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## **Prevalence of Hepatitis B among Blood Donors in Iran: A Systematic Review and Meta-analysis**

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### **ABSTRACT**

The global epidemic of Hepatitis B virus (HBV) is one of the most serious public health problems in the world and Blood transfusion is one of the most important transmission pathways of HBV. The present study was conducted to determine the prevalence of Hepatitis B in blood donor in Iran. This study was constructed based on the computerized literature database. English and non-English Articles were searched in PubMed database, ISI Web of Science, Iranmedex, Magiran, Google Scholar, SID, Scientific Journal of Iran Blood Transfusion Organization (SJIBTO) and Directory of Open Access Journals (DOAJ) from 1996 to 2008. Infection rates and 95% CI calculated by random affect model. Statistical analyses were performed using STATA 10.0, R Ver. 2.3 and ArcGIS 3.2a was used for map construction. Thirty papers from 83 studies involving 23671296 patients met our inclusion criteria. The prevalence of HBV infection in blood donors was 0.7% (CI 95: 0.5-0.8%). The highest rate of prevalence of hepatitis B in blood donors were found in Gilan,-Mazandaran,-Golestan and Semnan provinces with 1.1% (CI 95:0.6-1.6%). Prevalence of hepatitis B in blood donors from 1996-2008 is decreased, therefore national vaccination of hepatitis B after 1993, awareness programs and screening of bloods transfusion has led this fact.

**Key words:** Hepatitis B, prevalence, blood donors, Iran, meta-analysis

### **INTRODUCTION**

Hepatitis B virus (HBV) is one the most important causes of hepatic infectious diseases in humans. Hepatitis B has a global distribution with a prevalence of 360 million cases of the chronic type of the disease. About 600,000 deaths occur every year as a result of the acute and chronic consequences of HBV infection. About 45% of the world population reside in hyper-endemic where prevalence of Hepatitis B surface antigen (HBsAg) is more than 8, 43% live in midendemic areas where HBsAg prevalence is 2 to 7 and 12% live in hypo-endemic areas where HBsAg prevalence is less than 2% (Merican *et al.*, 2000; Lavanchy, 2004; Mast *et al.*, 2005). According to the report of World Health Organization and Centers for Disease Control and Prevention, prevalence of chronic Hepatitis B infection in Iran is between 2-7% (Poorolajal and Majdzadeh,

2009). In different parts of the world prevalence of HBV infection is rates ranging from 0.1 to 20% (Alavian *et al.*, 2007). Generally, 45% of the world population lives in high prevalence regions (Hepatitis B surface antigen positivity rates > 8%), resulting in the massive global burden associated with the infection (Alexander and Kowdley, 2006). The Middle East, Bahrain, Iran and Kuwait are areas of low endemicity. Iraq and the United Arab Emirates have intermediate endemicity and Jordan, Oman, Palestine, Yemen and Saudi Arabia have high endemicity (Andre, 2000). At present, vaccination is the most effective and cost saving means of prevention of HBV infection (Poorolajal and Majdzadeh, 2009). Hepatitis B vaccine was introduced within National Immunization Program (NIP) in Iran in 1993 for all neonates and vaccination of high risk groups and teenagers under 18 years old since 2006 (Hassan and Ziba, 2007). In order to prevent HBV transmission through blood transfusion in Iran serological screening for HBsAg was implemented (Said, 2011). Ali *et al.* (2011) reported that prevalence rate of Hepatitis B in Pakistani professional blood donors more than 5%, volunteer blood donors less than 5% Ali *et al.* (2011) in a study in Mexico. Prevalence of Hepatitis B in blood donors was 3.13% (95% CI, 3.01-3.24) in Yemen between 2000-2005 (Bajubair *et al.*, 2008) found prevalence of HBsAg to be 8% in healthy volunteers, 10.8% in blood donors (Bajubair *et al.*, 2008). In Thailand (Chimparlee *et al.*, 2011) indicted the prevalence of HBV infection in new blood donors has decreased gradually from 7.1% in 1988 to 2.6% in 2009 (Chimparlee *et al.*, 2011).

**Objectives:** This study aims to evaluate the prevalence rate of Hepatitis B in blood donors in Iran according to year and geographic areas of country.

## METHODOLOGY

**Eligibility criteria:** Cross sectional studies about prevalence of HBV among Iranian blood donor and No language, publication date, or publication status restrictions were imposed to our study.

**Information sources and search:** Literatures on Published studies in the English and Persian language on HBV were acquired by searching PubMed database, ISI Web of Science, Iranmedex, Magiran, Google Scholar, SID, Scientific Journal of Iran Blood Transfusion Organization (SJBTO) and Directory of Open Access Journals (DOAJ) for relevant articles from 1990 to 2008 using a search criterion combination of the following key words: Hepatitis, blood donor, Hepatitis B, HBV, prevalence, incidence and Iran. To maximize the number of studies for our analysis, we also combined the above key words.

**Study selection, data collection process and data items:** All identified studies were screened and the articles were selected by reviewing their titles and/or abstracts. Two observers independently reviewed the full texts of the remaining articles. We excluded studies were (1) not published at full length, (2) studies with a sample size less than 20, (3) studies without specific sample origin. When participant recruitment overlapped by more than 30% in two or more articles by the same author (s), the one with the largest population of participants or most recently published was selected. HBV infection was defined by a positive result of HBV infection markers: Hepatitis B surface antigen (HBsAg), Hepatitis B e antigen (HBeAg), anti-Hepatitis B surface antibody (HBsAb) and antiHepatitis B core antibody (HBcAb); this was confirmed by ELISA or enzyme immunoassay (EIA), also molecular diagnosis by PCR.

**Risk of bias in individual studies:** We used funnel plot model to check the existence of publication bias in our article.

**Planned methods of analysis:** Variance of prevalence in each study was estimate using binomial distribution. Pooled estimation of prevalence was computed using random effects models. Heterogeneity between studies was tested with the Cochran Q test ( $p < 0.10$  was considered as statistically significant heterogeneity) and the  $I^2$  statistic (values of 50, 25 and 75% were defined to represent low, medium and high heterogeneity respectively). Analyses were made with STATA (version 10.0, Stata Corp., College Station, TX, USA) and SPSS ver. 19. The significance was measured at  $p < 0.05$ . Subgroups analysis was done according to region, year and age group. Meta-regression was used to explore heterogeneity among studies (Sterne and Egger, 2001). And ArcGIS 3.2a was used for map construction.

## RESULTS

**Study selection:** In a total of 83 studies identified 17 studies from international database, 55 studies from Iranian databases and 11 studies by manual searching. The 25 studies were excluded for lacked study criteria. The 8 studies were repeated and don't involving in this study. The 5 studies lacked full text and were excluded. After full texts review, 15 studies were excluded (12 articles lacked study criteria and 3 studies were repeated). The remaining 30 studies were included in the analysis, reference numbers (Taheri Azbarmi *et al.*, 2008; Pedram, 2007; Attarpour Yazdi, 2009; Assarehzadegan *et al.*, 2008; Salem *et al.*, 2010; Rahimi-Movaghar *et al.*, 2010) which had prevalence 26, 19, 52, 38, 94 and 50%, respectively, were excluded in analysis (Fig. 1).

It was impossible to integrate and estimate the general widespread of Hepatitis B infection because of the variety of personal characteristics in the accepted studies. Therefore, the studies were divided to different categories based on participants, personal characteristics and then the results were categorized and analyzed in various groups. After searching the database, a total of 83 studies were identified, screened for retrieval. The characteristics of the 30 studies are given in Table 1. The number of patients participating in the studies ranged from 478 to 14599783. We draw the funnel plot model to decrease the bias of data (Fig. 2).

## RESULTS OF INDIVIDUAL STUDIES

**Synthesis of results:** The 30 studies were conducted about Hepatitis B prevalence in blood donors in all parts of Iran from 1996 to 2008. The sample size different from 478 (Ramezani *et al.*, 2007) to 14599783 (Kafi-Abad *et al.*, 2009a) in different studies. The highest and lowest prevalence of infection were 2.5% (CI: 2.3-2.6%) (Kazeminejad *et al.*, 2005) and 0.1% (CI: 0.05-0.15%) (Pourabuli *et al.*, 2006), respectively. The meta analysis estimated of infection prevalence with 95% interval confidence. According, Hepatitis B prevalence in blood donor was 0.7% (CI: 0.5%-0.8%) (Fig. 3, Table 1). Heterogenicity test was significant ( $p < 0.00001$ ,  $I^2 = 99.9\%$ ).

**Additional analyses:** Trend B Hepatitis in Iran during 1996-2008, Meta-regresion line with 95% confidence interval indicated of decrease of prevalence of Hepatitis B (Fig. 4, 5).

**Distribution of Hepatitis B in blood donor inside different parts of country:** The 30 studies were conducted about Hepatitis B prevalence in blood donors in all parts of Iran from 1996 to 2008. Table 2 the highest and lowest number of studies were done in part 8 of the country (24 studies)

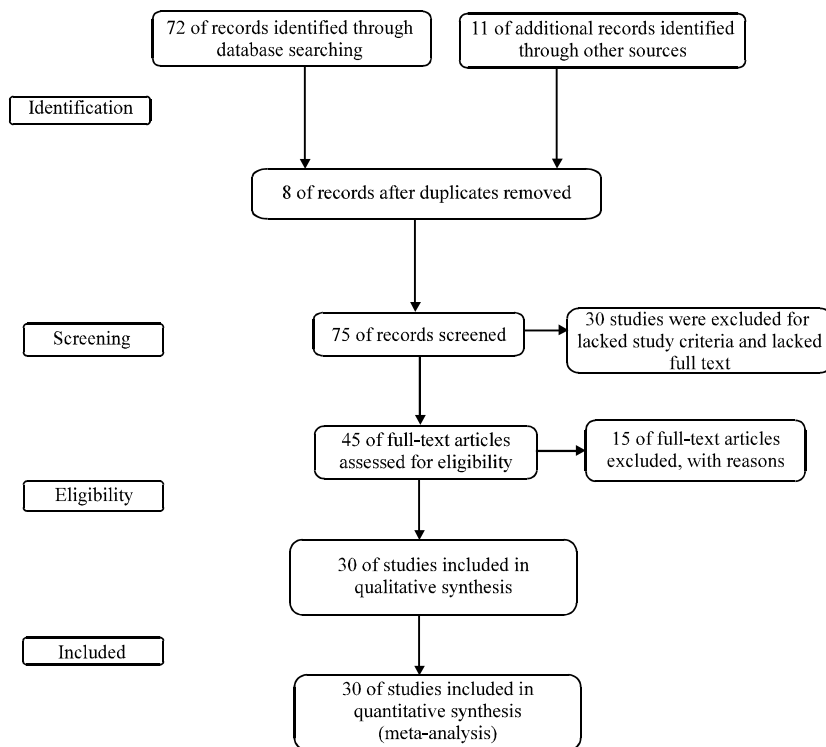


Fig. 1: Selection of studies and extraction process

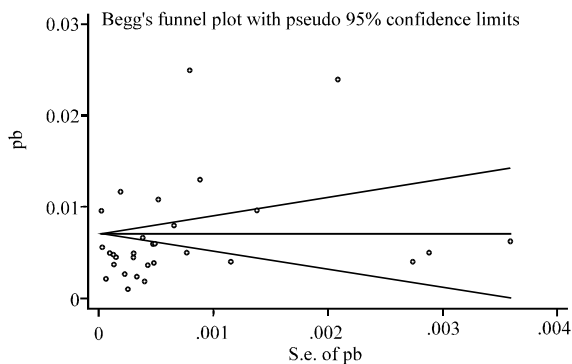


Fig. 2: Funnel plot for publication bias

and part 5 of the country (14 studies). Meta analysis estimated infection prevalence with 95% interval confidence. The highest and lowest rate of prevalence of infection were found in group 3 (Gilan-Mazandaran-Golestan-Semnan) (Kazeminejad *et al.*, 2005; Aghajanipoor and Zandieh, 2006; Ghanaei *et al.*, 2008; Taheri Azbarmi *et al.*, 2008) 1.1% (CI:0.6-1.6%), group 5 (Isfahan-Yazd-Kerman-Chaharmahalobakhtiari) (Ardekani *et al.*, 2002; Moniri *et al.*, 2004; Pourabuli *et al.*, 2006; Doosti *et al.*, 2009; Ebrahimian *et al.*, 2011) 0.3% (CI:0.2-0.5%) of the country, respectively. In parts 6 and 7 only one study carried out (Rezazadeh *et al.*, 2006) (Fig. 6).

Table 1: Study design and sample size of studies included in the Meta-analysis Hepatitis B prevalence in blood donors in all parts of Iran

Sl. No. Author	Ref. No.	Location	Sample population	Years	Method used	Prevalence	95% CI	
							Lower	Upper
Kasraian L	(Kasraian and Jahromi, 2007)	Shiraz	507531	2002-2005	ELISA	0.0049	0.00473325	0.00511675
Vahid T	(Vahid <i>et al.</i> , 2005)	Qazvin	39598	2001	ELISA	0.0108	0.009782	0.011818
Esmaeili H	(Esmaeili <i>et al.</i> , 2009)	Boushehr	20294	2006	ELISA	0.0023	0.001641	0.002959
Afzali Hasan	(Ardekani <i>et al.</i> , 2002)	Kashan	43731	1996	ELISA	0.0066	0.005841	0.007359
Rezazadeh M	(Rezazadeh <i>et al.</i> , 2006)	Hamedan	18306	2004	ELISA	0.0080	0.006709	0.009291
Esmaeili H	(Esmaeili <i>et al.</i> , 2007)	Boushehr	19627	2005	ELISA	0.0036	0.002762	0.004438
Ramezani A	(Ramezani <i>et al.</i> , 2007)	Tabriz	478	2005	PCR	0.0062	0.00084	0.013237
Souffan M	(Souffan <i>et al.</i> , 2009)	Arak	531	2008	PCR	0.0040	0.00137	0.009369
Agha Jani Poor K	(Aghajaniipoor and Zandieh, 2006)	Babol	16576	2002	ELISA	0.013	0.011276	0.014724
Masaeli Z	(Masaeli <i>et al.</i> , 2006)	Isfahan	16620	2002	ELISA	0.00385	0.002908	0.004792
Emamghorashi F	(Emamghorashi <i>et al.</i> , 2006)	Jahrom	3000	2001	ELISA	0.0040	0.001741	0.006259
Mansour Ghanei F	(Ghanei <i>et al.</i> , 2008)	Guilan	221508	1997	ELISA	0.0045	0.004221	0.004779
kazeminejad V	(Kazeminejad <i>et al.</i> , 2005)	Gorgan	38920	2003	ELISA	0.025	0.023449	0.026551
Ebrahimian Z	(Ebrahimian <i>et al.</i> , 2011)	Isfahan	542705	2004	ELISA	0.0021	0.001978	0.002222
Ghafouri M	(Ghafouri and Ameli, 2011)	Khorasan.s	42652	2006	ELISA	0.00492	0.004324	0.005516
Vossoughinia H	(Vossoughinia <i>et al.</i> , 2010)	Mashhad	310518	2003	ELISA+PCR	0.0117	0.001162	0.022238
Taheri Azbarmi Z	(Taheri Azbarmi <i>et al.</i> , 2008)	Rasht	49820	2003	ELISA	0.0026	0.002561	0.002638
Bozorgi SH	(Bozorgi <i>et al.</i> , 2006)	Qazvin	48116	2002	ELISA	0.0045	0.003902	0.005098
Attarchi Z	(Attarchi <i>et al.</i> , 2006)	Tehran	26645	2003	ELISA	0.0060	0.005073	0.006927
Torabi Zadeh	(Maatoghi <i>et al.</i> , 2006)	Ahwaz	39032	2005	ELISA	0.0060	0.005057	0.006943
Maatoghi j								
Jabbari H	(Jabbari <i>et al.</i> , 2009)	Chabahar	5409	2002	ELISA	0.024	0.019921	0.028079
Moniri R	(Moniri <i>et al.</i> , 2004)	Kashan	600	2001	ELISA	0.0050	0.00064	0.010644
Nabavizadeh S.H	(Nabavizade, 2000)	Yasuj	4980	2000	ELISA	0.0096	0.006892	0.012308
Arab M	(Pourabuli <i>et al.</i> , 2006)	Bam	15375	2006	ELISA	0.0010	0.0005	0.0015
Ranjbarian P	(Ranjbarian, 2008)	Hamedan	8468	2005	ELISA	0.0050	0.003498	0.006502
Amini Kafi-abad S	(Kafi-Abad <i>et al.</i> , 2009b)	Iran	6499851	2004-2007	ELISA	0.0056	0.00554	0.00565
Doosti A	(Doosti <i>et al.</i> , 2009)	shahrekind	11200	2003-2004	ELISA	0.0018	0.00101	0.00258
Kasraian L	(Kasraian and Tavasoli, 2010; Kasraian <i>et al.</i> , 2012)	Shiraz	204419	2006-2008	ELISA	0.0037	0.00343	0.00396
Khedmat H	(Khedmat <i>et al.</i> , 2007)	Tehran	318029	2005-2006	ELISA	0.0048	0.00456	0.00504
Amini Kafi-abad S	(Kafi-Abad <i>et al.</i> , 2009a)	Iran	14599783	1998-2007	ELISA	0.0096	0.00955	0.00965
Total	30		23671296			0.007	0.005	0.008

Table 2: Hepatitis B prevalence in blood donors in all parts of Iran from 1996-2008

Group No.	Regions	No. of studies	Prevalence	Lower	Upper
1	Tehran and suburban	2	0.005	0.004	0.006
2	Alborz-Qom-Markazi-Qazvin-Hamedan	4	0.007	0.004	0.01
3	Gilan-Mazandaran-Golestan-Semnan	4	0.011	0.006	0.016
4	North Khorasan-Khorasan Central-South Khorasan-SistanoBaluchestan	3	0.007	0.001	0.013
5	Isfahan-Yazd-Kerman -Chaharmahalobakhtiari	6	0.003	0.002	0.005
6	Kurdistan-Kermanshah-Ilam-Lorestan	1			
7	East Azarbaijan-West Azarbaijan-Ardabil-Zanjan				
8	Hormozgan- Bushehr-Fars-Khuzestan-KohgelouyeoBoyerahmad	8	0.006	0.004	0.007
9	Unclassified	2	0.008	0.004	0.012

**Age distribution of prevalence of Hepatitis B in blood donor:** All of 30 studies were done in undetermined age. In general, blood donor ranges 17 to 65 years old.

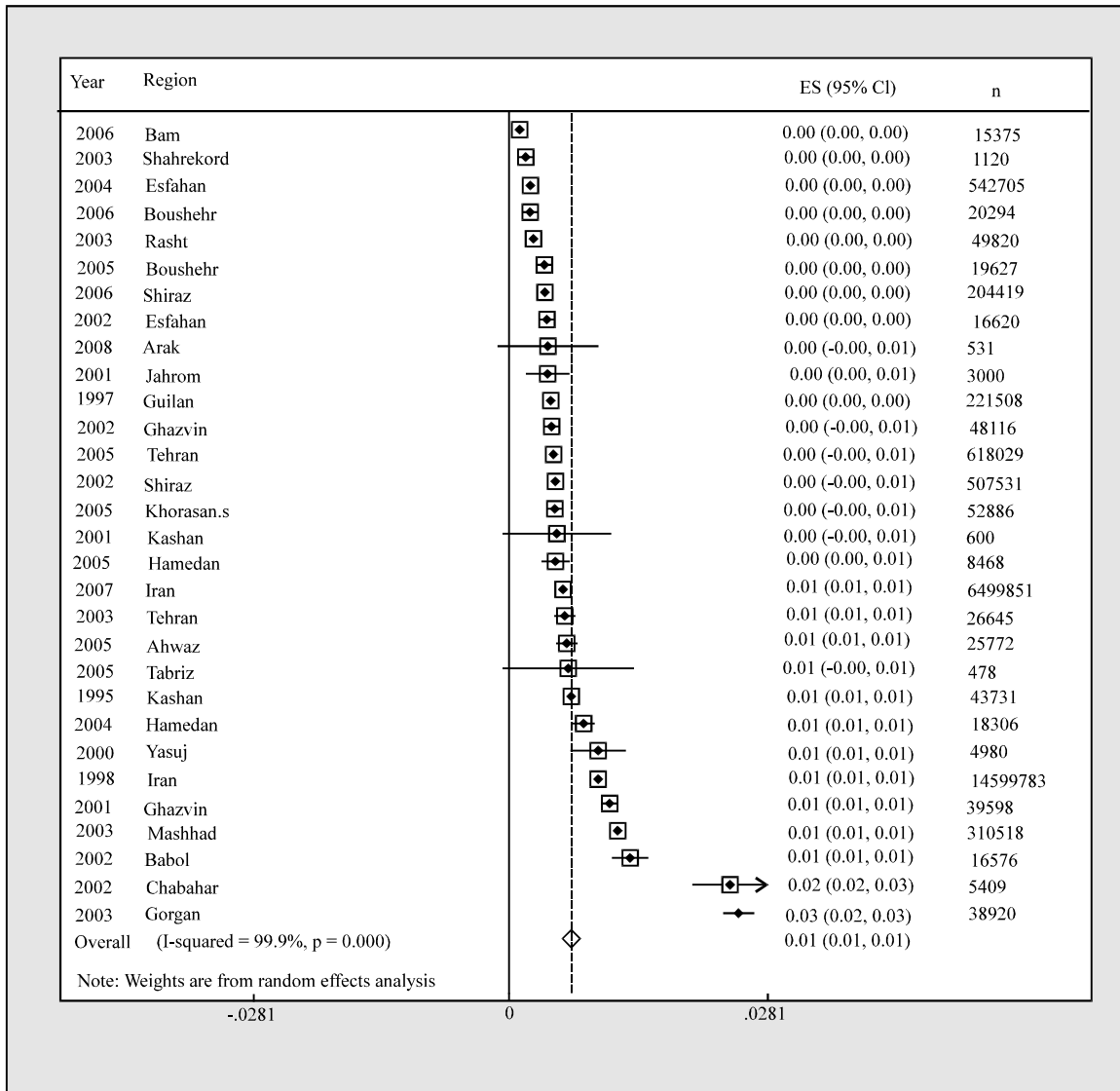


Fig. 3: Forest plot of studies on prevalence of Hepatitis B in voluntary blood donor, showing two types of population

**Diagnostic methods:** The most and lowest method was used ELISA (27 studies) and combination of PCR-ELISA (1 study), respectively.

## DISCUSSION

This is the first meta-analysis study of Hepatitis B prevalence in blood donor in Iran. In our analysis, the results showed significant heterogeneity ( $p < 0.00001$ ,  $I^2 = 99.9\%$ ). Because of conducting various studies in different years, regions and sample sizes.

Nearly 83% the studies we have analyzed are cross-sectional studies with period of one year and are therefore indicative of the point prevalence of the disease, but these studies contain about 8 million of all samples. Fortunately about 17% the studies we have analyzed, i.e., 15.5 million of

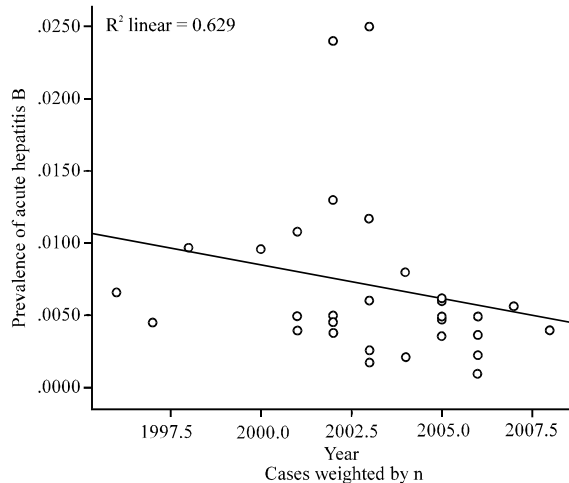


Fig. 4: Prevalence of Hepatitis B in voluntary blood donor during 1996-2008 years shows decrease of prevalence of Hepatitis B

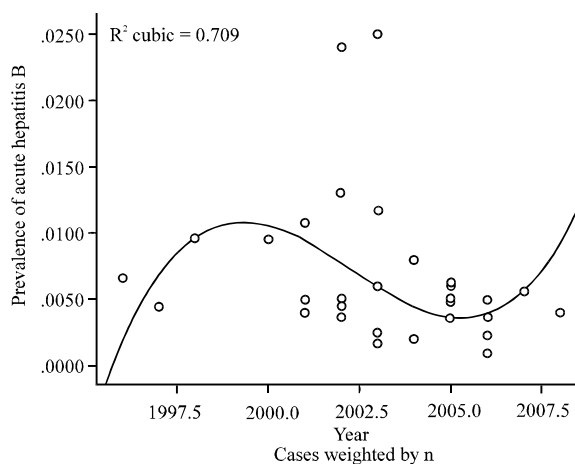


Fig. 5: Prevalence of Hepatitis B in blood donor during 1996-2008 years shows 1996-2005 decrease of infection and during 2005-2008 increase of infection while infection is decreasing generally

all samples are cross-sectional studies with period of more than one year and one study with period of 10 years. Therefore these results are a real estimation of Hepatitis B prevalence in blood donor in Iran. Overall, the rate of prevalence of Hepatitis B in blood donors from 1996-2008 was decreased [0.7%(CI 95: 0.5-0.8%)] ( $R = -79\%$ ), former studies Hepatitis B infection prevalence in blood donors has been reported 0.8% and less than public population (1.7%) in during 2002-2008 in Fars province, Hepatitis B infection prevalence in blood donors from 0.0049 to 0.0037 was decreased (Kasraian and Jahromi, 2007; Kasraian *et al.*, 2012). In others studies in Bushehr province during 2005-2006, prevalence in blood donors from 0.0036 to 0.0023 was decreased (Esmaeili *et al.*, 2007; Esmaeili *et al.*, 2009b). In Ghazvin province, during 2001-2002, prevalence in blood donors from 0.0108 to 0.0045 was decreased (Vahid *et al.*, 2005; Bozorgi *et al.*, 2006). In Gilan-Mazandaran-Golestan-Semnan provinces prevalence in blood donors is higher than mean



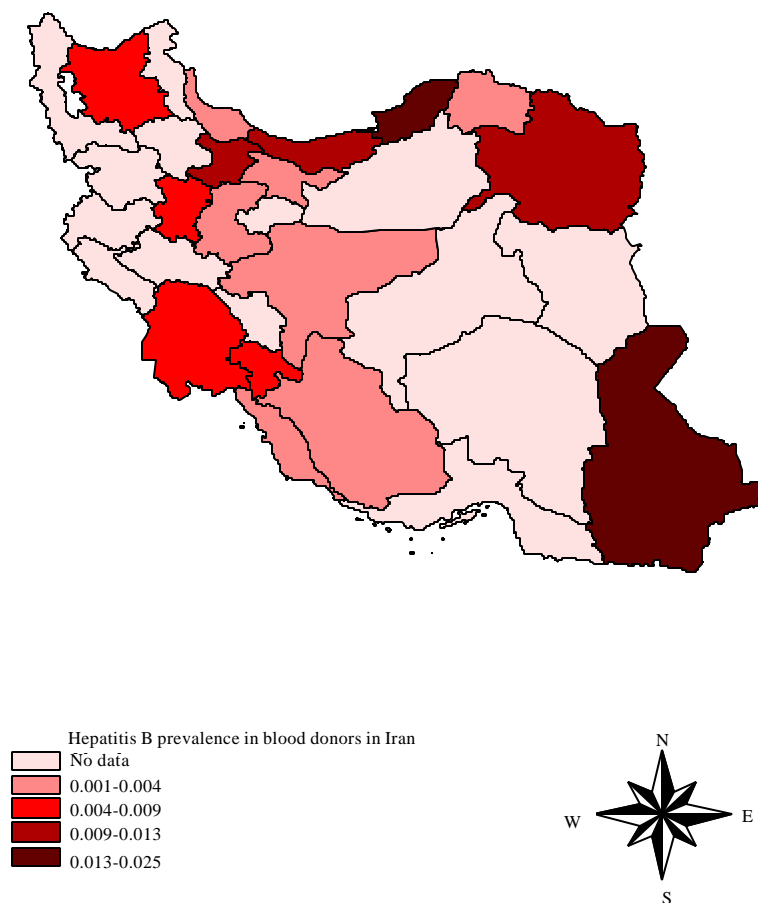


Fig. 6: Hepatitis B prevalence in blood donors in all parts of Iran from 1996 to 2008

of country (0.7%), this similar with prevalence Hepatitis B infection in public population of these regions. In 1979 Farzadegan, the prevalence of Hepatitis B surface antigen (HBsAg) in Iran was reported between 0.5 and 7.2% (Farzadegan *et al.*, 1979; Ghadir *et al.*, 2012). Almost 3% of the Iran population was affected. In the 1980s, divergent from a prevalence rate of 1.7% in the Fars province to 5% in Sistan-Balouchestan province (Ghadir *et al.*, 2012). Results of this meta-analysis indicated 87 and 13% of blood donor are male and female, respectively. According to world health organization, serological survey of free blood donor who gives their blood for the first time is a good indicator for investigating Hepatitis B infection prevalence in adults. While infection prevalence in repeated donors and those who give their blood instead of fee/payment, is more than public population. Serological survey of blood donor which has been done in Iran is not a good indicator for studying Hepatitis B infection prevalence in adults, for numbers of blood donors are male (83%, in this study). Accordingly, blood donors can not be a representative of general adults' population. Second, in the most studies, serological findings related to the first time blood donors were not separated from repeated blood donors while just 35 to 84% of blood donors did not mention their giving blood backgrounds. In fact, anyone can give his blood repeated provided that he/she

doesn't have any infection. Results of this meta-analysis indicated 90% studies used ELISA for detection of HBs antigen as diagnostic method, therefore in screening of blood donors in early of acute phase of Hepatitis B don't have HBs antigen they can't be diagnosed. In addition to the risk of transmission through the transfusion of infected blood, reactivation of Hepatitis B in Occult Hepatitis B infection (OBI) patients and recipients of their blood can lead to cirrhosis, hepatic cancer and reactivation of viral replication in the carrier (Kaviani *et al.*, 2006). Therefore, effective assays to assess and screen for OBI in blood donors are of paramount importance and require urgent attention.

In general, this reduction of Hepatitis B infection prevalence blood donors in Iran can be due to, national vaccination of Hepatitis B, screening of blood before transfusion, awareness of public population and education.

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