Patients with Childhood Leukemia are at High Risk for Transfusion-Transmitted HBV and HCV Infections

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ABSTRACT:

BACKGROUND:

This work presents estimation to the number of hepatitis B virus (HBV) and hepatitis C virus (HCV) infections among polytransfused leukemic children, who received chemotherapy.

METHODS:

A total of 88 serum specimens were collected from children with leukemia aged between 1-12 years (60 males and 28 females), attending Al-Mansoor Teaching Hospital, seen during the period from January to October 2004 to determine if the patients with childhood leukemia are at high risk for transfusion-transmitted HBV and HCV infections. Enzyme linked immunosorbent assay (ELISA) test was used to determined infected and non infected individuals.

RESULTS:

Out of the 88 children studied, Hbs Ag was detected in 18 (20.45%) including 12 (66.6%) males and 6 (33.3%) females, whereas anti HCV was detected only in 4 (4.54%) children including 3 (75%) males and 1 (25%) female. The peak prevalence of HBV infection was recorded in children of age 9-12 years and reached (23.33%) while in HCV the peak prevalence was in age group (6-9), being (66.6).

CONCLUSION:

In this study, the prevalence of anti HCV and Hbs Ag were high in patients who were treated for children leukemia. The high incidence of hepatitis infections was recorded in polytransfused leukemic children.

KEY WARDS: HBV, HCV, Leukemia, Children

INTRODUCTION:

Hepatitis B and C viral infections are the most common causes of chronic liver disease [1]. It is estimated that there are over 350 million of HBV carriers and 170 million of HCV world wide [2]. Patients treated for a pediatric malignancy are at high risk for parentrally transmitted viral hepatitis [3] [4].

Blood product transfusions are the major risk factors [5]. Moreover, when compared with immunocomponent patients, the immunodepression caused by chemotherapy increases the chronicity rate of viral hepatitis [4].During the last two decades, screening blood donors for the HBV has resulted in a remarkable reduction of post transfusion B-virus hepatitis, thus, non-A, non-B hepatitis has become the major form of parentrrally transmitted hepatitis [6] [7]. Before the discovery of the HCV and the implementation of anti-HCV tests for the screening of blood donors, patients with hematologic malignancies were at a very high risk of HCV infection, due to the large transfusional support they often needed and to the immunodeficiency status caused by the underlying disease and by chemotherapy [8]. At that time, about (70%) to (80%) of children with acute leukemia were found to have a persistent elevation of transaminase enzyme level with liver histologic lesions suggestive of chronic viral hepatitis that early Iraqi studies, were related to hepatitis B virus infection in about half of the children, the remaining being cases of non-A, non-B hepatitis [8]. More recently, several studies based on the detection of HCV markers in serum, mainly anti-HCV by ELISA, have reported variable prevalence of positive HCV serology in this clinical setting, in association with a wide spectrum of liver involvement [9] [10]. The aim of the study is to determine the prevalence of hepatitis B and C among polytransfused leukemic children on chemotherapy.

PATIENTS AND METHODS:

A prospective study of 88 sera of pediatric patients who had began chemotherapy treatment for malignancy were included in this study aged from (1-12) Years attending to Al-Mansoor Teaching hospital (60 males and 28 females), seen during the period from January to October 2004. The sera of all patients were analyzed for antibodies to HBV and HCV infections using ELISA following the manufactures instructions, for HBV

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(Biotest ELISA Hbs Ag (D-63303 Dreleich-Germany)) and (VIDAS Hbc IgM and IgG, BioMerieux) for the determination of anti-hepatitis B virus core antigen IgM and IgG (anti-Hbc IgM and IgG), while for HCV antibodies by using, the third generation of ELISA test (Bioelisa Kits (Biokits S.A. 08186 Lissa, Spain)). To define the specifity of the results obtained by ELISA, all HCV positive sera were also investigated by recombinant immunoblot assay (RIBA), according to the manufactures instructions (Microgen, Gmb, Germany), sera showing only a band or at least two bands were considered undetermined or positive, respectively.

A questionnaire was arranged for this purpose regarding age, sex, duration of the disease and frequency of blood transfusion.

RESULTS:

Of the 88 serum specimens of study group, Hbs Ag was found in 18 (20.45%) patients, 12 (66.66%) in Males and 6 (33.33%) in females (table 1).

Out of 18 sera with HBsAg positive only 2 (11.11%) patients were Hbc IgM positive while 16 (88.88%) were positive for Hbc IgG. Both anti-HCV antibodies and RIBA were positive in 4 (4.54%) patients, 3 (75%) were males and 1 (25%) was female. The highest rate of HBV infection was in males of age group (4-6) and (10- 12) years being (23.33%) and (36.84%), while the highest rate of HCV infection was in males of age group (7-9), being (66.66%). HbsAg and anti-HCV prevalence seemed to be increased with number of blood transfusion, 8 (44.44%) patients for HBV and 3 (75%) patients with positive for HCV infection had previously received blood transfusions (5-6) time/year for HCV infection and (3-4) times/year for HBV infection (figure 1). Regarding the effect of chemotherapy doses on viral marker, the highest rate was in high doses of chemotherapy, 8 (44%) for HBV and 2 (50%) for HCV (figure 2). Concerning the distribution of HBV and HCV according to different governorates, the peak morbidity of positive viral marker was recorded among leukemia patients in Baghdad City (33.3%) for HBV infection and (50%) for HCV infection (figure3).

Table 1: Prevalence of Hbs Ag and anti-HCV among leukemic children with different age groups .

Age years	No of cases	HBV +ve	%	♂	%	♀	%	HCV +ve	%	♂	%	♀	%
1-3	15	1	6.66	-	-	1	100	-	-	-	-	-	-
4-6	30	7	23.33	3	42.8	4	57.14	-	-	-	-	-	-
7-9	24	3	12.5	3	100	-	100	3	12.5	2	66.6	1	33.3
10-12	19	7	36.84	6	85.7	1	14.28	1	5.26	1	100	-	-
Total	88	18	20.45	12	66.6	6	33.33	4	4.54	3	75	1	25
♂: Males ♀: Females +ve: Positive													

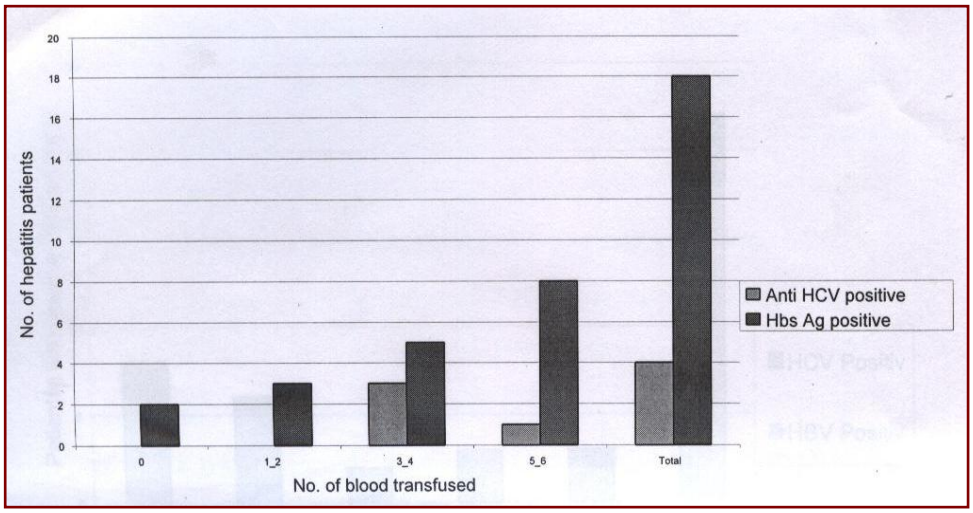

Figure (1): Prevalence of Hbs Ag and anti-HCV among leukemia children according to the number of blood compounds transfused .

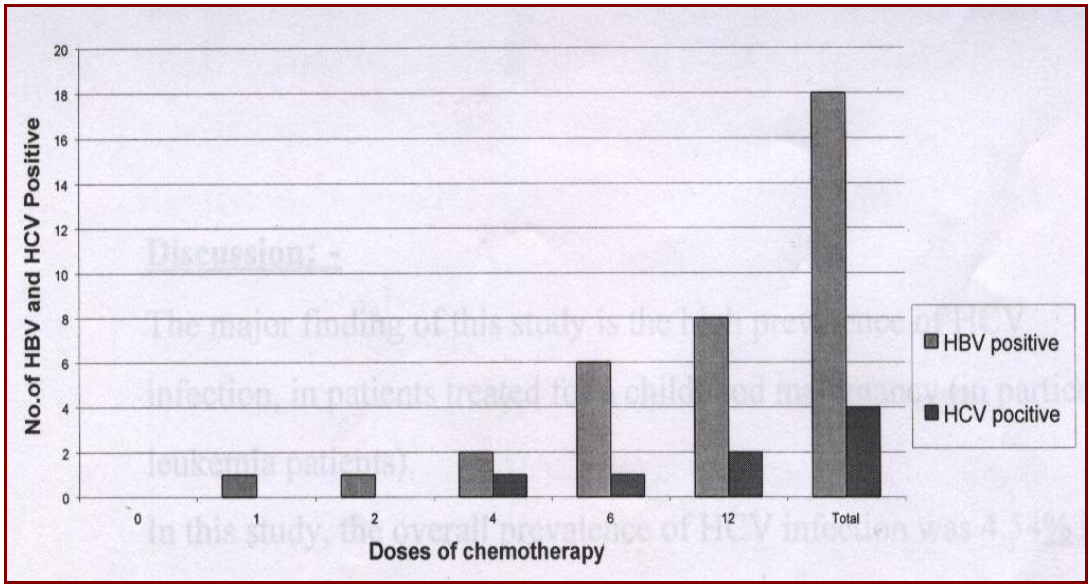

Figure (2): Prevalence of Hbs Ag and anti-HCV among leukemia children according to the number of chemotherapy doses

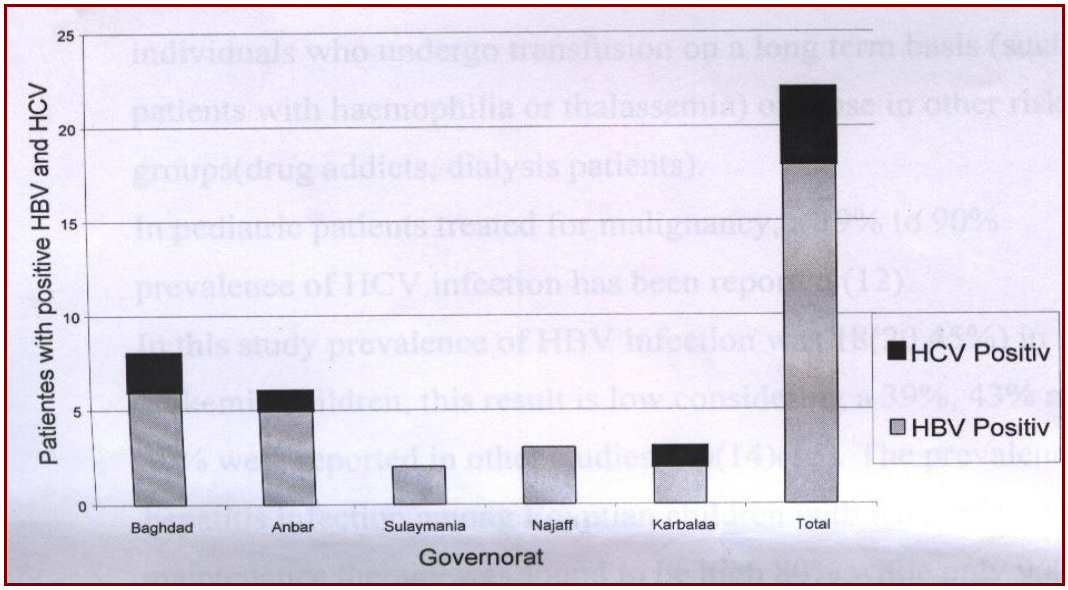

Figure (3): Prevalence of Hbs Ag and anti-HCV among patient with childhood leukemia according to different governorates

DISCUSSION:

The major finding of this study is the high prevalence of anti HCV in patients treated for a childhood malignancy (in particular, leukemic patients). The overall prevalence of HCV infection was (4.54%) in a group of patients that was receiving chemotherapy during the treatment of pediatric leukemia.

This figure is high considering a (0.36%) prevalence of HCV infection among Italian children [11], but it is relatively low considering other individuals who undergo transfusion on a long term basis (such as patients with hemophilia or thalassemia) or those in other risk groups (drugs addicts and dialysis patients)

[12]. In pediatric patients treated for malignancy, a (19%) to (40%) prevalence of HCV infection has been reported [12]. In this study prevalence of HBsAg was 18 (20.45%) in leukemia children, this result is low considering a (39%, 43% and 30% were reported in other studies [13] [14] [15]. The prevalence of hepatitis infection among Egyptian children with leukemia under maintenance therapy was found to be high (80%) while only (9.8%) Saudi children had evidence of exposure to HBV [16]. The common prevalence of HBV and HCV infection between leukemia children results from higher exposure to risk factors for hepatitis infection (more frequent blood- product transfusion [8]. The finding of this study revealed that there was an increased incidence of HCV and HBV infection with number of transfusion, (44.44%) for children with HBV infection who have transfused blood from (5-6) times/ year, while in HCV infection (75%) for leukemic children who have transfused blood from (3-4) times/ year. The rate of HCV infection in another study was (6.8%) among those with (25-99) blood transfusion compared with (19.4%) among those with 100 or more blood transfusion [17], while in another study transfusion-acquired hepatitis (28%) in childhood acquired leukemia [18]. Transfusion of unscreened blood for anti –HC antibody is of the major causes of higher sero prevalence of HCV among patients [19].

CONCLUSION:

The finding of this study revealed that there was an increased incidence of anti HCV and HBsAg with numbers of chemotherapy doses, 8 (44.44%) for children with HBV infection who have received 12 doses of chemotherapy, while in HCV infection 2 (50%) for leukemic children who have received chemotherapy for 12 doses. Antimetabolite chemotherapy exposure was associated with early progression of fibrosis [20].

REFERENCE:

1. Serlok, S. and Dooley, J.; Viral hepatitis is of the liver and biliary system. Black well scientific publication, 1997: 17, 265-302.
2. Satoshi, O.; Fuji, M; Ku, Y.; Yoon, S. and Hotta, H.; Comparative sequence analysis of the core protein and its frameshift product. The F protein, of hepatitis C virus subtype 1b strains obtained from patients with and without hepatocellular carcinoma; Am. Soc. For Micr.; 2002; 40; 10: 3625-3627.
3. Armitigo, J.; Burns, C. and Kent, T.; Liver disease complicating the management of acute leukemia during remission; Cancer; 1978; 41; 41: 737.
4. Locasciulli, A.: Albert, A.; Rossetti, F. and Masera, G.; Acute and chronic hepatitis in childhood leukemia: A multicentric study from the Italian pediatric cooperative group for therapy of acute leukemia; Med. Pediatr. Oncol; 1985: 13; 203.
5. Hetherington, M. and Buchanam, G.: Elivated serum transaminase values during therapy for acute lymphoblastic leukemia correlated with prior blood transfusions; 1988; Cancer; 62: 1614.
6. Colombo, M.; Oldani, S.; Donato, M.; Borzio, M.; Santese, R.: Roffi, L.: Vigano, P.; Cargnel, A.; A multicenter prospective study of posttransfussion hepatitis in main. Hepatology; 1978; 7: 709.
7. Rossetti, F.; Messina, C; Pillon, M. and Zanesco, L.; Liver disease and childhood leukemia; 1991; Riv. Ital Pediatr.; 17: 16.
8. Locasciulli, A.; Albert, A.; Barbieri, R.; Realdi, G.; Uderzo, C.; Pormann, B. and Vergani, B.; Histologic evidence of hepatitis B virus infection with negative serology in children with acute leukemia who develop chronic liver disease; 1982; Lancet; 1: 361.
9. Arico, M.; Maggiore, G.; Silni, F.; Bono, F.; Vigano, C.;Cernio, A. and Mondelli, M.; Hepatitis C virus infection in children treated for acute lymphoblastic leukemia; 1994; Blood; 84: 2919.
10. Frikhoven, N., Wiesneth, M.; Jienta, C.;Hertenstein, B and Bainchi, L.; Hepatitis C virus infection is a risk factor for liver failure from venoocclusive disease after bone marrow transplantation. 1998: 83.
11. Romano, L.; Azara, A. and Zanetti, A.; Low prevalence of anti-HCV antibody among Italian children. Blood, 1994; 22: 350.
12. Locasciulli, A.; Cavalletto, D.; Pontisso, P; Cavalletto, L; Scovena, E. and Albert, A; Hepatitis virus C serum markers and liver disease in children with leukemia during and after chemotherapy; 1993; Blood; 82: 2564.
13. Meral, A; Seviner, B. and Gunay, U.; Efficacy of immunization against hepatitis B virus infection in children with cancer; 2000; J. Clin. Oncol.: 18:3273-9.

14. Yetgin, S.; Tunc, BG.; Koc, A. and Canara, G.; Two booster dose hepatitis B virus vaccination in patients with leukemia; 2001; Leuk. Res. : 25: 647-9.

15. Somjee, S.; Pai, S.; Kelkar, R and Advani, S.; Hepatitis B Vaccination in children with acute lymphoblastic leukemia; results of un intensified immunization schedule; 1999; Leuk. Res.; 23 : 365-7.

16. Meir, H.: Balawi, I.; Nayel, H.; El-Karaksy, H. and El- Hadad, A.; Hepatic dysfunction in children with acute lymphoblastic leukemia in remission: relation to hepatitis infection; 2001; Med. Pediatr. Oncol; 36: 469-73.

17. Lopez, J; Cacelas, J.; Ramos, P.; Ordizola, J. and Navrro, J.; Post transfusion hepatitis after induction chemotherapy in acute non lymphoblast leukemia: implications for long-term management and outcome; 1995; Transfusion; 35: 313.

18. Leung, W.; Melissa, M.; Donald, K,; Raul, C.; Williiam, E. and Ching, P.; Late effect of treatment in survivors of childhood acute myeloid leukemia; 2000; J. Clinc. Oncol.; 18: 3273-3279.

19. Majeed, M.; Prevalence of hepatitis B and Hepatitris C infections among Thalassaemic children in Najaf City, Kufa Med. J.; 2002; 1: 192-196.

20. Castellino, S.; Lensing, S; Riely, C. and Hudson, M.; The epidemiology of chronic hepatitis C infection in survivors of childhood cancer; Blood; 2004; 103: 2460-2466.