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RESEARCH ARTICLE

Prevalence of Hepatitis B and C Virus Infections among Iraqi Patients Registered to Babylon Center for Inherited Blood Disorders

Dr. Najlaa B. Alawadi

Assistant professor and head of Department of Pathology, College of Medicine, Babylon University, Babylon, Iraq.

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Abstract

Aims: To assess the prevalence of hepatitis B virus (HBV) and hepatitis C virus (HCV) infections among Iraqi patients registered to Babylon Center for Inherited Blood Disorders (BCIBD).

Methods: The study included 1024 patients representing all patients registered to BCIBD by the date of 1^{st} July 2012. At the time of registration to the center and every six months later on, all patients are tested routinely for hepatitis B surface antigen (HBs Ag) and hepatitis C virus antibody (anti-HCV Ab). In this study, the results of these tests were reviewed and the prevalence of HBV and HCV infections was evaluated.

Results: 0.09% (1/1024) of the patients in the center were positive for HBs Ag and 11.72% (120/1024) of them were positive for anti-HCV Ab.

The prevalence of HBV infection is less than that in general population in Babylon. Routine and repeated HBV vaccinations might be the cause.

The prevalence of HCV infection is higher than that in general population in Babylon, however it is still less than that recorded in multi-transfused patients in other countries. Low prevalence of HCV infection in Babylonian general population might be the cause.

Conclusion: HBV vaccine proved effective in protecting multi-transfused patients from getting HBV infection. However; the absence of HCV vaccine until nowadays, calls for new and better HCV detection tests and viral inactivation methods in donated blood and blood products.

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Introduction

Regular transfusion of whole blood, blood components or clotting factors concentrates is the mainstay of treatment in patients with thalassemia and hemophilia. These transfusions have improved overall survival, although they carry a definite risk of infection with blood-borne viruses that can lead to complications contributing to the morbidity and mortality.

Transfusion transmitted hepatitis was first recognized in 1943, almost all patients received clotting factor concentrates before 1985 developed non-A non-B hepatitis (now recognized as HCV)⁽¹⁾.

Blood transfusion safety can be improved by reducing the pre-seroconversion window period when patients are highly infective but have neither symptoms nor detectable antigen or antibody concentrations. This is done by testing for anti-HBc Ab and nucleic acid amplification tests (NAT). Viral DNA (in HBV) and RNA (in HCV) detection tests have not been developed to be implemented in the blood screening laboratories because of high cost and complexity with the need for specialized facilities and training^(2,3,4). However, a routine nationwide NAT for HBV, HCV and HIV-1 of donated blood was implemented on July 1999 by Japanese Red Cross blood transfusion services⁽⁵⁾.

Furthermore, routine HBV vaccination of multiply transfused patients with post-vaccination checking for response (anti-HBs Ab > 10 IU/L) will definitely reduce the risk of acquiring HBV infection.

Methods

This is a cross sectional descriptive study including all Iraqi patients registered to Babylon Center for Inherited Blood Disorders (BCIBD) which is a specialized center established on 1997 in Alhilla city, center of Babylon governorate, middle of Iraq. It provides a specialized, facilitated and scientific care for patients with hemoglobinopathies (thalassemia, sickle cell anemia and sickle thalassemia) and inherited bleeding tendency disorders (factor deficiency diseases).

Until the 1st of July 2012, 1024 patients were registered to the center including 648 males and 376 females. All was taken in this study and classified into two major groups; hemoglobinopathy group and bleeding tendency group.

Hemoglobinopathy group included 735 patients, 422 males and 313 females. It consisted of 421 patients with thalassemia major, 219 patients with thalassemia intermedia, 15 patients with thalassemia minor, 63 patients with sickle-thalassemia and 17 patients with sickle cell anemia.

Bleeding tendency group included 289 patients, 231 males and 58 females. It consisted of 168 patients with factor 8 deficiency, 63 patients with factor 9 deficiency, 43 patients with vonWillibrand disease, 7 patients with factor 7 deficiency, 5 patients with factor 13 deficiency and 3 patients with factor 1 deficiency.

All patients in the center are tested routinely for hepatitis B surface antigen (HBs Ag) and anti-hepatitis C virus antibody (anti-HCV Ab) at the time of registration and every six months later on. In this study, the center's records of these tests were rechecked and reviewed.

The tests were carried out in the general health laboratory in Babylon where the patient's sera are sent. Samples are tested for HBs Ag and anti-HCV Ab using the enzyme linked immunosorbent assay (ELISA) test. Any positive result for anti-HCV Ab was retested by second generation recombinant immunoblot assay (RIBA) as a confirmatory test which was done in the Central Health Laboratory in Baghdad, the capital of Iraq.

The data were analyzed using Chi-square and significant p-value was <0.05.

Results

1024 patients were enrolled in this study. 735 of them were in hemoglobinopathy group with male:female ratio of 1.3:1 and age range from 10 months to 49 years, whereas 289 of them were in bleeding tendency group with male:female ratio of 4:1 and age range from 7 months to 54 years.

In hemoglobinopathy group, 0.14% (1/735) of them were positive for HBs Ag who was one male patient. 11.16% (82/735) of them were positive for anti-HCV Ab. From the anti-HCV Ab positive patients, 42.68% (35/82) were females and 57.32% (47/82) were males (non significant difference, p-value is 0.18). (Table 1)

In bleeding tendency group, all patients were HBs Ag negative while 13.15% (38/289) were anti-HCV Ab positive. From the anti-HCV Ab positive patients, 10.5% (4/38) were females and 89.5% (34/38) were males. The infected females represented 6.89% (4/58) of all females in this group, whereas infected males represented 14.71% (34/231) of all males in this group (a significant difference, p-value is <0.001). (Table 1)

89.2% (107/120) of HCV infections were acquired before July 2008 with average of 9.7 cases/year (from the foundation date of the center on 1997 to July 2008) compared to 10.8% (13/120) of infections acquired after July 2008 with average of 3.25 cases/year (a significant difference, p-value <0.01).

The group	Numbers			HBVs Ag +ve		Anti-HCV Ab +ve	
	Male	Female	Total	Number	%	Number	%
Hemoglobinopathy	422	313	735	1	0.14	82	11.16
Bleeding tendency	231	58	289	0		38	13.15
Total	653	371	1024	1	0.09	120	11.72

Table 1: Prevalence of HBs Ag and Anti-HCV Ab among hemoglobinopathy and bleeding tendency groups.

HBsAg : hepatitis B surface antigen, Anti-HCV: Anti-hepatitis C virus antibody, +ve: positive.

Discussion

Nowadays with the use of sensitive screening tests, the risk of transfusion-transmitted HBV is about 1 per 63,000 units of blood transfused, and HCV, about 1 per 125,000 units⁽⁶⁾. In low-income countries, the risk is even higher. Jayaraman et al. (2010)⁽⁷⁾ found that the risk of acquiring HBV was 4.3 per 1000 units transfused in sub-Saharan Africa, and HCV, 2.5 per 1000 units. This means 28,595 HBV and 16,625 HCV new infections every year. Prevalence of HBV infection:

In this study, the prevalence of HBV infection among patients registered to BCIBD was negligible (0.09%) which is even less than that in Babylonian general population (0.8%), healthy blood donors (0.47%) and high risk groups (1.17%) (*Abbas MA, Atallah MT, Hanan AG. National survey of viral hepatitis in Iraq during 2011. Annual statistics of Iraqi ministry of health: Feb 2012 - Internally published with restricted distribution to Iraqi health centers*). Surprisingly, the prevalence of HBV was high (32.3%) in multiply transfused leukemic patients in Baghdad (capital of Iraq, 100 Km to the north of Babylon)⁽⁸⁾.

The prevalence of HBV infection in my study is even lower than that in multiply transfused patients from adjacent countries and worldwide as the prevalence was 4.9% in Zahedan-Iran⁽⁹⁾, 1.5% in Shiraz-Iran⁽¹⁰⁾, 29% in Egypt⁽¹¹⁾, 52.9% in Tunisia⁽¹²⁾, 5% in Pakistan⁽¹³⁾, 1% in Malaysia⁽¹⁴⁾, 45% in India⁽¹⁵⁾ and 25% in Brazil⁽¹⁶⁾.

This low prevalence may be due to regular vaccination against HBV infection offered for all patients in the center at the time of registration in 3 doses (time zero, after one month and after 6 months) with regular booster doses later on (within 5-10 years). Anti-HBs Ab is routinely checked after completed vaccination course and the course is repeated in non responder patients (titer less than 10 IU/L). In Iraq, HBV vaccination was added to National Vaccination Program by the end of nineties of the last century, hence most Iraqis born after that date had been vaccinated at birth, but not those born before. During 2011, 88% of live births in Iraq were vaccinated at delivery with 1st dose HBV vaccine (*Abbas MA et al. National survey of viral hepatitis in Iraq during 2011. Annual statistics of Iraqi ministry of health: Feb 2012*).

The dependence of this study upon HBsAg solely for the diagnosis of HBV infection might have some role in the low prevalence rates. Singh et al.(2003)⁽¹⁷⁾ found positive HBs Ag in 5.7% of their thalassemic patients, while positive anti-HBc Ab was found in 20%, and HBV-DNA in 32% of the same patients group.

HBV can be transmitted even by HBsAg negative blood units when they are positive for anti-HBc Ab, HBV-DNA or both. Behzad et al.(2006)⁽¹⁸⁾ found that 6.5% of HBsAg negative healthy blood donors were anti-HBc Ab positive. Similar results were found by O'Brien et al.(2007)⁽¹⁹⁾ who concluded that anti-HBc Ab should be tested routinely on blood donor volunteers and positive units should be discarded. Prevalence of HCV infection:

The prevalence of HCV infection among patients registered to BCIBD was 11.72% which is higher than that in Babylonian general population (0.32%), healthy blood donors (0.17%) and high risk groups (0.8%). (Abbas MA et al. National survey of viral hepatitis in Iraq during 2011. Annual statistics of Iraqi ministry of health: Feb 2012). It is also higher than the results of Tawfeeq et al.(2013)⁽²⁰⁾ who found that the prevalence of HCV in healthy blood donors from Babylon was (0.29%). This high rate of infection is principally due to multiple blood and blood products transfusions in the absence of effective vaccine against HCV infection. The contaminated factor VIII used for treating hemophiliac patients could be responsible for disease acquisition as 66% of HIV-infected hemophiliacs in Baghdad were positive for anti-HCV Ab despite that 68% of them had no history of blood transfusion⁽²¹⁾.

Al-Kubaisy et al. $(2006)^{(22)}$ found high prevalence of HCV infection among thalassemic children in Baghdad's center as 67.3% of them were positive for anti-HCV Ab and 61.5% positive for HCV-RNA. Surprisingly low rates of HCV infection (3.4%) was found by Omar et al. $(2011)^{(8)}$ among multiply transfused leukemic patients in Baghdad.

In the present study, the majority of infections were acquired before July 2008. The economic sanctions against Saddam's regime before 2003 and bad security circumstances during American occupation between 2003 and 2008 caused a great shortage of the essential screening tests for viral infections in the Iraqi blood banks, so donated blood and blood products were given to patients without virology screen especially at emergencies. In spite of these periods of shortage in virology testing for donated blood, the infection rate in Babylon center isn't very high when compared to other centers in the nearby countries. This may be due to low prevalence of infection in the general population and healthy blood donors in Babylon. Also, most blood donors are regular donors who were surely tested during their previous blood donation visits.

The high prevalence of HCV infection in this study is still less than that recorded in multiply transfused patients from adjacent countries or worldwide. The prevalence was 29.6% in Zahedan-Iran⁽⁹⁾, 19% in Shiraz-Iran⁽¹⁰⁾, 40% in Egypt⁽¹¹⁾, 50% in Tunisia⁽¹²⁾, 43% in Pakistan⁽¹³⁾, 13% in Malaysia⁽¹⁴⁾, 17.5% in India⁽¹⁵⁾ and 46% in Brazil⁽¹⁶⁾. Early implementation of mandatory screening of donated blood for HBV and HCV in Argentina at 1993 might explain it's lower infection rates in multiply transfused patients (HBV is 0.2% and HCV is 9.3%)⁽²³⁾.

Higher HCV infection rates in Iran might be partially due to higher prevalence in general population of southeast $Iran^{(24)}$ (3.1% vs. 0.32% in Babylon).

Virucidal procedures:

Previously it was said that "It is probable that every vial of coagulation factor concentrate contained infective $HCV^{(25)}$. Modern concentrates have a greatly improved safety records arising from the implementation of virucidal procedures that are based on various methods of pasteurization, heating in lyophilized state at 80°C, vapor heating and addition of solvent/detergent⁽²⁶⁾. All methods can definitely decrease the risk of HBV and HCV infections. Treatment of infected patients:

In spite of availability of HBV and HCV treatment in the Gastroenterology and Liver Center in Babylon, no one of the infected patients in this study was treated. No reasonable cause could be found other than underestimation of the benefits of treatment by responsible doctors. Anti-viral treatment in those patients dose not differ from that of other patients, however, current treatment of HCV necessitates the use of ribavirin, which is associated with dose-dependent hemolysis, requiring adjustment of the transfusion protocol for thalassemia patients⁽²⁷⁾. Remote consequences:

From other point of view; legal, financial and public health consequences had been faced with transfusion-transmitted HCV in hemophiliac patients as compensation funds were allocated in some countries^(28,29).

Conclusion and recommendations

Despite that it is less than the recorded rates in adjacent countries, the prevalence of HCV infection among patients registered to BCIBD is still high compared to Babylonian general population. This fact calls for a critical look into the adoption of stricter donor selection criteria and implementation of more specific and sensitive HCV detection methods in Babylon including HCV-RNA detection tests. Anti-viral therapy should be offered for all patients with confirmed chronic hepatitis.

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