 IU/L are considered nonreactive and with concentrations ≥ 10 IU/L are considered reactive in the Elecsys anti-HBs test.

Hypothesis of the study

[1] HBsAg and anti-HBs seroprevalence in the study universe is consistent with the seroprevalence in similar studies conducted previously in Turkey.

[2] Prevalence is high among nonimmunized individuals.

[3] There is an association between HBsAg seroprevalence and certain sociodemographic variables.

Statistics

Dependent variables analyzed in the study were HBsAg positivity and anti-HBs positivity, verified by ELISA following serological tests. The independent variables analyzed were age, gender, reference year, and hepatitis B vaccination status.

Statistical analysis was evaluated using the Statistical Package for the Social Sciences software version 22.0. (SPSS Inc., CA, USA). Chi-square, independent *t*-test, Pearson correlation, Spearman correlation, and regression analyses were performed for statistical analysis. A value of $P < 0.05$ was considered statistically significant.

Results

A total of 101666 patients were studied by scanning 113096 HBsAg records. There were 57938 (57%) men and 43728 (43%) women. The mean age was 47.68 ± 20.04 years.

Overall HBsAg prevalence was found to be 4% (4080/101666). HBsAg prevalence was 1.1% (55/4933) for 0-18 years age group and 3.58% (537/15011) for 19-29 years age group. For older than 28-year-old patient groups, HBsAg prevalence were determined as 5.2%, 5.8% for, 5.1%, 3.2% and 2%. There was a significant difference in HBsAg seropositivity between different age groups (chi-square = 560.42; $P = 0.00$) [Figure 1].

HBsAg prevalence was 4.4% (2501/57938) in male and 3.6% (1579/43728) in female patients [Table 1], and a significant difference was found between men and women (chi-square = 32.2; $P = 0.00$).

According to the immunization status, HBsAg seropositivity was 1.1% (55/4933) for the immunized group, 3.7% (537/15011) for the partially immunized, and 4.3% (3420/80363) for the nonimmunized patient groups [Table 1]. We found a significant difference between HBsAg seropositivity and immunization status (chi-square = 124.12; $P = 0.00$) [Figure 3].

Anti-HBs were studied in 38066 patients (18913 males, 19153 females). The mean age was 50.23 ±19.33 years. Overall anti-HBs seropositivity was 38.3% (14572/38066); it was 82.4% (1648/1993) for the immunized 0-18 years age groups; 51.50% (2059-2159/3999) for the partially immunized 19–29 years age groups. For older than 28-year-old nonimmunized patient groups, anti-HBs seropositivities were 30.5% (1576/5173), 31.3% (1789/5713), 32.6% (2261/6943), 35.3% (2404/6810), and 38.2% (2835/7435) for 29-38, 39-48, 49-58, 59-68 and ≥ 69 years age groups, respectively. A significant difference in anti-HBs seropositivity was observed between different age groups (chi-square = 222.3; $p = 0.00$) [Figure 2].

Anti-HBs seropositivity was 37.9% (7163/18913) for male and 38.7% (7409/19153) for female patients [Table 1]. There was no significant difference in anti-HBs seropositivity between males and females (chi-square = 3.02; $P = 0.22$).

According to the immunization status, anti-HBs seropositivity was 82.4% for the immunized group, 51.50% for the partially immunized, and 33.9% for the nonimmunized patient groups [Table 1]. There was a significant difference between anti-HBs seropositivity and immunization status (chi-square = 209.08; $P = 0.00$) [Figure 4].

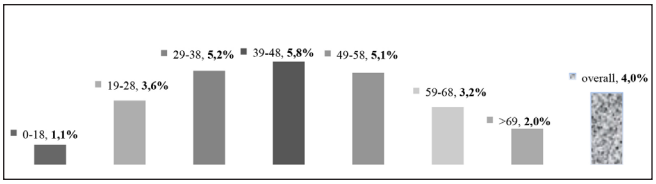

Figure 1: Seropositivity of HBsAg according to age groups (%)

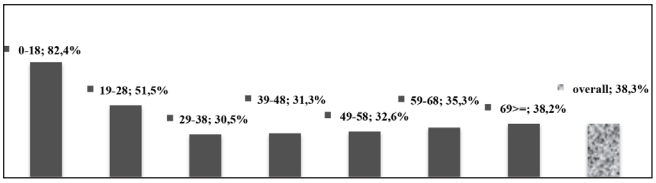

Figure 2: Seropositivity of anti-HBs according to age groups (%)

Table 1: Distribution of HBsAg and anti-HBs seropositivities according to age groups

	0–18 years	19–28 years	29–38 years	39-48 years	49–58 years	59–68 years	69 years and above	Total
HBsAg (+) %	1.11%	3.58%	5.24%	5.75%	5.13%	3.22%	2.01%	4.01%
n/N	(55/4933)	(537/15011)	(812/15487)	(919/15974)	(909/17720)	(516/16037)	(332/16504)	(4080/101666)
AntiHBs(+)%	82.41%	51.46%	30.48%	31.34%	32.57%	35.31%	38.15%	38.28%
n/N	(1648/1993)	(2059/3999)	(1576/50173)	(1789/5713)	(2261/6943)	(2404/6810)	(2835/7435)	(14572/38066)

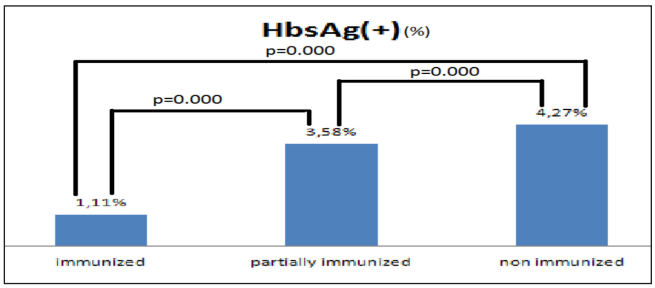

Figure 3: Seropositivity of HBsAg according to immunization status

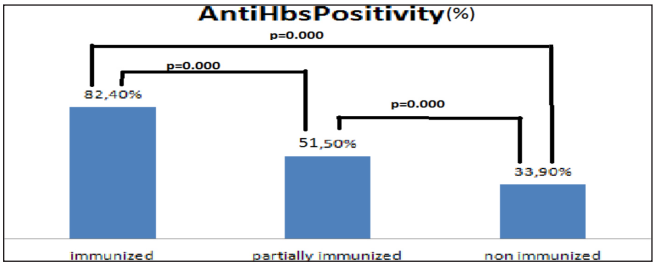

Figure 4: Seropositivity of anti-HBs seropositivity according to immunization status

Table 2: Distribution of HBsAg and anti-HBs seropositivity according to the gender

		HBsAg(+)	*P* value	AntiHBs(+)	*P* value
Sex	Male (%)	4.3%	< 0.05	37.9%	> 0.05
	n/N	2501/57938		7163/18913	
	Female (%)	3.6%		38.7%	
	n/N	1579/43728		7409/19153	

Table 3: Results of the multiple logistic regression analysis for HBsAg positivity with descriptive properties of the study group

HBsAg Seropositivity Negative	*P*	Exp(B)	95% Confidence Interval for Exp(B) Lower Bound	Upper Bound
Sex = Male	.000	.846	.792	.902
Age < 8	.000	9.704	3.109	30.288
Age = 9–18	.024	1.405	1.047	1.887
Age = 19–28	.000	.532	.398	.711
Age = 29–38	.000	.378	.332	.432
Age = 39–48	.000	.340	.299	.386
Age = 49–58	.000	.381	.335	.432
Age = 59–68	.000	.620	.539	.713
Age > 69 reference	.	.	.	.
Immune group	.000	3.942	3.016	5.154
Partially immune group	.001	1.158	1.061	1.265
Nonimmune group reference	.	.	.	.

Table 4: Results of the multiple logistic regression analysis for anti-HBs positivity with descriptive properties of the study group

				95% Confidence Interval for Exp(B)	
Anti-HBs Seropositivity		Sig.	Exp(B)	Lower Bound	Upper Bound
Negative	Sex = Male	.000	1.087	1.041	1.135
	Age < 8	.000	7.57	6.68	8.58
	Age = 9–18	.000	.396	.310	.506
	Age = 19–28	.000	1.389	1.285	1.501
	Age = 29–38	.000	1.365	1.269	1.468
	Age = 39–48	.000	1.285	1.200	1.377
	Age = 49–58	.000	1.132	1.057	1.212
	Age = 59–68	.000	1.136	1.061	1.216
	Age > 69 reference	.	.	.	.
	Immune group	.000	.131	.115	.148
	Partially immune group	0001	1.501	1.191	1.892
	Nonimmune group reference	.	.	.	.

A significant correlation was found between age groups (= -0.17; 95% CI 1.04-1.05; *P* = 0.00), being male (= -0.18; 95% CI 1.04-1.05; *P* = 0.00), and HBsAg positivity.

A significant correlation was found between age groups (= -0.12; 95% CI 1.61-1.65; *P* = 0.00), being male (= 0.08; 95% CI 1.37-1.40; *P* = 0.12), and anti-HBs seropositivity.

HBsAg positivity with descriptive properties of the study group as age, gender, and hepatitis B vaccination status are presented in a multiple regression model [Table 3]. Anti-HBs positivity with descriptive properties of the study group as age, gender, and hepatitis B vaccination status are presented in a multiple regression model [Table 4].

Discussion

In September 2010, European Centre Disease Prevention and Control (ECDC) released data as between 2% and 8% reporting HBV seroprevalence in various regions of Turkey.[6] According to this report, large differences among European countries were observed from the standpoint of HBV findings including the prevalence of HBsAg and HBsAg carrier rates of high to low such as Turkey (8%), Romania (6%), Bulgaria (4%), Latvia (2%), and Greece (2%).[6] Compared with European countries, according to this report, Turkey is one of the countries with the highest prevalence of hepatitis B.[8,9]

It is known that Hepatitis B seroprevalence in Turkey also varies by region and the results are contradictory, indicating that the prevalence of HBsAg positivity ranges from 1% to 14.3%.[10] Thus, we aimed to study the seroprevalence of HBV surface antigen and antibodies against HBV by using the ELISA method in the general population of the Black Sea region of Turkey.

In our study, overall HBsAg and anti-HBs seropositivity were found to be 4.0% [Figure 1] and 38.3% [Figure 2], respectively. Based on these results, Turkey's northern side could be considered a region with medium endemicity for HBV infection. However, looking at these results can lead to incorrect conclusions. This kind of false inferences for different age groups must be prevented by taking into consideration the date of beginning of the national HBV vaccination program.

Hepatitis B vaccination has been implemented since 1982; it is probably the major global preventive measure against the development of HBV infection and its complications. In Turkey, Hepatitis B vaccine was included in the routine immunization program by Turkish Ministry of Health in 1998. The primary goal of the vaccination program was to immunize all newborns to prevent the occurrence of HBV infection later in the early childhood.[11]Vaccination coverage rates in the post-national hepatitis B vaccination program (NHPVP) era in Turkey were 72% in 2002, 96% in 2010, and 95% in 2014.[12] As a result of the mass vaccination program, Turkey was included in low-risk countries for HBV infection by the World Health Organization.[13]

The major limitation of this study was its retrospective design, which lacked concurrent assessment of HBsAg and anti-HBs.

In the study, we divided the population according their HBV infection immunization state into 3 groups; the first group comprised nonimmunized people borne before 1982, the date of first implementation of vaccine in the world. The second group, born between 1982 and 1998, comprised partially immune people because the routine HBV vaccination schedule was not available in Turkey before 1998. The third group comprised of immunized people born after 1998, i.e., the post-national hepatitis B vaccination program (NHPVP) period. When we compared HBsAg and Anti-HBs seroprevalence, the difference was significant ($P < 0.05$) between these groups. HBsAg and anti-HBs seroprevalence were, respectively, 1.1% and 82.40% for the immunized group, 3.58% and 51.50% for partially immunized group, and 4.27% and 33.90% for the nonvaccinated group [Figure 3] and [Figure 4]. Seropositivity rates for the post-NHPVP group (1.1%), less than 18 years old individuals, was consistent with the low endemicity (< 2%). Rates in other groups were consistent with moderate endemicity (2–8%). While the overall HBsAg seropositivity rate was 4%, it was 4.27% for nonvaccinated group, 3.58% for partially vaccinated group, and 1.1% for vaccinated group.

When we analyzed population according to age groups other than immunization status, we found different aspects. As expected, the lowest HBsAg seropositivity and the highest anti-HBs positivity were in the post-NHPVP groups with a rate of 1.1% and 82.40%, respectively; partially immunized (19–28 years age group) showed the second highest rates. When we examined nonimmunized age groups, highest HBsAg and lowest anti-HBs seropositivity rates were observed in the younger age groups [Table 1]. It was found that there was significant gradual transition ($P < 0.05$) of young people to the elderly in both the HBsAg seropositivity and anti-HBs seropositivity [Figure 1] and [Figure 2]. The possible infection burden among the sexually active adult age group might be expected because of high titer seropositivity in this age group. Another reason may be decreased immunity to HBV in the elderly. Similar study was done in the same city by Karatekin[5] expressing high HBsAg seropositivity of 6.5–8.2% in 11–18 years age group after evaluating records from 2007 to 2009 years retrospectively. However, they evaluated only children and adult female records, and their study group ($n = 12057$) was smaller compared with our population. We believe that our data not only show the success of the vaccination program it gives a chance to see all population immunization status reflecting the Black Sea region globally, enabling the development of new strategies against HBV infection.

We found that there was significant, strong inverse relation between HBsAg and anti-HBs seropositivities

(P = 0.014, Pearson correlation: -0.757). Hence, it is clear that immunization programs have achieved their goal and was successful. However, potential sources of HBV infection still persist, especially for the 29–38 years age group.[1] Thus, it is extremely important for healthcare providers, public health workers, and the general public to be educated about the fact that HBV infection can occur in anyone, especially persons who practice risky behavior, such as injection drug use or unprotected sex with multiple partners. We believe that a national policy should be developed for follow-up of persons with chronic HBV infection, especially in this age group. In addition, a catch-up immunization program targeted at adults age groups in Black Sea region would be useful to decrease HBV infection rate in the future.[12]

The higher prevalence of hepatitis B markers in males compared to females was reported in some studies.[2,14,15] Similarly in this study, the prevalence of HBV infection was found different between males (4.4%) and females (3.6%) (P < 0.05). It may be associated with risky sexual behavior, in which men are more relaxed than women in sexual relationships in Turkey, along with risky procedures with nonaseptic and antiseptic measures applied, such as circumcision. This high frequency of HBsAg positivity in males is likely explained by the fact that all healthy Turkish men are required to complete at least one period of army service. During this time, barbers could expose them to potential blood transmission via instruments such as scissors, razor blades, straight razors, etc. during haircutting/shaving procedures. Anti-HBs seropositivity was similar for both sexes (p > 0.05) [Table 2].

Samsun is the largest and most crowded city of the region and the study conducted in the reference hospital of Black Sea region, therefore, we found 33.16% of 101648 patients were from other cities of the region. Hence, we believe that our results reflect not only the city of Samsun but reflect overall Black Sea region of Turkey.

Conclusion

In conclusion, the national vaccination program started in 1998 has changed the HBV epidemiology in Turkey and resulted in an apparent trend towards reduced disease levels. However, the prevalence of HBV infection is still high in adolescent and young adults. Therefore, a catch-up immunization program, education, and follow-up policy for these groups in addition to routine infant immunization will decrease the HBV infection rate, reduce morbidity and mortality rates, and will help to reduce hepatitis B transmission in Turkey.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. McMahon BJ, editor. Epidemiology and natural history of hepatitis B. Seminars in liver disease. New York, NY, USA: Thieme Medical Publishers, 2005.
2. Gogos C, Fouka K, Nikiforidis G, Avgeridis K, Sakellaropoulos G, Bassaris H, *et al.* Prevalence of hepatitis B and C virus infection in the general population and selected groups in South-Western Greece. Eur J Epidemiol 2003;18:551-7.
3. McMahon B. Hepatocellular carcinoma and viral hepatitis. Ganstreoenterol and Hepat 1997;4:315-30.
4. McMahon BJ, Holck P, Bulkow L, Snowball M. Serologic and clinical outcomes of 1536 Alaska Natives chronically infected with hepatitis B virus. Ann Intern Med 2001;135:759-68.
5. Karatekin G, Kilinc M, Oksuz BG, Igde M. Hepatitis B seroprevalence in children and women and the impact of the hepatitis B vaccination program in the Black Sea Region of Turkey. J Infect Dev Ctries 2013;7:960-5.
6. (ECDC) ECfDPaC. Hepatitis B and C in the EU neighbourhood: prevalence, burden of disease and screening policies. Technical Reports 2010 Sep 14; (2010).
7. Wong DK, Cheung AM, O'Rourke K, Naylor CD, Detsky AS, Heathcote J. Effect of alpha-interferon treatment in patients with hepatitis B e antigen-positive chronic hepatitis B: A meta-analysis. Ann Intern Med 1993;119:312-23.
8. Igde M, Acici M, Igde FA, Umur S. Carpet Beetle Anthrenus Verbasci, Linnaeus 1767: A New Seasonal Indoor Allergen: Case Report. Turkiye Klinikleri Tip Bilimleri Dergisi 2009;29:1729-31.
9. Ay P, Torunoglu MA, Com S, Cipil Z, Mollahaliloglu S, Erkoc Y, *et al.* Trends of hepatitis B notification rates in Turkey, 1990 to 2012. Euroo Surveilll 2013;18:
10. Mistik R, Balik I. Epidemiological analysis of viral hepatitis in Turkey. Viral Hepatitis İstanbul 2001;10-55.
11. Mast EE, Margolis HS, Fiore AE, Brink EW, Goldstein ST, Wang SA, *et al.* A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States. MMWR 2005;54:1-32.
12. Köse MR, Başara BB, Güler C, Yentür CK, *et al.* chapter 5: Prevention of Diseases and Protection of Health. THE MINISTRY of HEALTH of TURKEY HEALTH STATISTICS YEARBOOK 2014. 2014:59.
13. Konrath SH, O'Brien EH, Hsing C. Changes in dispositional empathy in American college students over time: a meta-analysis. Personality Soc Psychol Rev 2011;15:180-98.
14. Demirtürk N, Demirdal T, Toprak D, Altindiş M, Aktepe O. Hepatitis B and C virus in West-Central Turkey: seroprevalence Seroprevalence in healthy individuals admitted to a university hospital for routine health checks. The Turki J Gastroenterol 2006;17:267-72.
15. Thierfelder W, Hellenbrand W, Meisel H, Schreier E, Dortschy R. Prevalence of markers for hepatitis A, B and C in the German population. Results of the German National Health Interview and Examination Survey 1998. Eur J Epidemiol 2001;17:429-35.