

The prevalence of hepatitis B virus (HBV) among turkish immigrants in Germany

K.M. BURGAZLI, M. MERICLILER, C. SEN¹, M. TUNCAY¹, Y GÖKCE¹,
B. NAYIR¹, H.U. KLÖR¹, K. SINTERHAUF¹, E. KARATAY¹, Y. BILGIN²

Internal Medicine, Research and Medical Center Wuppertal, Wuppertal, Germany

¹Turkish-German Health Foundation, Giessen, Germany

²Department of Internal Medicine, Giessen University, Giessen, Germany

Abstract. – AIM: To determine the seroprevalence of Hepatitis B (HBV) among Turkish immigrants living in Germany.

SUBJECTS AND METHODS: A cross-sectional, multi-centered study was conducted among 1319 Turkish immigrants who were living in Germany and admitted to the clinics for any reason. Participants were tested for Hepatitis B surface antigen (HBsAg), hepatitis B surface antibody (Anti-HBs) and antibodies to hepatitis B core antigen (Anti-HBc).

RESULTS: 37.3% of the participants were tested positive for Anti-HBc. Of these, 45.8% percent was showed positivity for anti-HBc. 25.6% of all donors were showed positive results for Anti-HBc. HbsAg seroprevalence was found as 5%. Furthermore, 90% of participants with positive HBsAg had positive results for Anti-HBc. Males had significantly higher rates of Anti-HBc and HBsAg positivity than females.

CONCLUSIONS: Turkish immigrants living in Germany represented higher seroprevalence rate of HBV than total population of Germany.

Key Words:

Hepatitis B virus, Immigrants, Turkish, Germany, HBV seroprevalence.

Introduction

Hepatitis B virus (HBV) is one of the major infectious diseases worldwide, with the estimated number of infected people being more than 2 billion¹. Of these, approximately 350 million people remain infected chronically². Hepatitis B virus is the most common cause of hepatitis, liver cirrhosis and responsible for 80% of hepatocellular carcinomas¹. HBV has high mortality rates of 600,000 deaths every year resulting from its short and long term consequences³. Since the prevalence of chronic hepatitis differs geographically, countries classified as low (< 2%), intermediate (2-7%) and high (> 8) prevalence based on the serum Hepatitis

B surface antigen (HBsAg) positivity. Although the highest incidence rates of the disease occur in Asia; sub-Saharan Africa, South America and Alaska are also considered in the high incidence category⁴. Additionally, high rates of the disease occur in southern sides of the Central and Eastern Europe³. HBV is transmitted through the body fluids of the person with HBV infection, and highest titers of the virus are found in blood and serum while the semen and saliva have the lower concentrations.¹ The HBV is mainly transmitted perinatally, parenterally and with sexual contact. Perinatal transmission occurs majorly in the areas with high-endemicity. On the other side, sexual route is thought to be the major transmission pathway worldwide; however, it is principally seen in low-endemicity areas. Parenteral transmission is seen in United States and Western Europe and, intravenous drug usage is an important risk factor. Moreover, parenteral transmission includes the transmission during the surgery, dialysis, tattooing and piercing.⁵

There is a diversity of the prevalence of the HBV in Europe and the estimated HBV carrier rates ranges between 0.1% to 8.0%. In Germany, the HBV seroprevalence ranges from 0.5% to 1.5% and the incidence had been decreased from 7.5 to 1.4 cases per 100,000 inhabitants from 1995 to 2005⁶. However, it is difficult to estimate the true annual incidence due to under-reporting and missed subclinical cases⁷. Studies showed that HBsAg prevalence in migrants is higher than in general population⁸. 84% of adult migrants in Germany are from intermediate/high HBV prevalence countries⁹. Germany has 7.3 million foreigners in its population and 2.4% of the total population of Germany is constituted by Turks¹⁰. The HBV infection prevalence in Turkey is stated as 4.57% and it is considered as intermediated-endemicity¹¹. Since Turkey is the major source of

immigration to Germany, screening Turkish immigrants living in Germany has a significant importance. In order to provide an effective health control, it is essential to know the epidemiology of the illness in specific regions and subpopulations.

In this cross-sectional study we investigated the seroprevalence of HBV infection in Turkish immigrants living in six different cities of Germany.

Subjects and Methods

Study Design

A cross-sectional descriptive study was conducted among 1319 Turkish immigrant patients from 6 different centers of Germany (Dreieich, Frankfurt, Ludwigsburg, Ludwigshafen, Stuttgart, and Wuppertal), during a 12 months period. Study was done with the approval of Giessen University Ethics Committee. The participants who administered to corresponding clinics for any reason were randomly selected. The number and sexual distribution of included patients according to centers were shown in Table I.

Data Collection and Serological Parameters

An informed consent was taken from every participant before the clinical examination. The patients, who were Turkish being in any of these six cities for the purpose of tourism were excluded from study. Venous blood samples were drawn

from every participant in order to measure serological markers for HBV infection. Enzyme immunoassays were performed in order to analyze the venous blood samples for anti-HBc, HBsAg, and Anti-HBs.

Anti-HBs analysis was performed in order to find out the participants who were provided immunity to HBV infection via vaccination or previous infection. Anti-HBc antigen from serum was measured in order to determine whether any participant ever had an HBV infection previously, was having at that moment or not. Furthermore, HBs-Antigen analysis was done for detection of participants who were infectious.

Statistical Analysis

Each parameter collected from six different cities was distributed as male and female. The comparison of the male-female values and comparison of the values of four different ranges of age were done based on the Fisher's exact test using the SPSS 20.0 program. $p < 0.05$ was considered as statistically significant. Data was expressed in mean \pm SD.

Results

1318 donors were tested for Anti-HBs antibody and 37.3% of them demonstrated positive results. Stuttgart was the city having the highest rate which was 40%, on the contrary, Ludwigshafen had the lowest rate for Anti-Hbs positivity of 28%. When genders were compared,

Table I. Participants from six different centers by sex.

Clinics		Sex			Total
		Male	Female	U.G.*	
Dreieich	Number (n)	19	19	0	38
	Percentage (%)	50%	50%	0%	100%
Frankfurt	Number (n)	180	243	3	426
	Percentage (%)	42%	57%	1%	100%
Ludwigsburg	Number (n)	4	2	73	79
	Percentage (%)	5%	3%	92%	100%
Ludwigshafen	Number (n)	42	71	0	113
	Percentage (%)	37%	63%	0%	100%
Stuttgart	Number (n)	0	0	40	40
	Percentage (%)	0%	0%	100%	100%
Wuppertal	Number (n)	285	336	2	623
	Percentage (%)	46%	54%	0%	100%
Total	Number (n)	530	671	118	1319
	Percentage (%)	40%	51%	9%	100%

*U.G.: Unknown sex.

Anti-Hbs analysis did not show any significant differences ($p > 0.05$). Serological results of Anti-HBs antibody were shown in Table II.

It was found that there was a rate of 25.6% Anti-HBc positivity among 1287 Turkish immigrants, highest in Dreieich, lowest in Ludwigshafen. When the results of total Anti-HBc analysis were distributed by sex, it was found that the rates of the male patients were significantly higher than that of female patients ($p < 0.05$). The study further showed that the rate of Anti-HBc raised with the increase in age groups. Additionally, it was stated in each of four age groups, except the group aged 55 and older, men had significantly higher rates of Anti-HBc positivity than women (Figure 1).

Of those with positive Anti-HBs antibody, 45.8% percent was showed positivity for anti-HBc while 51.7% had negative results. There were 12 participants who were not tested for Anti-HBc. When the patients were distributed into four age groups, it was shown that the age groups younger than 35 had significantly higher negative rates than the age groups ($p < 0.0001$) (Table III).

5% of 1285 patients who were tested for HBsAg had positive results. Highest rates of HBsAg positivity was shown in Frankfurt and Ludwigsburg whereas Ludwigshafen had the lowest rates (Table IV). This positivity was significantly higher in men with the rate of 7% than in women with that of 3.5% ($p < 0.05$). No significant differences were shown among four age groups regarding the antigenic positivity ($p > 0.05$). Moreover, of participants with positive HBsAg ($n=64$), 58 had positive results for Anti-HBc.

Discussion

Hepatitis B viral infection is a common infection worldwide affecting about 350 million people chronically⁸. The prevalence of the disease is changeable in a population due to various factors such as ethnic differences and population movements^{12,13}. Migration is an important factor affecting prevalence of HBV infection because of the fact that immigrants have higher prevalence of HBsAg and Anti-HBc than the generalized population since they live in poorer conditions. In Germany, 19% of all population has a history of migration and 84% of this migrant population is immigrated from countries which have high or intermediate HBV prevalence. Three major countries from which the migrants are coming are Turkey, Italy and Former Yugoslavia⁹. Since Turkey is considered as an intermediate risk country for Hepatitis B virus with the estimated prevalence of 4.57%, migration from this country should be taken importance in terms of the epidemiology of the disease.

In our study we investigated the seroprevalence of the HBV in Turkish immigrants who migrated to six cities of Germany. The average HbsAg prevalence was found as 5% among Turkish immigrants. On the other side, although Germany is considered as a country with low (< 2%) hepatitis B virus endemicity, total HbsAg positivity of the three major migrant groups living in Germany was formerly found as 4.0%^{9,14,15}. Moreover, Germany has the ratio of 5.9% indicating the percent of all immigrants with chronic HBV¹⁵.

Table II. Distribution of Anti-HBs according to study centers.

		Anti-HBs			
		Negative	Positive	Total	
Centers	Dreieich	Number (n)	25	13	38
		Percentage (%)	66%	34%	100%
	Frankfurt	Number (n)	260	166	426
		Percentage (%)	61%	39%	100%
	Ludwigsburg	Number (n)	49	30	79
		Percentage (%)	62%	38%	100%
	Ludwigshafen	Number (n)	81	32	113
		Percentage (%)	72%	28%	100%
	Stuttgart	Number (n)	24	16	40
		Percentage (%)	60%	40%	100%
	Wuppertal	Number (n)	388	234	622
		Percentage (%)	62%	38%	100%
Total		Number (n)	827	491	1318
		Percentage (%)	63%	37%	100%

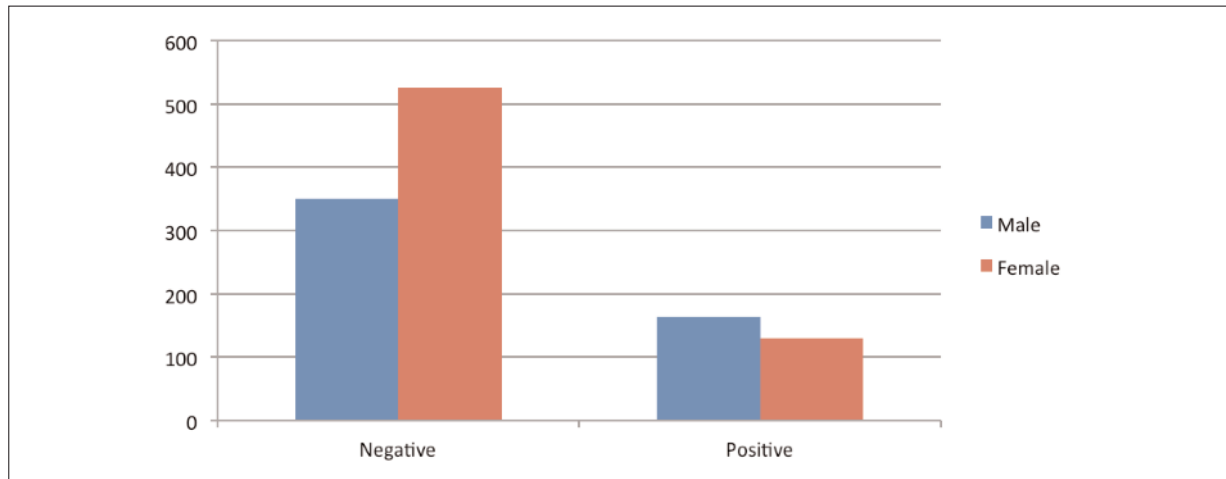


Figure 1. Serological results of Anti-HBc by sex.

Based on a systemic review done by Toy et al¹¹, total seroprevalence of HbsAg in Turkey is between 4.0%-5.0%. However, no recent data showing the prevalence of HBV infection in Turkey was found. Furthermore, it is known that Turks who are living in their nature country or migrated to another country are in the high risk groups and should be screened for HBV⁸. In our study, the positivity of HBsAg and Anti-HBc in Turkish participants were found 5% and 25.6% respectively and these rates are higher than those of total population of Germany.

Fisher et al¹⁶ showed in their multi-centered study that 37% of chronically active patients from 74 German centers were HbeAg-positive and 63% of these patients were immigrants mostly consisted of Turks. This study stated the epidemiology of chronic hepatitis B was affected by the migration from countries with higher HBV

prevalence. Another study done by Back E et al¹⁷ showed that Assyrian children who migrated from Turkey were represented a HBV transmission risk which was the same risk in Turks' general population whereas those migrated from Sweden did not showed any risk for this transmission.

According to van der Veen YJ et al¹⁸, the Turkish immigrants living in the Netherlands also had higher HBV prevalence compared with the total population of the Netherlands. As reported, positive factors for getting screened for HBV included responsibility, religious beliefs, feeling obligated due to the periodic invitations and provided social support. On the other side, factors limiting the screening were association of HBV with sexually transmitted diseases, and the thought that the health care services were not effective enough.

Table III. Anti-HBc seropositivity in participants with + Anti-Hbs according to age groups.

		Anti-HBc		Total	
		Negative	Positive		
Age groups	<= 34 Years	Number (n)	65	15	80
		Percentage (%)	81%	19%	100%
	35-44 Years	Number (n)	48	46	94
		Percentage (%)	51%	49%	100%
	45-54 Years	Number (n)	53	64	117
		Percentage (%)	45%	55%	100%
	>=55	Number (n)	56	70	126
		Percentage (%)	45%	55%	100%
Total		Number (n)	222	195	417
		Percentage (%)	53%	47%	100%

Table IV. Seroprevalence of HBs-Ag by six cities.

		HBsAg			
		Negative	Positive	Total	
Centers	Dreieich	Number (n)	25	13	38
		Percentage (%)	66%	34%	100%
	Frankfurt	Number (n)	260	166	426
		Percentage (%)	61%	39%	100%
	Ludwigsburg	Number (n)	49	30	79
		Percentage (%)	62%	38%	100%
	Ludwigshafen	Number (n)	81	32	113
		Percentage (%)	72%	28%	100%
	Stuttgart	Number (n)	24	16	40
		Percentage (%)	60%	40%	100%
	Wuppertal	Number (n)	388	234	622
		Percentage (%)	62%	38%	100%
Total		Number (n)	827	491	1318
		Percentage (%)	63%	37%	100%

Niederau et al¹⁹ investigated the epidemiology of chronic HBV in Germany in 250 patients. They stated that two thirds of the patients with chronic HBV were immigrants from other countries and they had serious financial problems. Furthermore, a population based prospective study conducted in 524 patients in Hamburg²⁰ showed that the incidence was 3.5 times higher in immigrants than in Germany-born patients. Additionally, the main risk factors were stated as parenteral drug use with the rate of 17.7% and immigration with the rate of 13.9%.

Authors acknowledge that the number of participants were not equally distributed in each study centers. Moreover, there were missing data on some baseline characteristics and serological results. However, we assume that these missing data had minor influence on the analysis outcome.

In the comparison of these investigations with our study, there is a parallel relationship highlighting that the seroprevalence of the Hepatitis B virus occurred in higher rates in Turkish immigrants. The recommendation strategies has common points based on the prevention and screening programmes focusing on the high risked, targeted groups such as Turkish immigrants.

Conclusions

Turkish immigrants living in Germany have higher seroprevalence of HBV compared to total population of Germany. Therefore, the prevention and screening programs should be improved.

Acknowledgements

The authors thank Prof. Klaus Sinterhauf and Gilead Sciences, Inc. for their contribution to this study.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

References

- 1) HEPATITIS B. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention, 07 May 2012. Web. 28 Jan. 2014.
- 2) DIENSTAG JL. Hepatitis B virus infection. *N Engl J Med* 2008; 359: 1486-500.
- 3) HEPATITIS B. WHO. N.p., n.d. Web. 28 Jan. 2014 retrieved from: <http://www.who.int/mediacentre/factsheets/fs204/en/index.html>
- 4) Chapter 3 Infectious Diseases Related To Travel. Hepatitis B. N.p., n.d. Web. 27 Jan. 2014. Retrieved from: <http://wwwnc.cdc.gov/travel/yellowbook/2014/chapter-3-infectious-diseases-related-to-travel/hepatitis-b>.
- 5) HOU J, LIU Z, GU F. Epidemiology and prevention of hepatitis B virus infection. *Int J Med Sci* 2005; 2: 50-57.
- 6) RANTALA M, VAN DE LAAR MJ. Surveillance and epidemiology of hepatitis B and C in Europe—a review. *Euro Surveill* 2008; 13.
- 7) HARBARTH S, SZUCS T, BERGER K, JILG W. The economic burden of hepatitis B in Germany. *Eur J Epidemiol* 2000; 16: 173-177.
- 8) LOK ASF, McMAHON BJ. Chronic hepatitis B. *Hepatology* 2007; 45: 507-539.
- 9) CHU JJ, WÖRMANN T, POPP J, PÄTZELT G, AKMATOV MK, KRÄMER A, REINTJES R. Changing epidemiology

- of hepatitis B and migration--a comparison of six Northern and North-Western European countries. *Eur J Public Health* 2013; 23: 642-647.
- 10) LIBRARY OF CONGRESS – Federal Research Division. Country Profile: Germany 2008. Web. Retrieved from: <http://lcweb2.loc.gov/frd/cs/profiles/Germany.pdf>
 - 11) TOY M, ÖNDER FO, WÖRMANN T, BOZDAYI AM, SCHALM SW, BORSBOOM GJ, VAN ROSMALEN J, RICHARDUS JH, YURDAYDIN C. Age- and region-specific hepatitis B prevalence in Turkey estimated using generalized linear mixed models: a systematic review. *BMC Infect Dis* 2011; 11: 337.
 - 12) ROUSSOS A, GORITSAS C, PAPPAS T, SPANAKI M, PAPADAKI P, FERTI A. Prevalence of hepatitis B and C markers among refugees in Athens. *World J Gastroenterol* 2003; 9: 993-995.
 - 13) EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER. EASL clinical practice guidelines: Management of chronic hepatitis B virus infection. *J Hepatol* 2012; 57: 167-185.
 - 14) EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL. (2010) Hepatitis B and C in the EU neighbourhood: prevalence, burden of disease and screening policies. Web. Retrieved from: http://ecdc.europa.eu/en/publications/Publications/TER_100914_Hep_B_C20%_EU_neighbourhood.pdf
 - 15) ROSSI C, SHRIER I, MARSHALL L, CNOSSEN S, SCHWARTZMAN K, KLEIN MB, SCHWARZER G, GREENAWAY C. Seroprevalence of chronic hepatitis B virus infection and prior immunity in immigrants and refugees: a systematic review and meta-analysis. *PLoS One* 2012; 7:e44611.
 - 16) FISCHER C, MAUSS S, ZEHNTER E, BOKEMEYER B, HEYNE R, HÜPPE D. Epidemiology and clinical characteristics of patients with chronic hepatitis B (CHB) in Germany – results of a nationwide cross-sectional study. *Z Gastroenterol* 2012; 50: 22-29.
 - 17) BÄCK E, DANIELSSON D, LUNDOVIST BO. Difference in prevalence of hepatitis B markers in children born either in Sweden or in Turkey of Assyrian immigrants. *Scand J Infect Dis* 1985; 17: 147-150.
 - 18) VAN DER VEEN YJ, DE ZWART O, VOETEN HA, MACKENBACH JP, RICHARDUS JH. Hepatitis B screening in the Turkish-Dutch population in Rotterdam, the Netherlands; qualitative assessment of socio-cultural determinants. *BMC Public Health* 2009; 9: 328.
 - 19) NIEDERAU C. Epidemiology of hepatitis B in Germany. *Med Klin (Munich)*. 2007; 102: 351-357.
 - 20) DIEHL R, SCHNEIDER S. Transmission of hepatitis A in Hamburg, Germany, 1998-1999--A prospective population based study. *Eur J Epidemiol* 2001; 17: 175-182.