Hepatitis Screen in Children with Malignancy at Al-Emamain Al-Kadimain Medical City

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ABSTRACT:

BACKGROUND:

Transfusion-transmitted infections continue to be a threat to the safety of the blood supply, in particular the risk is high for parent rally transmitted viral hepatitis in pediatric malignancy.

OBJECTIVE:

The aim is to estimate the prevalence of hepatitis in children with malignancy, identify some variables that could affect the prevalence of hepatitis in these patients, and to have an idea about the effect of vaccination in controlling hepatitis infection.

PATIENTS AND METHODS:

A cross sectional study was done over ten months period between December 1st, 2013 to September 30th, 2014 at the Pediatric Oncology Unit in Al- Emamain Al -Kadimain Medical City, A total of (54) children between the age of [1-15] years with malignancy who were diagnosed and treated at the pediatric oncology department before 6 months and more were studied. Information regarding age, gender ,residence, hepatitis vaccine received ,number of blood transfusion ,any surgical intervention for solid tumors and lymphoma was done, history of hepatitis screen at diagnosis were taken from hospital record and pediatric oncology consultation clinic files ,re- evaluation of hepatitis screen were done through with screen for HBs Ag , Anti HCV. Among those children with malignancy, testing for HBV and HCV were done through blood samples taken from the patients and sent to lab. of the hospital

RESULTS:

From (54) patients with malignancy, 46 patients were with hematological malignancy(85%) and 8 cases(15%) with solid malignancy, from them 8 (14.8%) cases were HBV positive and 4 (7.4%) cases with HCV positive. Most of the patient were from Baghdad 37 cases (68.5%), male to female ration(1.7:1) and also most dominant age group was from (4-9 year).The number of blood transfusion had significant positive impact on prevalence of hepatitis virus infection , and also the vaccine status had significant positive influence.

CONCLUSION:

There is a low frequency of HBV &HCV infection in patients with malignancy treated in Al-Emamain Al- Kadimain Medical City with lower incidence of HCV infections than HBV.

Blood transfusions (more than 3 times) is significantly increasing the incidence of HBV infection and HBV vaccine is significantly reducing the incidence of HBV infection.

KEYWORDS : viral hepatitis, malignancy, children.

INTRODUCTION:

Viral infections are important causes of liver disease world-wide. The five primary hepatitis viruses that have been identified are A, B, C, D (or delta), and E. Other viruses such as cytomegalovirus and Epstein-Barr virus also can result in hepatitis as part of a systemic infection. In addition, medications , toxins, autoimmune hepatitis, or Wilson's disease may cause acute or chronic hepatitis. [1] Hepatitis syndromes divided into acute and chronic forms. Acute hepatitis can last from weeks up to 6 months and is often accompanied by jaundice with anorexia, malaise, dark urine, fever, and mild abdominal pain. In chronic hepatitis, patients are often asymptomatic but may complain of fatigue[1] . Blood product transfusion is the major risk factor. [2] Immune suppressed persons on cytotoxic chemotherapy, especially if the regimen includes high dose corticosteroids , with acute hepatitis B virus infection are more likely to become chronically infected, presumably because of an insufficient immune response against the virus [2] . Reactivation of hepatitis B virus infection is a well-recognized complication in infected patients who undergo cytotoxic

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chemotherapy for cancer [3]. Reactivation of "dormant" infection with an acute hepatitis has been reported in both HBsAg-positive & negative patients treated with chemotherapy or immunosuppression. [3] Important consequences of hepatitis B virus reactivation is that it often leads to premature termination of chemotherapy or disruption in treatment schedules, which can impact patient survival. [3] . Hepatitis C virus (HCV) was identified in 1989 as a major cause of the parenterally transmitted non - A non - B hepatitis. The majority of patients develop chronic hepatitis C infection that has a global prevalence of 2.2% [4] .Groups at risk for HCV infection include transfusion recipients, injection drug users, hemodialysis patients, and health care workers [5,6]

AIMS OF THE STUDY:

1. To find out the overall prevalence of HBV and HCV among children with malignancy in Al-Imamin Alkhadimain Medical City
2. To find out the effect of frequent blood transfusion or blood product transfusion on the prevalence of hepatitis B and C.
3. To find out the effect of surgical intervention on the prevalence of hepatitis B and C concerning solid tumor.

PATIENTS AND METHOD:

A cross sectional study was carried out in the pediatric oncology unit of Al- Emamin Al-Kadimain Medical City ,Baghdad, Iraq .

A total of (54) children between the age of [1-15] years with onclogical diease including(acute lymphocytic leukemia , acute myeloblastic leukemia ,Hodgkin and non Hodgkin lymphoma ,neuroblastoma, Wilm's tumor) were collected over ten months between December 1st, 2013 to september 30th, 2014 ,patients diagnosed before 6 months and more and treated in Al- Emamin Al-Kadimain Medical City were studied.

Informations regarding (name of the patient, date of birth, gender , date of diagnosis, hepatitis screen at time of diagnosis, number of hepatitis vaccines given, number of blood transfusion) were obtained.

Surgical interventions including lapratomy for resection for neuroblastoma , nephrectomy in Wilm's tumor, lymphoma (Hodgkin and non-Hodgkin) , excisional biopsy of lymph node were included.

These data were taken from hospital records, questionnaire of the parents & from the patient's own medical file in pediatric Hemato-Onclogy consultation clinic which contain all information regarding inpatient & outpatient visits with the detailed management.

The results of hepatitis screen at time of diagnosis of cancer were taken from the hospital records.

Patients were evaluated for HBV and HCV through venous blood sample aspirated in plain tube and sent for screening for hepatits B and C in the laboratory of Al- Emamin Al-Kadimain Medical City

Hepatitis B surface Antigen and Anti Hepatitis C virus Antibody were investigated by commercially available ELISA diagnostic kit techniques.

For Hepatitis B; Bioelisa HBsAg 5,6 (Biokit) for screening tests made in Spain.

For Hepatitis C;HCV Ab screening ELISA test, Biorex made in UK

Patient with positive test were referred to GIT department in medical city for further tests and management.

Statistical analysis were performed with the statistical package for social science version 20(SPSS Inc., Chicago ,IL,USA).Chi-square were used to compare between groups of variables, a 2-tailed p-value less than 0.05 was considered significant.

RESULTES:

In fifty four cases studied ,the incidence of hepatitis B virus was 8 (14.8%)cases, and only 4 (7.4%) cases were infected with HCV as figures-1, 2- shows

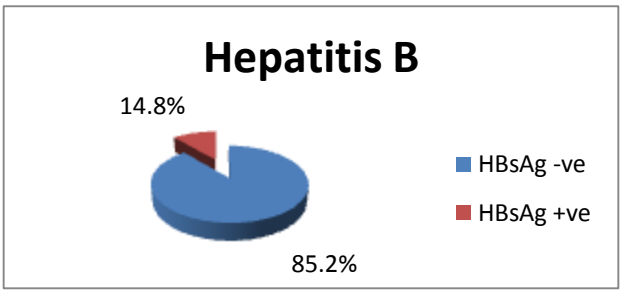

Figure 1: Hepatitis B ratio in 54 patients .

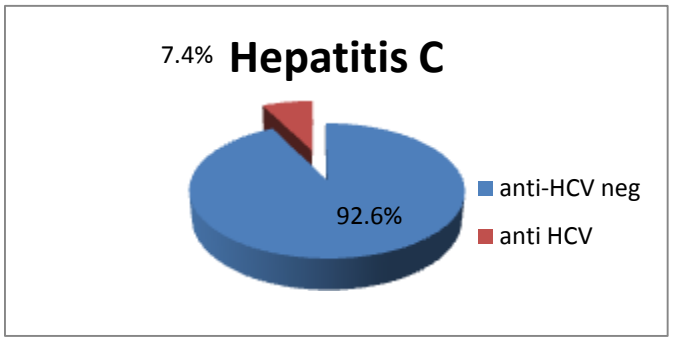

Figure 2:Hepatitis C frequency ratio in 54 patients.

of 54 patients there were 24 cases(44.4%) with acute leukemia including lymphocytic and myelocytic leukemia ,of them 4 cases were HBsAg positive and one case was hepatitis B and C positive and 2 cases with leukemia infected with hepatitis C only, while from 22(40.7%) lymphoma cases only 4 cases infected with hepatitis B and one case infected with hepatitis C, from 6 (11.1%) cases with neuroblastoma and 2 (3.7%) cases with wilm's tumor, no case was positive for hepatitis B or C as shown in table -1-

Table 1 : Oncological disease percentage and prevalence of hepatitis B and C.

Disease	No.	%	HBsAg +ve	Anti-HCV	HBs Ag +ve And anti HCV
Acute leukemia	24	44.4	4	2	1
Lymphoma	22	40.8	4	1	0
Neuroblastoma	6	11.1	0	0	0
Wilm's tumor	2	3.7	0	0	0

The age (years) range was 1-15years and mean age was 6.5 ± 3.96 years, [1-4, 15 patients (27.8%), >4-9, 31(57.4%), >9-15, 8 (14.8%)] .Most of the hematological malignancy were in the age group >4—9 years , 27 cases(87%) while solid tumor equally found in the age group 1-4 and>4—9 years 4,4 cases (26.7 % and 13%) respectively . Males were more predominant than females [34(62.9%) & 20(37.1%] respectively, male to female ratio was (1.7:1). The patients were referred from different parts of the country; however the majority were from Baghdad [37(68.5%)] . Most of the patients received 3 vaccines 34 (63%) as (Table- 2-) shows

Table 2: Demographic & clinical data of 54 patients.

Parameters	No.	%	Type of malignancy			
			Solid tumor		Hematological malignancy	
Age in years			No.	%	No.	%
1—4	15	27.8	4	26.7	11	73.3
>4—9	31	57.4	4	13	27	87
>9—15	8	14.8	0	0	8	100
gender						
Male	34	63	18	33	16	30
Female	20	37.1	12	22	8	15
Residence						
Baghdad	37	68.5	5	15	32	85
Others	17	31.5	3	18	14	82
Heptitis B vaccines						
3 vaccines	34	63	6	18	28	82
Incomplete<3	12	22.2	1	8	11	92
Not vaccinated	8	14.8	1	12.5	7	87.5

of the fifty four patients, all were tested for HBsAg. The impact of some variables on prevalence of HBV infection includes age, sex, and residence were studied. There was equal number of cases in two age groups (>4-9 years and >9-15 years which was 4 cases in both). There was significant association between age and Hepatitis B infection [p. value <0.05].Gender had a significant effect on the prevalence of hepatitis B virus ,male 6 cases(75%), female 2 cases (25%) with (p. value =0.023). The residence had significant effect on prevalence of HBV which was more prevalent in Baghdad than other governorate [7, (87.5%); 1 (12.5%)] respectively.[p .value= (0.038)]. As (Table -3-) shows

Table 3: Impact of Age, Sex &Residence of patients on the prevalence of HBV infection.

Factors studied		HBsAg positive		HBsAg Negative		P value
		No. Total (8)	% within HBV%	No. Total (46)	% within HBV %	
Age (years)	1—4	0	0	15	32.6	0.005*
	>4—9	4	50	27	58.7	
	>9—15	4	50	4	8.7	
Sex	Male	6	75	28	60.8	0.023
	Female	2	25	18	39.2	
Residence	Baghdad	7	87.5	30	65.3	0.038
	Others	1	12.5	16	34.7	

*Significant using Pearson Chi-square test at 0.05 level of significance.

All patients were tested for HCV. The impact of some variables including age ,gender and residence on prevalence of HCV infection reveal that these variables had no impact on prevalence of HCV infection [age(p. value =0.227), sex(p. value 0.11), residence(p. value 0.159) as in(table -4-) .

Table 4 :Impact of Age, gender &Residence of patients on the prevalence of HCV infection.

Parameters		Anti-HCV positive		Anti-HCV Negative		P value*
		No. (4)	%	No. (50)	%	
Age (years)	1—4	0	0	15	30	0.227
	>4—9	4	100	27	54	
	>9—15	0	0	8	16	
Gender	Male	4	100	30	60	0.111
	Female	0	0	20	40	
Residence	Baghdad	4	100	33	66	0.159
	Others	0	0	17	34	

*Significant using Pearson Chi-square test at 0.05 level of significance

All patients who were vaccinated with 3 doses of hepatitis B vaccine had positive results for anti-HBs Ag ,while all patients with incomplete vaccination or unvaccinated results were with negative results.

Out of 8 cases with hepatitis B infection [2,(25%),2,(25%),4,(50%)], received (3 doses, <3 doses and not vaccinated),respectively and that was statistically significant (p. value<0.05) as table -5- shows.

Table 5: Impact of hepatitis vaccine on hepatitis B infection

Number of doses of HB vaccines	Anti-HBs Ag positive		Negative Anti-HBsAg		P value*
	No.	%	No.	%	0.016
3 doses	2	25	32	69.6	
Incomplete(< 3 vaccine)	2	25	10	21.7	
Not vaccinated	4	50	4	8.7	

*Significant using Pearson Chi-square test at 0.05 level of significance.

of fifty four patients only 26 cases (48%) patients did not receive blood transfusions ,10 cases(19%) received 1 -3 times and 18 cases (33%) received more than 3 times blood transfusion as(table -6-) shows .Hepatitis B was more common in cases who had more than 3 blood transfusion 8,(100%) and that was statistically significant (p .value <0.05),as (table -6-) shows

Table 6: Impact of blood transfusion and its frequency on infection with hepatitis B infection

Number of blood transfusion	Total No.	Total%	HBs Ag positive		HBsAg negative		P. value*
			No.	%	No.	%	0.0001
No transfusion	26	48	0	/	26	56.6	
1-3	10	19	2	/	10	21.7	
>3	18	33	8	100	10	21.7	

*Significant using Pearson Chi-square test at 0.05 level of significance

HCV infection occurred in 4 cases in cases with blood transfusion (1-3 times),Blood transfusion was significantly associated with HCV infection(p value =0.0001). as table -7- shows.

Table 7: Impact of blood transfusion and its frequency on infection with hepatitis C infection

Number of blood transfusions	Total No.	Total %	Anti-HCV positive		Anti HCV negative		P. value*
			No.	%	No.	%	
No transfusion	26	48	0	0	26	52	0.0001
1—3	10	19	4	100	6	12	
>3	18	33	0	0	18	36	

*Significant using Pearson Chi-square test at 0.05 level of significance

of the 54 patients 29 (53.7%) cases underwent surgical intervention(excisional biopsy, tumor resection in neuroblastoma, nephrectomy) as table -8- shows

Table 8: Number of surgical intervention.

Surgical intervention	Total No.	% out of total	No. Solid tumor and lymphoma	% surgery within solid tumor and lymphoma
Surgical intervention	29	53.7	29	96.6
No surgical intervention	25	46.3	1	3.4

Hepatitis B was found in 4 cases (50%) underwent surgery and 4 cases (50%) who did not undergo surgery as show in table -9- .Hepatitis C was also found in 1 case (25%) underwent surgery and 3 cases (75%) of cases with no surgical intervention. There is no significant relation between surgery and the infection with hepatitis B or C (p value=0.809, 0.232) respectively, as show in(table -9-).

Table 10: Impact of surgical intervention with hepatitis B and hepatitis C infection

Surgical intervention	HBsAg negative No.	%	HBsAg positive No.	% from hepatitis B +ve	P. value	Anti HCV No.	%from anti-HCV -ve	P. value*
Surgery	25	54.3	4	50	0.809	1	25	0.232
No surgery	21	45.7	4	50		3	75	

*Significant using Pearson Chi-square test at 0.05 level of significance

DISCUSSION:

The prevalence of HBs Ag. among the patients was(14.8%) ,and the prevalence of anti-HCV was(7.4%). The prevalence of HBsAg was less than that of a study done in Children Welfare Teaching Hospital [7] that found the prevalence of HBS Ag was (27.3%) in 2008 but the same prevalence of HCV was (7.8%) ,this is may be related to the application of more intensive vaccination programs in the country since that time. Another study carried by Ali S.M . in 2007 [8] included 607 patients with leukemia& lymphoma at Child Central Teaching Hospital over 3 years period, hepatitis B surface antigen was positive in 20/607 (3.29%) and Anti-HCV was 6/607 (0.98%), In most western countries and North America, the prevalence of HCV ranges from 0.3 to 0.7% [9], In a study conducted in Iran , among the patients who had been treated for leukemia, 2% were HCV positive, 0.2% of patient had combined HBsAg and HCV positive infection, and 2.5 % were HBsAg positive [10] , the explanation of this difference may be related to criteria of sample size and short period of study.

Children with cancer require multiple transfusions during intensive therapy ,and are at an increased risk of blood transmissible infections, such as HBV and HCV infections. The need for frequent blood counts, intravenous therapy and surgery in addition to the immune suppressed status of these patients further increase the risk. [11]

Hematological malignancy was more than solid tumor taken in this study which was 46(85%) of

total cases , as in a Turkish study done by Serap Karaman et al, in which in total of 159 cases , acute leukemia (n=66), non-Hodgkin lymphoma (n=27), Hodgkin lymphoma (n=20) constitute 71%, and solid tumors (n=46) contribute to 29% .[11]

The variables are age, sex and residence which may have an impact on the prevalence on HBV &HCV infection . The effect of age on the prevalence of hepatitis in the younger age group is lower due to high efficacy of hepatitis vaccine received through the national immunization programs . [12] This study shows significant association between prevalence of hepatitis and older age group.

Regarding the sex ,In this study number of males were more than female (75 %)for cases of hepatitis B infection , this was the same as research done by Ali S.M. [8] who found that the prevalence of HBV was more in boys than girls (75%) while in HCV there was no difference between boys and girls, Same result also found with Yeo W, et al. done in korea in 2000. [13]

The residence of patient might have an impact on infection as there were more cases of hepatitis B and C in Baghdad than other government which may be related to the fact that most of patients screened were from Baghdad, this was not the same result reached by Dr. fadhil H.K in research done at Child's Central Teaching Hospital in 2011 [14] who found that hepatitis is more prevalent in governorate state than Baghdad that was 91 % of cases of hepatitis B from governorate state and 9 % from Baghdad. this may be related to fact that most cases treated in Al-Emamain Al-Kadimain Medical City are referred from Baghdad.

This study showed that patients received three doses of HBV vaccine had better protection against HBV in comparison with those who received less than three doses or never taken any dose of HBV vaccine, on the other hand some children who received three doses of vaccine but do not get protection against infection with HBV, which might raise the question of the efficacy of the vaccines given, the possibility of attenuation of immune system during period of receiving chemotherapy and the reliability of the history taken from the parents because the lack of medical records regarding vaccination these results was the same as S. Yetgin et al, who suggested that a high protective role of HBV vaccination was observed in non-sero-conversion acute leukemia patients. [15] Although children who have not received routine childhood vaccination can be immunized during cancer therapy, vaccination may not be sufficient, as cancer therapy can cause loss of acquired vaccination status. The type of cancer and the therapy applied may influence the level of antibody titer. [16]

In another study done in turkey by Serap Karaman et al in 2011 who investigated antibody titers in a heterogeneous group of patients, including those with leukemia, lymphoma, and solid tumors. The loss of antibody titers after therapy was determined to be the highest in patients with leukemia (63.6%), and diagnosis of the disease was the unique factor that statistically significantly affected the antibody titers [11]

This study showed the risk of blood transfusion for transmission of HBV ,HBC increases with the increased number of blood transfusion which was the same result as in Mansour AK [17] from Egypt who showed that The HBV and HCV-markers were found significantly more often among multi-transfused thalassaemic children than among the controls in terms of 39 (19.5%) were anti-HCV positive ; 58 (29.0%) were HBsAg positive. [10]

Another study done in Brazil showed that the overall prevalence of HCV, HIV, HBV and co-infection among multi-transfused patients were 16.7%, 1.7%, 0.8% and 1.7% respectively. [18]

Children with cancer require multiple transfusions during intensive therapy are at an increased risk of blood transmissible infections, such as HBV and HCV infections. However, the risk for acquiring HCV infection from blood products has decreased significantly since the initiation of routine blood donor screening, ,while risk of transfusion transmitted viral infection (HCV, HBV) in France for the 2001-2003 periods was estimated at 1 in 10 million for HCV and at 1 in 640 000 for HBV. [19]

Surgical intervention was found in 29 cases (53.7%) and that was not significantly associated with either hepatitis infection B or C virus as a Pakistani study also showed that there no significant association between surgical intervention and infection with hepatitis B and C. [20]

CONCLUSION:

1-The frequency of hepatitis B in children with malignancy treated in Al- Emamain Al-Kadmain Medical City is low but higher than hepatitis C .Factors that might significantly affect the prevalence of hepatitis B infections are the number of blood transfusions received & number of hepatitis B vaccines given and residence of the

patients .Solid tumor carry lower risk of activation or infection with hepatitis B or C than hematological malignancy.Higher frequency of hepatitis in male patients, among children age from 4-9 years and among patients from Baghdad city. No significant association between surgical interventions and hepatitis B and C.

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