Frequency of blood-borne viral infections among leukemic patients in central Iraq

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ABSTRACT

الأهداف: تحديد مدى انتشار فيروس التهاب الكبد (ب)، وفيروس التهاب الكبد (ج)، والفيروس المُضخم للخلايا، وفيروس ايبشتاين بار، وفيروس نقص المناعة لدى مرضى سرطان الدم، بالإضافة إلى دراسة بعض الخواص الوبائية لهذا المرض من أجل معرفة كيفية رعاية المرضى في المستقبل.

الطريقة: أُجريت هذه الدراسة المقطعية في مستشفى الأطفال المركزي التعليمي ومستشفى المدينة الطبية، بغداد، العراق وذلك خلال الفترة من فبراير 2006م إلى يونيو 2008م. لقد تم جمع 641 عينة من مصل الدم (291 عينة من المجموعة المُصابة بسرطان الدم و350 عينة من مجوعة التحكم الغير مُصابة). وبعد ذلك تم عمل مسح مصلي عن وجود مؤشرات الفيروسات التالية: فيروس التهاب الكبد (ب)، وفيروس التهاب الكبد (ج)، والفيروس المُضخم للخلايا، وفيروس ايبشتاين بار، وفيروس نقص المناعة.

النتائج: أشارت نتائج الدراسة بأن هناك ارتفاعاً واضحاً في معدل انتشار المستضد السطحي لفيروس التهاب الكبد (ب) لدى مرضى سرطان الدم (32.3%) مقارنةً بمجموعة التحكم (2.3%)، وكانت نسبة انتشار الأجسام المضادة للمستضد السطحي لفيروس التهاب الكبد (ب) 29.9% في المجموعة المُصابة و20.6% في مجموعة التحكم. ولقد كان الفرق بين المجموعتين عالياً من الناحية الإحصائية. لقد لوحظ وجود ارتفاعا كبيراً في معدل الأجسام المضادة لفيروس التهاب الكبد (ج) لدى مرضى سرطان الدم(3.4%) وذلك بالمقارنة مع مجموعة التحكم (0.3%). وكان هناك ارتفاعاً واضحاً في معدل مؤشرات الفيروس المُضخم للخلايا والتي تتمثل في الغلوبين المناعي م والغلوبين المناعي ج لدى مرضى سرطان الدم، حيث كانت النسبة 96.2% و12% في المجموعة المُصابة، و91.6% و8% في مجموعة التحكم، كما كان هناك ارتفاعاً واضحاً في هذه المؤشرات الدالة على فيروس ايبشتاين بار لدى المرضى وكانت النسبة 88.3% و26.5% في المجموعة المُصابة، و75.1% و13.4% في مجموعة التحكم. لم تشير النتائج إلى إصابة المجموعتين بفيروس نقص المناعة من النوع 1و2.

خاتمة: أظهرت الدراسة أن الإصابة بفيروسات التهاب الكبد (ب)، والتهاب الكبد (ج)، والفيروس المُضخم للخلايا، وفيروس ايبشتاين بار كانت متفشية بين مرضى سرطان الدم وذلك عند مقارنتهم بالأصحاء. وقد ازداد معدل الإصابة بهذه الأمراض بزيادة عمر المرضى، بالإضافة إلى زيادة معدل الإصابة بهذه الأمراض بين المرضى الذكور عند المقارنة بالإناث.

Objectives: To determine the prevalence of hepatitis B virus (HBV), hepatitis C virus (HCV), cytomegalovirus (CMV), Epstein-Barr virus (EBV), and human immunodeficiency virus (HIV) and other epidemiological criteria among leukemic patients to establish basic knowledge for future leukemic patient's care.

Methods: This cross-sectional study was carried out between February 2006 and June 2008 in the Children's Central Teaching Hospital and Medical City Teaching Hospital in Baghdad, Iraq. A total of 641 blood samples (291 samples from leukemic patients and 350 samples from controls) were collected and the sera were tested for the presence of HBV, HCV, CMV, EBV, and HIV serological markers.

Results: A significantly higher prevalence of hepatitis B surface antigen (HBsAg) was detected among leukemic patients (32.3%) than controls (2.3%). The seroprevalence of anti-HBs was 29.9% among patients, and 20.6% among controls. This difference was also found to be statistically significant. A significantly higher prevalence of anti-HCV antibodies among leukemic patients (3.4%) than controls (0.3%) was also detected. A higher prevalence of IgG and IgM markers specific for CMV (96.2% and 12% for patients; 91.6% and 8% for controls), and for EBV (88.3% and 26.5% for patients; 75.1% and 13.4% for controls), were detected among leukemic patients than controls, while none of the patients and controls were positive for HIV I and II markers.

Conclusions: We conclude that HBV, HCV, CMV, and EBV infections are more prevalent among leukemic patients. There was an increase in the seropositivity rates of HCV, CMV, and EBV infections with increasing ages of leukemic patients. The male leukemic patients were more exposed to HBV, HCV, and EBV infections than females.

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Leukemias are a group of malignant disorders of the hematopoietic tissues characteristically associated with increased numbers of primitive white cells in the bone marrow. The cause of leukemia is unknown in most patients. Several etiological factors are associated with development of leukemias such as: ionizing radiation, cytotoxic drugs, retroviruses, immunological, and genetic factors.[1] There are many types of leukemia, and chronic lymphocytic leukemia (CLL) is the most common adult leukemia in the Western world. However, CLL is less common among people of African or Asian origin.[2] Acute leukemia is the most common childhood malignancy representing 30% of all childhood cancers under the age of 15 years, and 80% of these are acute lymphocytic leukemia (ALL).[3] In Iraq, CLL accounts for 7.6% of all leukemias with an incidence of 0.19/100000.[4] Although regular blood transfusions improve the overall survival of leukemic patients, it carries a definite risk of infection with blood-borne viruses, such as hepatitis B virus (HBV), hepatitis C virus (HCV), cytomegalovirus (CMV), Epstein-Barr virus (EBV), and human immunodeficiency virus (HIV) in the world. The problem is more serious in the developing countries with lower economic means due to the high rate of morbidity and mortality among immunocompromised patients, as well as immunocompetent recipients, such as leukemic patients. Multi-transfused patients in these countries are at high risk of these infections, and studies of infections in those patients can be a useful index for examining the blood safety filters in place.[5] In infections caused by these viral agents, each has their own epidemiological, clinical, and immunological characteristics, however, they share many features since all these viral agents are transmitted parentally, flourish in states of immunosuppression, and most of these infections are asymptomatic. In developed countries, the medical community and general public are becoming increasingly aware of transmissible transmitted infections concerning bacterial infections, parasitic infections, and other emerging pathogens, and this leads to the request for more information of the risk of these infections to prevent or limit their spread, particularly among multi-transfused patients, such as leukemic patients.[5-7] In developing countries, including the Middle East, the risk of transfusion-transmitted infections is still considerable.[5,8] In Iraq, there is a lack of comprehensive studies on the seroprevalence of all these blood-borne viral infections among leukemic patients. Therefore, this study was carried out to determine the prevalence of these viral infections, and other risk factors among Iraqi leukemic patients to establish basic knowledge for future leukemic patient care in Iraq.

Methods. This study was carried out in the Children's Central Teaching Hospital and Medical City Teaching Hospital in Baghdad, Iraq between February 2006 and June 2008. The total sample included in this study was 641 subjects, of which 291 were leukemic patients, and 350 were apparently healthy control subjects. All the control subjects were blood donors, and those attending primary health care centers for vaccination, as well as leukemic patients family. The diagnosis of acute and chronic leukemia was based on characterization of the leukemic cells, obtained from bone marrow and/or peripheral blood. The criteria established by the World Health Organization classification were considered for the diagnosis.[9] All patients were referred by their clinicians from several governorates in Iraq, and attending the Children's Central Teaching Hospital and Medical City Teaching Hospital in Baghdad, Iraq for further management. All the participants or their relatives gave written informed consent, and the ethical institutional approval was also obtained from the Scientific Research Committee of the College of Medicine, Al-Anbar University, Baghdad, Iraq. Concerning inclusion and exclusion criteria, we included all proven leukemia patients exposed to blood transfusions, and patients without a history of blood transfusions were excluded from this study.

Blood samples were collected from all leukemic patients, and control subjects and their sera were separated, and tested for the presence of hepatitis B surface antigen (HBsAg), hepatitis B surface antibody HB(sAb), hepatitis B core antibody (HBcAb)-immunoglobulin (Ig)M and IgG, hepatitis C virus antibody (HCVAb), cytomegalovirus antibody (CMVAb)-immunoglobulin (Ig) M and IgG, Epstien-Barr virus antibody (EBVAb)-IgM and IgG and human immuno-deficiency virus antibody (HIVAb)/ human immuno-deficiency virus antigen (HIV Ag) serological markers. Serum testing was carried out at the Central Public Health Laboratory/Viral Hepatitis Reference Center in Baghdad using an enzyme linked immuno-sorbent assay (ELISA) (BioElisa kit, Biokit, Barcelona, Spain), and an enzyme immuno-florescent assay (EIFA) (Biomeriuox kit, Biomerieux Ltd., Paris, France) according to the manufacture's instructions. To decrease or limit the false positive rate in HCV testing, all anti-HCV positive sera from both the study and control groups were tested again to confirm the presence of anti-HCV antibodies using confirmatory tests (Lia Tik HCV iii Kits, Organon-Teknika, Turnhout, Belgium), which is a third generation recombinant immunoblot assay (RIBA 111) that detects antibodies reactivities to

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several HCV antigens, and this procedure will prevent or limit the false positive rate in the anti-HCV antibody test. A questionnaire form was completed either by direct interview with the patients or by their family or their relatives, and the data requested concentrated mainly on age, gender, occupation of the patient, or his family, residence, history of chemotherapy, history of frequent hospitalizations, frequent injections, history of blood transfusions, and surgery, in addition to the results of serological tests obtained.

Statistical analysis was carried out using Statistical Package for Social Sciences version 17.O (SPSS Inc., Chicago, IL, USA) for analyzing the data. Chi-square test with Yates correction was also used to analyze categorical variables with 95% confidence intervals. A p value ≤0.05 was considered statistically significant.

Results. Out of the leukemic patients, there were 190 (65.3%) males and 101 (34.7%) females with a female to male ratio of 0.5:1, and their mean age was 26.4 ± 9.2 years with age ranging from 1-72 years. Of the 291 leukemic patients, 193 (66.3%) were below 15 years old, and 98 (33.7%) were adults (more than 15 years old). Within the leukemic patients, there were 198 (68.1%) patients with ALL, 18 (6.2%) with CLL, 33 (11.3%) with acute myeloid leukemia (AML), and 42 (14.4%) patients with chronic lymphocytic leukemia (CML). A significantly higher prevalence of HBsAg was detected among leukemic patients compared with healthy control subjects (p=0.0001) (**Table 1**). As shown in this table, the seroprevalence of anti-HBs was also found to be significantly higher among leukemic patients than in the healthy control subjects (p=0.0001). Significantly higher rates of anti-HBc IgG and IgM, anti-HCV antibodies, IgG and IgM specific for CMV and for EBV were also observed among leukemic patients than in the controls, while none of the patients and controls were positive for serological markers of HIV I and II, as well as human T-cell lymphotropic virus (HTLV) I and II. As shown in **Table 2**, the prevalence of HBsAg, anti-HBs, anti-HBc IgG, and anti-HBc IgM were significantly higher among young leukemic patients than in adults, while there was a significantly higher prevalence of anti-HCV among adult leukemic patients than in the children. This table also shows a significantly higher total prevalence of both IgG and IgM specific for CMV and EBV among adult leukemic patients than in children. The overall prevalence of CMV IgG and IgM

Table 1 - Seroprevalence of HBV, HCV, CMV, and EBV markers among leukemic patients and controls.

Markers	Leukemic n= 291	Controls n=350	*P*-value
	n (%)		
HBsAg	94 (32.3)	8 (2.3)	0.0001
Anti-HBs	87 (29.9)	72 (20.6)	0.0001
Anti-HBc IgG	66 (22.7)	24 (6.9)	0.0002
Anti-HBc IgM	51 (17.5)	13 (3.7)	0.0017
Anti-HCV	10 (3.4)	1 (0.3)	0.0001
Anti-CMV IgG	280 (96.2)	320 (91.4)	0.0000
Anti-CMV IgM	35 (12.0)	28 (8.0)	0.0004
Anti-EBV IgG	257 (88.3)	263 (75.1)	0.0000
Anti-EBV IgM	77 (26.5)	47 (13.4)	0.0008

HBV - hepatitis B virus, HCV - hepatitis B virus, CMV - cytomegalovirus, EBV - Epstein-Barr virus, HBsAg - hepatitis B surface antigen, anti-HBs - antibody to hepatitis B surface antigen, anti-HBc IgM and IgG - antibody to HB core immunoglobulin (IgM) and IgG, anti-HCV - antibody to hepatitis C virus, anti-CMV IgM and IgG - antibody to cytomegalovirus IgM and IgG, anti-EBV IgM and IgG - antibody to Epstein-Barr virus IgM and IgG

Table 2 - Seroprevalence of HBV, HCV, CMV, and EBV markers among leukemic patients according to age.

Markers	Childhood ≤15 n=193	Adults >15 n=98	Total N=291	*P*-value
	n (%)			
HBs Ag	89 (46.1)	5 (5.1)	**87 (29.9)**	0.0026
Anti-HBs	71 (36.8)	16 (17.8)	**87 (29.9)**	0.0000
Anti-HBc IgG	59 (30.6)	7 (7.8)	**66 (22.7)**	0.0003
Anti-HBc IgM	46 (23.8)	5 (5.1)	**94 (32.3)**	0.0035
Anti-HCV	3 (1.5)	7 (7.8)	**10 (3.4)**	0.0014
Anti-CMV IgG	183 (94.6)	97 (99.0)	**280 (96.2)**	0.0029
Anti-CMV IgM	11 (5.7)	24 (24.5)	**35 (12.0)**	0.0005
Anti-EBV IgG	166 (86.0)	91 (92.9)	**257 (88.3)**	0.0005
Anti-EBV IgM	42 (21.8)	35 (35.7)	**77 (26.5)**	0.0019

HBV - hepatitis B virus, HCV - hepatitis B virus, CMV - cytomegalovirus, EBV - Epstein-Barr virus, HBsAg - hepatitis B surface antigen, anti-HBs - antibody to hepatitis B surface antigen, anti-HBc IgM and IgG - antibody to HB core immunoglobulin (IgM) and IgG, anti-HCV - antibody to hepatitis C virus, anti-CMV IgM and IgG - antibody to cytomegalovirus IgM and IgG, anti-EBV IgM and IgG - antibody to Epstein-Barr virus IgM and IgG

Table 3 - Seroprevalence of HBV, HCV, CMV, and EBV markers among leukemic patients according to gender.

Markers	Male n=190	Female n=101	Total N=291	*P*-value
	n (%)			
HBs Ag	71 (37.4)	23 (22.8)	**94 (32.3)**	0.0006
Anti-HBs	68 (35.8)	19 (18.8)	**87 (29.9)**	0.0022
Anti-HBc IgG	46 (24.2)	20 (19.8)	**66 (22.7)**	>0.5
Anti-HBc IgM	35 (18.4)	16 (15.8)	**51 (17.5)**	>0.5
Anti-HCV	8 (4.2)	2 (2.0)	**10 (3.4)**	0.0027
Anti-CMV IgG	181 (95.3)	99 (98.0)	**280 (96.2)**	0.0003
Anti-CMV IgM	13 (6.8)	22 (21.8)	**35 (12.0)**	0.0001
Anti-EBV IgG	179 (94.2)	78 (77.2)	**257 (88.3)**	0.0016
Anti-EBV IgM	56 (29.5)	21 (20.8)	**77 (26.5)**	0.0035

HBV - hepatitis B virus, HCV - hepatitis B virus, CMV - cytomegalovirus, EBV - Epstein-Barr virus, HBsAg - hepatitis B surface antigen, anti-HBs - antibody to hepatitis B surface antigen, anti-HBc IgM and IgG - antibody to HB core immunoglobulin IgM and IgG, anti-HCV - antibody to hepatitis C virus, anti-CMV IgM and IgG - antibody to cytomegalovirus IgM and IgG, anti-EBV IgM and IgG - antibody to Epstein-Barr virus IgM and IgG

Table 4 - Seroprevalence of HBV, HCV, CMV, and EBV markers among leukemic patients according to types of leukemia.

Markers	ALL n=198	CLL n=18	AML n=33	CML n=42	Total N=291	*P*-value
			n (%)			
HBs Ag	81 (40.9)	0 (0.0)	9 (27.3)	4 (9.5)	**94 (32.3)**	0.0001
Anti-HBs	48 (24.2)	13 (72.2)	12 (36.4)	14 (33.3)	**87 (29.9)**	0.0002
Anti-HBc IgG	60 (30.3)	0 (0.0)	5 (15.1)	1 (2.4)	**66 (22.7)**	0.0001
Anti-HBc IgM	42 (21.2)	1 (5.5)	8 (24.2)	0 (0.0)	**51 (17.5)**	0.0027
Anti-HCV	10 (5.1)	0 (0.0)	0 (0.0)	0 (0.0)	**10 (3.4)**	0.0049
Anti-CMV IgG	193 (97.5)	17 (94.4)	31 (93.9)	39 (92.8)	**280 (96.2)**	0.0013
Anti-CMV IgM	29 (14.6)	1 (5.6)	2 (6.1)	3 (7.1)	**35 (12.0)**	0.0003
Anti-EBV IgG	179 (90.4)	15 (83.3)	29 (87.9)	34 (81.0)	**257 (88.3)**	0.0015
Anti-EBV IgM	58 (29.3)	4 (22.2)	7 (21.2)	8 (19.0)	**77 (26.5)**	0.0007

HBV - hepatitis B virus, HCV - hepatitis B virus, CMV - cytomegalovirus, EBV - Epstein-Barr virus, ALL - acute lymphoblastic leukemia, CLL - chronic lymphoblastic leukemia, AML - acute myeloid leukemia, CML - chronic myeloid leukemia HBsAg - hepatitis B surface antigen, anti-HBs - antibody to hepatitis B surface antigen, anti-HBc IgM and IgG - antibody to HB core immunoglobulin (IgM) and IgG, anti-HCV - antibody to hepatitis C virus, anti-CMV IgM and IgG - antibody to cytomegalovirus IgM and IgG, anti-EBV IgM and IgG - antibody to Epstein-Barr virus IgM and IgG

antibodies was also significantly higher among adult leukemic patients than in the children. **Table 3** shows significant between gender differences in the positivity rates of HBsAg, and anti-HBs, with non-significant between gender differences for anti-HBc IgG and IgM. A significantly higher rate of anti-HCV was also detected among male leukemics than females. This table also shows a significantly higher prevalence of anti-EBV IgG and IgM markers in male leukemic patients than in females, and a significantly higher total prevalence of IgG and IgM specific for CMV among female leukemic patients than males. **Table 4** shows a significantly higher prevalence of HBsAg among patients with ALL than in patients with other types of leukemia, while the prevalence of anti-HBs was higher among patients with CLL than in other types, and this difference was also of statistically significant. The prevalence of anti-HBc IgG and anti-HBc IgM was significantly higher among patients with ALL than other types. It was also found that all positive anti-HCV cases were from patients with ALL (5.1%). The overall prevalence of antibodies specific for CMV and EBV was also found to be significantly higher among patients with ALL than in other types.

Discussion. The present study revealed a high risk of blood-borne viral infections among Iraqi leukemic patients, and may represent a serious economic and public health problem in the community. Regarding HBV infection, our results show very high prevalence of HBsAg (32.3%) among leukemic patients comparing with normal healthy control subjects (2.3%). In the last decade, there is a marked decline in the prevalence of HBsAg among Iraqi normal blood donors and the normal population (<2%),[10] which reflects the awareness of the people and the public of the serious impact of HBV infection on the community, as well as the good standard of hygiene, vaccination, and introducing compulsory screening tests for HBsAg among blood donors. Our findings are higher than that reported by Al-Hilli and Ghadhban,[11] where the prevalence of HBsAg was 10% among multi-transfused patients, and 1.6% among blood donors. It was also higher than rates previously reported among patients with different blood disorders in different regions of Iraq.[12-15] Comparing reports from developed countries, which enjoy a high standard of hygiene, our findings were higher.[16-20] However, our results were lower than that reported by Kocaba et al,[21] who reported a 47.4% prevalence of Turkish children with cancer (acute leukemia, lymphoma, and solid tumors), with 20% of child control subjects positive for HBsAg. These data reflect that the association between HBV infection and risk of leukemia is controversial, and there are variations in the prevalence of HBV infection among leukemic patients from one country to another, and also variations among different provinces within the same country. The higher prevalence of HBsAg among leukemic patients might be explained by the increased exposure to the risk factors for HBV, such as repeated hospitalizations, frequent injections, frequent blood withdrawal for laboratory tests, and may be also due to multifactorial impairments in cellular and humeral immunological integrity in leukemia.[22] The prevalence of anti-HCV among leukemic patients in this study was 3.4%, which is less compared to other reports from different regions in our country.[11,13-15,23] However, it is in line with a study conducted in the North of Iraq, where the prevalence of anti-HCV antibodies among thalassemic patients was 2.4%.[24] This prevalence is lower when compared to reports from different countries. In Turkey, Kocaba et al[21] found that 5.8% of Turkish children with acute leukemia and lymphoma were positive for anti-HCV antibodies and in Brazil, a high prevalence of HCV

infection (46.8%) was detected in a population of multi-transfused patients,[25] and in Malaysia this rate was 22.3%,[26] while in Japan it was 7.3%,[19] and in Egypt, it was 4.2%.[27] Therefore, data on an association between HCV infection and risk of leukemia remain controversial. While some workers reported a positive correlation,[28-31] others found none.[32,33] Our findings are in agreement with the first group. The high rate of HCV infection among leukemic patients may be due to the fact that patients are immunocompromised, increasing their susceptibility to this infection, and this may reflect a possible contribution of other etiological factors (environmental, genetic, and the effect of multiple exposure to HCV to neoplastic transformation).[34,35]

The detection of a high prevalence of CMV antibodies among leukemic patients and apparently healthy Iraqi people indicates that CMV infection is endemic in our country. This finding is similar to that reported by Alizi and Omer,[36] who found that 99.1% of the Iraqi immuno-compromised patients were positive for anti-CMV IgG, and 8.4% for IgM. In Egypt, Loutfy et al[37] also found a high seroprevalence of CMV antibodies in both leukemic children (100%) and their controls (100%). This supports the suggestion of CMV reactivation particularly among immunocompromised patients including leukemic patients. Our results show that there are at least 3 factors that may play role in active CMV infection among immunocompromised patients; first receiving large amount of blood ensuring transfer of viable cells latently infected with CMV. The second factor may be the course of immuno-suppressive therapy in different doses depending on their disease. Lastly, this variation may be due to the pathogenesis of their diseases.[38] In the present study, none of the study group and control subjects were positive for HIV serological markers. Similar findings have been reported in other developing countries,[26,35,39] meanwhile, researchers reported a high rate of HIV infection among multi-transfused patients.[20,40] This finding may indicate that Iraq is considered an area of low prevalence of HIV/AIDS (<0.01%) among the Iraqi population and blood donors.[41] Concerning EBV infection, this infection was more prevalent among patients with leukemia than controls. Similar findings have been also reported previously by Al-khalidi,[42] who found a significantly higher prevalence of EBV IgG and IgM among leukemic patients (86.81% and 37.2%) than in controls (77.6% and 25%). Our results agree with other studies,[37,43] and may reflect the pattern of past infection, silent, and persistent EBV infection. The immunosuppression state caused by therapy, and blood transfusion, which may be contaminated with EBV infected B-lymphocytes, in addition to the silent EBV infection, all these evidence reflects reactivation of EBV.[44]

The trend of these blood-borne viral infections varies with the age of the patients with leukemia. The rate of HBV infection was higher among young leukemic patients than adults, and in contrast to HCV, EBV, and CMV infections. Regarding HBV infection, our findings agree with previous reports.[13,15] Okan et al[45] found no differences in the prevalence of HBV infection in relation to the age of the patients. Our findings may be because most of the children are active, have low health education, and more exposed to accidental needlestick injuries. It is well known that a minute amount of HBV particles from a needle stick contamination can cause infection due to the high concentration of these particles, in addition to high stability to heat and other conditions compared with HCV. The seropositivity rate of anti-HCV in leukemic patients was found to be higher in adult leukemic patients than children. Several serological studies have revealed an increasing rate of HCV infection with increasing age among patients with hematological disorders in different regions of Iraq.[13,46] In Italy, Bianco et al[31] and Maso et al,[32] also found an increase in the seropositivity rate of HCV infection with increasing age in both cases and control subjects. Our findings may be due to the fact that the adult leukemics are exposed more frequently to risk factors to HCV infection during their lives (repeated hospitalization, operations, frequent injections, and blood transfusions), in addition to that, lacking or inadequate use of more sensitive screening tests for detection of anti-HCV antibodies from blood donors introduced in our country in 1995. Concerning EBV infection, our findings are in line with a study conducted in Iraq and Egypt, where the prevalence of EBV infection increased with age.[37,42] This finding could be due to multiple exposure to EBV infection, and most of the adult patients who received blood transfusion have antibodies to EBV. Our results showed higher prevalence of anti-CMV IgG and IgM antibodies among adult leukemic patients than children, and this finding is in agreement with a study conducted in Egypt by Loutfy et al.[42,47] Re-infection with CMV or reactivation CMV infection could explain the higher seroprevalence of anti-CMV antibodies with increasing age of leukemic patients.[48]

The results also showed that leukemic males were more infected by HBV, HCV, and EBV than leukemic females, and this finding is in contrast to CMV infection, where the rate was more prevalent among leukemic females. Concerning HBV infection, our findings are in agreement with that reported by Al-Hilli and Ghadhban,[11] although other workers reported increased prevalence of HBV infection in female leukemic patients.[13,24] The prevalence of HCV infection was also significantly higher in male leukemics than females. This finding is in agreement to that reported

in different provinces of Iraq,[11,13,23] and in contrast to that reported by Abdel-Kadir et al.[24] With regard to EBV infection, our findings are similar to those reported by Al-Khalidi,[42] and in contrast to that reported by Loutfy et al.[37] All these findings indicate that HBV, EBV, and HCV infections were found to be more common among male leukemics, which could be explained by the increased rate of exposure to HBV, HCV, and EBV. Occupational, travel, social, and life-style differences that are well known to be more identified with males may contribute to the higher exposure rates among the males. On the other hand, the prevalence of CMV infection was found to be higher in female leukemics than males. This finding is in agreement with a reports by Loutfy et al,[37] who found that both genders were equally exposed to CMV infection. Reactivation of the CMV during pregnancy together with the fact that females are more in contact with infants and children than males, may account for the significantly higher prevalence of CMV infection in females than males.[48] Within the types of leukemia, our results revealed a significantly higher prevalence of HBsAg, anti-HCV, anti-CMV, and anti-EBV among patients with ALL than other types. In contrast to our study, Bianco et al,[31] detected a higher prevalence of anti-HCV antibodies among Italian patients with CML (12.2%) followed in order by CLL (9%), AML (7.9%), and ALL (7.6%). The groups of patients in this study were not, however, large enough to allow these differences to be statistically significant.

One of the limitations of the study was the absence of genomic confirmation of HCV using a polymerase chain reaction test.

From the results of the present study, we can conclude that HBV, HCV, CMV, and EBV infections are most prevalent among leukemic patients, while none of the study group and control subjects were positive for HIV serological markers. There is a positive correlation in the seropositivity rates of HCV, CMV, and EBV infections in leukemic patients with increasing age. The male leukemic patients are exposed more frequently to HBV, HCV, and EBV than females, and this is in contrast to CMV infection. The prevalence of HBV, HCV, CMV, and EBV infections were more common among patients with ALL than other types, however, our data are not sufficient to draw conclusions concerning an association between these viral infections and risk of leukemias, as the group of patients in this study are not large enough to allow this association. Therefore, further studies with a larger population of patients with leukemias are needed to confirm the possibility of such association. The high prevalence of HBV and other viral infections in leukemic patients points to a high epidemiological risk of hemo-replacement therapy, unsatisfactory quality of donor blood testing, and necessity of updating methods of donor infection detection. To lower the risk of these viral infections in patients with leukemia, it is necessary to perform available vaccine prophylaxis of viral infections before initiation of chemotherapy. Implementation of more advanced serological techniques in pre-donation screening program is necessary to improve the safety of blood and blood products testing from the risk of transfusion-transmitted viral infections in these particular diseases and in general.

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