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Original Scientific Paper

THE IMPACT OF POSITIVE ANTI-HBc MARKER ON PERMANENT DEFERRAL OF VOLUNTARY BLOOD DONORS IN EASTERN CROATIA AND ESTIMATION OF OCCULT HEPATITIS B VIRUS INFECTION RATE

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SUMMARY – Recently an increase has been reported in the number of HBV transmissions from anti-HBc positive blood donors that were repeatedly negative in HBsAg and nucleic acid testing using the most sensitive tests available. The aim of the study was to show the effect of anti-HBc antibody testing performed in 2006 on permanent deferral of voluntary blood donors (VBDs), and to estimate occult hepatitis B infection (OBI) rate in this population after the introduction of mandatory molecular testing in the 2013-2016 period. More than 30,000 blood donations collected during the 2005-2007 period and more than 14,000 VBDs having donated blood during the 2013-2016 period after the introduction of molecular testing from eastern Croatia were included in the study. Serologic testing was performed with HBsAg assay throughout the study period, and anti-HBc assay was only performed in 2006. As part of the confirmatory algorithm testing, all HBsAg positive and unclear results were tested with molecular tests. Anti-HBc prevalence among VBDs in 2006 was 1.5%, with a rate of 1:197, whereas HBsAg prevalence was stable from 2005 to 2007 (0.04%, 0.1% and 0.1%, respectively). The calculated OBI rate from 2013 to 2016 was 1:30,250. Ten of 161 (12.4%) VBDs had serologic anti-HBc-only pattern. Anti-HBc testing in 2006 resulted in statistically more deferrals of VBDs compared to 2005 and 2007, and to the rest of Republic of Croatia. The strategy of universal anti-HBc testing of VBDs in addition to the existing HBsAg and molecular screening could be an additional measure to prevent HBV transmission by blood and blood components.

Key words: *Blood donors; Hepatitis B; Hepatitis B virus; Hepatitis B surface antigen; Croatia*

Introduction

Viral infections are a major cause of liver disease all over the world[1]. It is known that there are five primary hepatitis viruses, A, B, C, D and E. Other viruses such as cytomegalovirus, Epstein-Barr virus, herpes simplex virus, varicella zoster virus, human herpesvirus-6, adenovirus and yellow fever virus, as well as drugs, poisons, autoimmune hepatitis and Wilson's disease can cause acute or chronic hepatitis. Each hepatitis virus can cause acute hepatitis, but only hepatitis B, C and D can cause chronic hepatitis[2]. Hepatitis E virus can

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sometimes be the cause of chronic hepatitis in immunocompromised individuals[3].

Hepatitis B is a disease caused by hepatitis B virus (HBV) belonging to the Hepadnaviridae family and has traditionally eight genotypes (A-H, and recently reported J), which are geographically widespread. According to the European Association for the Study of Liver, chronic HBV infection is divided into five phases that are not strictly separated and stable, as follows: (I) HBeAg-positive chronic infection, (II) HBeAg-positive chronic hepatitis, (III) HBeAg-negative chronic infection, (IV) HBeAg-negative chronic hepatitis, and (V) HBsAg-negative phase[4]. Hepatitis B is a viral infection responsible for most chronic liver disease patients and is transmitted parenterally, as a sexually transmitted disease and by vertical transmission from mother to child. About 240 million people worldwide are infected with this virus and they have a risk of developing liver cirrhosis and hepatocellular carcinoma[5].

Although in the last two decades, major steps have been taken to reduce the risk of infection by blood transfusions, HBV is still a global risk in transfusion medicine. The residual risk of HBV is not restricted to the 'window period', but has been increased by including blood donors with occult hepatitis B infection (OBI), a condition when HBV DNA is present in the liver or plasma with undetectable HBsAg (hepatitis B surface antigen) and with or without anti-HBc antibodies (hepatitis B core, core refers to hepatitis B antigen) or anti-HBs, outside the 'window period'[6]. Updated statements of the Taormina Consensus Conference state that OBI is the presence of replication competent HBV DNA in the liver and/or HBV DNA in blood with HBsAg negative result by currently available assays with or without anti-HBc or anti-HBs[7]. When detectable, the amount of HBV DNA in serum is usually very low (<200 IU/mL). For more than thirty years, it has been known that HBsAg negative and anti-HBc positive blood donors can transmit HBV[8].

The introduction of molecular assays in blood donor testing has led to understanding the additional effect of anti-HBc marker in the detection of OBI, but a qualitative anti-HBc test can discriminate potentially infectious rather than truly infectious donors, making its use in high-prevalence populations conditioned with parallel molecular testing, antibody titer testing or other HBV marker testing[9-12]. Recently, increasing evidence of HBV transmissions from anti-HBc positive blood donors that were repeatedly negative in HBsAg and HBV individual nucleic acid testing (ID-NAT) using the most sensitive tests available has been reported[13].

In 2013, Croatia implemented the ID-NAT as a mandatory blood donor test for three viruses, i.e. HBV, hepatitis C virus (HCV) and human immunodeficiency virus (HIV-1) for all donations. In 2016, HIV-2 was added with the new ID-NAT test. Although the risk of transmissible infectious diseases in Croatia has been reduced significantly by the use of serologic tests (HBsAg, anti-HCV, anti-TP, HIV Ag/Ab) and consistent application of blood donor selection criteria, the notable challenge for transfusion therapy in Croatia was the risk of HBV transmission due to OBI. VBDs with positive anti-HBc results are deferred for further donations, regardless of anti-HBs status.

Transfusion service in eastern Croatia was reorganized in the 2011-2014 period. The Clinical Department of Transfusion Medicine (CDTM) of the Osijek University Hospital Centre (Osijek UHC) has taken over the tasks of collecting, testing, producing and supplying blood preparations for the hospitals in Našice, Vukovar, Vinkovci, Virovitica, Slavonski Brod and Nova Gradiška. Previously, these hospitals performed the above mentioned tasks for their needs. Currently, CDTM supplies blood to a total of seven hospitals and as a licensed health care facility for blood collection and supply is the second largest blood bank in the Republic of Croatia with over 30,000 blood donations collected annually since 2017.

The objective of the present study was to show the effect of testing VBDs for anti-HBc antibody with detection of total antibodies (IgM and IgG classes) on VBD permanent deferral, and to estimate OBI rate in VBDs at the Osijek UHC CDTM after the introduction of mandatory ID-NAT testing. The results of HBsAg testing in blood donations collected in the Osijek-Baranja County in 2005, 2006 and 2007 were analyzed, as well as the results of anti-HBc antibody testing in 2006 and HBsAg test results for the total number of donations collected in the Republic of Croatia.

Materials and Methods

Blood samples

The study included 10,579 serum samples from blood donations in 2005, 10,398 serum samples in 2006

Table 1. Testing results of VBDs for HBsAg and anti-HBc at the Clinical Institute of Transfusion Medicine, Osijek University Hospital Centre and in Republic of Croatia

	Number (%) of VBDs/donations tested			p*
	Osijek-Baranja County, n (%)	Other centers in Republic of Croatia, n (%)	Total, n (%)	
2005				
HBsAg positive	4 (0.04)	41 (0.03)	45 (0.03)	0.53
HBsAg negative	10,575 (99.96)	156,946 (99.97)	167,521 (99.97)	
Total number of donations tested	10,579 (100)	156,987 (100)	167,566 (100)	
2006				
HBsAg positive	6 (0.10)	34 (0.02)	40 (0.02)	**0.04**
HBsAg negative	10,392 (99.9)	156,906 (99.98)	167,298 (99.98)	
Total number of donations tested	10,398 (100)	156,940 (100)	167,338 (100)	
2006				
HBsAg positive + anti-HBc positive	167 (1.6)	34 (0.02)	201 (0.10)	**<0.001**
HBsAg negative	10,231 (98.4)	156,906 (99.98)	167,137 (99.9)	
Total number of donations tested	10,398 (100)	156,940 (100)	167,338 (100)	
2007				
HBsAg positive	6 (0.10)	29 (0.02)	35 (0.02)	**0.02**
HBsAg negative	10,555 (99.9)	161,009 (99.98)	171,564 (99.98)	
Total number of donations tested	10,561 (100)	161,038 (100)	171,599 (100)	

*Fisher exact test; VBDs = voluntary blood donors

and 10,561 serum samples in 2007 collected from VBDs in eastern Croatia (including the population of 5 counties: Osijek-Baranja, Vukovar-Srijem, Brod-Posavina, Požega-Slavonija and Virovitica-Podravina, with about 800,000 inhabitants). Blood samples were extracted in 10-mL Becton-Dickinson tube without anticoagulant and after the fibrin cluster was formed, they were centrifuged for 10 minutes at 3000 rpm.

Serologic testing

Serologic testing was performed by the microparticle enzyme immunoassay HBsAg (V2) on an AxSYM analyzer (Abbott, TX, USA) and anti-HBc chemiluminescence immunoassay on a Vitros ECIQ analyzer (Ortho Clinical Diagnostics, NJ, USA).

For statistical calculations, the number of VBDs tested in the Osijek-Baranja County that were rejected on the basis of serum markers was compared with the total number of VBDs tested in the Republic of Croatia; the latter data were kindly provided by the Croatian Institute of Transfusion Medicine, Zagreb.

Molecular testing

As part of confirmatory algorithm testing in 2005, 2006 and 2007, all HBsAg positive and unclear results were sent to the CDTM for HBV DNA testing with the HPS/HBV Cobas TaqMan 48 test; sensitivity 6 IU/mL. In the 2013-2016 period, the Procleix Ultrio Plus test with 95% level of detection for HBV, 3.4 IU/mL was used on ID-NAT.

Ethics

All the procedures in the study were in accordance with ethical standards of the institutional or regional board on human experimentation and Helsinki Declaration of 1975, as revised in 1983.

Statistical methods

The results of the study were processed by descriptive and tabular statistics. Categorical data were expressed as absolute and relative frequencies and statistically analyzed by χ^2-test or Fisher exact test using

Table 2. Number of permanently deferred VBDs at the Clinical Institute of Transfusion Medicine, Osijek University Hospital Centre

	Number VBDs tested in Osijek-Baranja County				
	HBsAg positive	Anti-HBc positive	Anti-HBc only positive	Other positive HBV markers	Total number of donations tested
2005	4	Not performed	Not performed	Not performed	10,579
2006	6	161	21	140	10,398
2007	6	Not performed	Not performed	Not performed	10,561
Total	16	161	20	140	31,538

VBDs = voluntary blood donors

Table 3. Distribution of permanently deferred VBDs due to HBV testing relative to the number of blood donations at the Clinical Institute of Transfusion Medicine, Osijek University Hospital Centre and in Republic of Croatia

	Number (%) of permanently deferred VBDs			p*
	Osijek UHC CDTM	Other centers in Republic of Croatia	Total	
2005				
Repeat VBDs	3 (75)	12 (29.1)	15 (33.3)	0.10
New VBDs	1 (25)	29 (70.7)	30 (66.7)	
Total	4 (100)	41 (100)	45 (100)	
2006†				
Repeat VBDs	155 (92.8)	8 (23.5)	163 (81.1)	**<0.001**
New VBDs	12 (7.2)	26 (76.5)	38 (18.9)	
Total	167 (100)	34 (100)	201 (100)	
2007				
Repeat VBDs	2 (33.3)	8 (27.6)	10 (28.6)	>0.99
New VBDs	4 (66.7)	21 (72.4)	25 (71.4)	
Total	6 (100)	29 (100)	35 (100)	

*Fisher exact test; VBDs = voluntary blood donors; CDTM = Clinical Department of Transfusion Medicine; Osijek UHC = Osijek University Hospital Centre; †HBV testing included HBsAg + anti-HBc assays

Prism 5 (GraphPad Software, San Diego, CA, USA) statistical software. The level of statistical significance was set at $p<0.05$.

Results

Anti-HBc testing

In the 2005-2007 period, 31,538 blood donations were collected by CDTM in the Osijek-Baranja County. Along with HBsAg testing, in 2006 all donations were tested for anti-HBc as well.

There were no significant differences in the number of HBsAg positive or negative VBDs in the Osijek-Baranja County and other Croatian centers in 2005. During 2006, there were significantly more HBsAg positive VBDs in the Osijek-Baranja County (Fisher exact test, p=0.04), and significantly more HBsAg + anti-HBc positive VBDs (Fisher exact test, p<0.001) as compared to other centers in the Republic of Croatia. In 2007, there were significantly more HBsAg positive VBDs in the Osijek-Baranja County than in other centers in the Republic of Croatia (Fisher exact test, p=0.02) (Table 1).

Deferral of VBDs due to positive anti-HBc test

During 2005 and 2007, Osijek UHC did not use anti-HBc and other HBV markers. In 2006, of the total number of donations tested in Osijek UHC, there were 6 (0.06%) HBsAg positive (and anti-HBc positive together with/without other HBV markers) VBDs, 161 (1.5%) anti-HBc positive VBDs including 21 (0.02%) only-anti-HBc positive VBDs, and 140 (1.3%) VBDs positive for other HBV markers as well. Anti-HBc positive VBDs were not reconfirmed with other anti-HBc assay but additional follow-up sample was obtained and testing for other HBV markers was performed. HBsAg and all anti-HBc positive VBDs were permanently deferred (Table 2). In 2006, there were significantly more permanently deferred repeat VBDs in Osijek-Baranja County compared to other

Table 4. HBV serologic profiles of permanently deferred VBDs at the Clinical Institute of Transfusion Medicine, Osijek University Hospital Centre in 2006

	Anti-HBc only positive	Anti-HBc + anti-HBs + anti-HBe positive	Anti-HBc + anti-HBs positive	Anti-HBc + anti-HBe positive	Total
HBsAg positive	0	0	0	6	6
HBsAg negative	21	68	64	8	161
Total	21	68*	64	14	167

VBDs = voluntary blood donors; *one VBD had HBeAg positive result; the range of anti-HBs titer was 12-1000 mIU/mL

Table 5. Distribution of occult HBV infection frequency and permanent deferral of VBDs relative to the number of blood donations in the Clinical Institute of Transfusion Medicine, Osijek University Hospital Centre and other 4 counties in the 2013-2016 period

	Number (%) VBDs tested			p*
	Osijek-Baranja County, n (%)	Other 4 counties†, n (%)	Total, n (%)	
2013 (May 1 to Dec 31)				
OBI positive	0	4 (0.1)	4 (0.04)	**0.02**
OBI negative	5,922 (100)	3,173 (99.9)	9,095 (99.96)	
Total number of VBDs tested	5,922 (100)	3,177 (100)	9,099 (100)	
2014				
OBI positive	1 (0.01)	1 (0.02)	2 (0.01)	>0.99
OBI negative	7,462 (99.99)	6,183 (99.98)	13,645 (99.99)	
Total number of VBDs tested	7,463 (100)	6,184 (100)	13,647 (100)	
2015				
OBI positive	0	2 (0.03)	2 (0.01)	0.17
OBI negative	8,728 (100)	6,118 (99.97)	14,846 (99.99)	
Total number of VBDs tested	8,728 (100)	6,120 (100)	14,848 (100)	
2016				
OBI positive	0	0	0	-
OBI negative	8,137 (100)	6,182 (100)	14,319 (100)	
Total number of VBDs tested	8,137 (100)	6,182 (100)	14,319 (100)	

*Fisher exact test; VBDs = voluntary blood donors; †Vukovar-Srijem, Požega-Slavonija, Brod-Posavina and Virovitica-Podravina; OBI = occult HBV infection

centers in the Republic of Croatia (Fisher exact test, p<0.001), whereas in 2005 and 2007 there were no significant differences between Osijek UHC and other centers in Croatia (Table 3). HBV serologic profiles of permanently deferred VBDs at the Osijek UHC CDTM in 2006 are shown separately in Table 4.

OBI rate from 2013 to 2016

In the period from May 1, 2013 until the end of 2016, eight cases of OBI were recorded, one in the Osijek-Baranja County and 7 in the other four counties (Vukovar-Srijem, Požega-Slavonija, Brod-Posavina and Virovitica-Podravina). Only in the last six months of 2013, there were significantly more OBIs in the other four counties than in Osijek-Baranja County, whereas in the 2014-2016 period there were no significant differences in the number of OBIs (Table 5). Detailed report of eight cases of OBI among VBDs diagnosed at the Osijek UHC CDTM during the study period is shown in Table 6.

Table 6. Detailed report of eight cases of occult HBV infections among VBDs diagnosed at the Clinical Institute of Transfusion Medicine, Osijek University Hospital Centre during study period

Year	Case/donor*	Age (yrs)	HBV-DNA (IU/mL)	Anti-HBc	Anti-HBs (IU/L)	Anti-HBe
2013	OBI 1	58	<20	Pos	24	Neg
2013	OBI 2	51	ND	Pos	12	Neg
2013	OBI 3	64	ND	Pos	Neg	Neg
2013	OBI 4	52	ND	Pos	789	Pos
2014	OBI 5	52	<20	Pos	24	Neg
2014	OBI 6	35	<20	Pos	Neg	Pos
2015	OBI 7	61	NP	Pos	NP	NP
2015	OBI 8	56	ND	Pos	18	Neg

VBDs = voluntary blood donors; OBI = occult HBV infection; ND = not determined; NP = not performed; Pos = positive; Neg = negative; *all eight cases were anti-HBc IgM and HBeAg negative

Discussion and Conclusion

The anti-HBc test was introduced into routine blood screening in the mid-1980s in HBV ethnically diverse countries such as the USA. In 1989, Japan introduced an anti-HBc blood donor test with a modified algorithm in which anti-HBc reactive with <1:32 or ≥32 with anti-HBs ≥200 mIU/mL levels were accepted for transfusion. The prevalence of anti-HBc is related to regional HBV prevalence (USA 0.23%, UK 0.56%, Germany 1.88%, Italy 4.85%, India 10.82%, Greece 14.9%, etc.)[13-16]. In Italy, in 2013, there was no recommendation for anti-HBc testing in routine practice due to the relatively high prevalence of other serologic infections (HBsAg and/or HBV DNA). The number of rejected VBDs would therefore be too large and unacceptable for this reason[16]. While OBI prevalence in VBD population varies from 0.0002% to 0.084%[15,17-20], it is 0.18% in China, which is a highly endemic HBV region[21]. According to data from the Croatian Public Health Institute, at the beginning of the 21st century, the prevalence of HBs Ag in new blood donors was 0.4% (in 2002) *versus* 0.1% in 2011, continuing to decrease to 0.047% in 2018[22-24] . Based on the HBsAg seroprevalence data in different population subgroups, it is estimated that approximately 20,000-30,000 people in Croatia are chronically infected with HBV[25].

The results of this study showed the prevalence of anti-HBc among VBDs in eastern Croatia (Osijek-Baranja County) in 2006 to be 1.5%, with a rate of 1:197, while the HBsAg prevalence during the 2005-2007 period was stable (0.04%, 0.1% and 0.1%, respectively). The calculated OBI rate from 2013 to 2016 was 1:30,250. Ten of 161 (12.4%) VBDs had the anti-HBc-only pattern. Considering that in Croatia anti-HBc test is not obligatory in VBD screening, VBDs with anti-HBc positive results are permanently deferred for blood donation and there is no re-entry national policy using anti-HBs results, anti-HBc testing in 2006 resulted in a statistically higher VBD deferral compared with 2005 and 2007, and with the rest of the Republic of Croatia. The number of VBDs lost after anti-HBc screening at the Osijek UHC CDTM was substantial although it did not significantly affect the overall blood supply. It is important to note that in 2006, VBDs from Osijek-Baranja County were screened for anti-HBc, while VBDs from the other four counties whose serologic screening testing was taken over by the Osijek UHC CDTM in 2011-2014 were not tested for anti-HBc. The results of ID-NAT testing revealed that all seven VBDs where OBI was detected were from those counties, except for a new VBD from the Osijek-Baranja County who donated blood for the first time. The result of our research on a larger number of permanently deferred repeat blood donors (repeat VBDs/new VBDs=155/12) coincides with the OBI prevalence in the Republic of Croatia, which is significantly higher among multiple blood donors (45/50, 90%), male sex (86%) and older donors (median age 58) in relation to the general population of blood donors[26]. In addition, it is also apparent from the results that after the introduction of routine ID-NAT testing, OBI had a declining tendency in the eastern part of Croatia in 2013, 2014, 2015 and 2016.

According to a recent study in Croatian donors conducted over a 14-year period, the anti-HBc prevalence significantly decreased among Croatian VBDs (from the Croatian Institute of Transfusion Medicine), from 5.24% in 2004 through 2.56% in 2013 to 1.32% in 2017[27]. Similarly, the prevalence of anti-HBc-only profiles decreased from 0.62% in 2004 through 0.25% in 2013 to 0.21% in 2017. A fourfold decrease was observed in all age groups of VBDs from 2017 but mostly among repeat donors (from 5.90% to 1.38%). In the group of first-time donors, there was a nonsignificant difference in anti-HBc prevalence during the study period, probably due to their younger age (<29 years), and were mostly vaccinated against HBV according to the mandatory vaccination policy in Croatia since 1999[27].

However, similar anti-HBs carriage rates (80.56%, 87.57%, and 82.09%) were reported in anti-HBc positive donors during the study period. HBsAg and HBV DNA were not detected. In the first year of blood donor testing in Croatia with ID-NAT tests (2013), the frequency of OBI was 1:7,031, whereas after the 3-year period it was 1:10,900 donations, followed by further significant decrease, i.e. 1:98,494 in 2016, 1:28,495 in 2017 and 1:195,815 in 2018. Analysis of 23 OBI donor archival samples showed consistency of anti-HBc positive results (100%), as opposed to ID-NAT (63%) and ID-NAT reproducibility (50%), as expected for samples with a low HBV DNA viral load. These data support the importance of anti-HBc testing in identifying OBI donors. HBV decreasing residual risks of 68, 88, and 12 *per* million donations were estimated for the years 2004, 2013 and 2017[27].

Taking into consideration that anti-HBc *per se* is an irreplaceable serologic marker in the detection of end phase HBV infection, which preludes convalescence in the detection of seropositive OBI infection that is characterized by negative HBsAg test and HBV DNA blood level is mostly undetectable or intermittent, it is assumed that anti-HBc would be a more useful marker in the detection of OBI in VBDs. Results of this study, the anti-HBc rate/OBI rate (1:197/1:30,250) and the previous Croatian study from 2013 (anti-HBc rate/OBI rate 1:19/1:11,213; 2017 anti-HBc rate/OBI rate 1:76/1:30,932) show that due to the high consistency of anti-HBc in Croatian OBI VBDs, the strategy of universal testing of blood donors for this marker in addition to the existing HBsAg and ID-NAT screening in Croatia would represent an additional measure to prevent HBV transmission by blood and blood components.

The true value of universal anti-HBc screening of blood donors remains controversial and mostly depends on HBV prevalence in a population. It is estimated that in moderate- and high-endemic countries, where anti-HBc prevalence in blood donors ranges between 8% and >50%, such as the Mediterranean area, East Asia, and sub-Saharan Africa, anti-HBc testing would affect blood product availability too severely and probably cannot be implemented without compromising blood supplies[13].

Similarly, universal VBD anti-HBc testing in HBV low-endemic countries is still debated. While some HBV low-endemic and developed countries such as Germany and the Netherlands in EU, as well as Canada, have recently implemented anti-HBc screening, some other developed countries, i.e. Australia and Switzerland, have not implemented it but decided to introduce different strategies to reduce the risk of HBV infection (i.e. NAT testing)[28].

It is well recognized that anti-HBc may be the only detectable serologic marker of HBV infection in blood donors, which may be an HBV-naïve subject (false positive anti-HBc test), a person with a past HBV infection, or having OBI, i.e. a low-level carrier negative for HBsAg[29]. False positivity of anti-HBc test is one of the possible outcomes and such isolated test reactivity can be overcome by additional testing with alternative anti-HBc assay, as well as testing for other HBV markers and HBV DNA, which could provide additional helpful information, along with additional sample testing.

Occult HBV infection is considered a rare event in developed low-endemic HBV countries, whereas in developing moderate- and high-endemic countries the risk is much higher and depends on screening policies and methods implemented. A recently conducted study in Croatia during a three-year period showed the incidence of OBI infection of 1 *per* 10,900 donations. Since 2013, the Croatian screening policy for blood borne viruses includes NAT screening, which resulted in deferral of 50 VBDs with OBI and there were only two potential HBV DNA transmissions to blood recipients in Croatia due to OBI in VBDs[26].

The requirements for safe transfusion therapy are increasing and new history exclusion criteria for blood

donors are constantly being added. At the same time, due to the growing demand for blood products and prolonged life span, medical procedures are becoming ever more complicated and there is no appropriate synthetic replacement for all the functions blood carries. Some authors point out that with the current strategy, in the near future, we will not be able to meet the needs for blood and blood products[30]. So further cost-benefit analyses should be conducted concerning decision of including mandatory anti-HBc testing in the existing VBD screening strategy in Croatia.

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Sažetak

UTJECAJ POZITIVNOG ANTI-HBc BILJEGA NA TRAJNU ODGODU I PROCJENA UČESTALOSTI OKULTNE HEPATITIS B INFEKCIJE U POPULACIJI DOBROVOLJNIH DAVATELJA KRVI U ISTOČNOJ HRVATSKOJ

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U posljednje vrijeme uočen je porast prijenosa HBV infekcije putem krvi dobrovoljnih davatelja koji su pozitivni na anti-HBc biljeg, dok su u isto vrijeme ponovljeno negativni u serološkom testiranju na HBsAg biljeg i testiranju tehnikama umnožavanja nukleinskih kiselina pričem su korišteni najosjetljiviji dostupni testovi. Cilj ovoga istraživanja bio je ispitati utjecaj testiranja anti-HBc biljega provedenog u 2006. godini na trajno odbijanje dobrovoljnih davatelja krvi i procijeniti stopu okultne infekcije hepatitis B virusom u navedenoj populaciji nakon uvođenja obveznog molekularnog testiranja u razdoblju od 2013. do 2016. godine. U istraživanje je bilo uključeno više od 30.000 donacija pune krvi prikupljenih u razdoblju od 2005. do 2007. godine te više od 14.000 dobrovoljnih davatelja koji su donirali krv nakon uvođenja obveznog molekularnog testiranja u razdoblju od 2013. do 2016. godine među davateljima s područja istočne Hrvatske. Serološka testiranja HBsAg testom provedena su tijekom cijeloga razdoblja istraživanja, dok je anti-HBc test rađen samo tijekom 2006. godine. Kao dio algoritma potvrdnog testiranja svi pozitivni i nejasni rezultati HBsAg testiranja testirani su molekularnim testovima. U 2006. godini učestalost pozitivnih anti-HBc biljega među dobrovoljnim davateljima bila je 1,5% sa stopom 1:197, dok je učestalost pozitivnih HBsAg biljega od 2005. do 2007. godine iznosila 0,04%-0,1%. Izračunata stopa okultne infekcije hepatitis B virusom od 2013. do 2016. iznosila je 1:30.250. Isključivo na anti-HBc biljeg pozitivno je bilo 10/161 (12,4%) dobrovoljnih davatelja. Statistički gledano, testiranje na anti-HBc biljeg u 2006. godini u usporedbi s 2005. i 2007. godinom rezultiralo je većim brojem odbijenih dobrovoljnih davatelja u cijeloj Hrvatskoj. Strategija univerzalnog testiranja dobrovoljnih davatelja krvi na anti-HBc biljeg uz postojeći test na HBsAg biljeg i molekularni probir može predstavljati dodatnu mjeru za sprječavanje prijenosa HBV-a transfuzijom krvi i krvnim pripravcima.

Ključne riječi: *Krv, davatelji; Hepatitis B; Hepatitis B virus; Australijski antigen; Hrvatska*