Prevalence of hepatitis c infection among multitransfused thalassemia major patients in ibn-albalady center of thalassemia

Abdul karem jasem Albahadle* ,Areege Abdul Abass* and Ali Hussein Ali**

الخلاصة

الهدف من هذه الدراسه هو تحديد مدى انتشار عدوى التهاب الكبد الفيروسي نوع(ج) بين مرضى فقر دم البحر الابيض المتوسط (الثلاسيميا).

تمت مراجة ملفات 206 مريض من مرضى الثلاسيميا الكبيره في مركز امراض الثلاسيميا واعتلال الهيموغلوبين في مستشفى ابن البلدي للفتره من ايار ولغاية ايلول 2011 ،وتم جمع المعلومات حول العمر،الجنس،عدد مرات نقل الدم،رفع الطحال و نتائج فحص التهاب الكبد الفيروسي نوع (ج)و(ب)ونقص المناعه المكتسبه(الايدز) لكل مريض من ملفات المرضى في المستشفى. تم جمع النتائج وتحليلها احصائيا للحصول على قيمة (p).

من مجموع 206 مريض، كان عدد الذكور والاناث كالاتي؛99 ذكر (48.1%) و 107 انثى(51.9%). ست واربعون مريضا (22.3%) كانت اعمارهم تحت الخمس سنوات ،77مريضا(37.4%) كانت اعمارهم تتراوح بين 5-10 سنوات و 83 مريضا(40.3%) كانت اعمارهم فوق 10 سنوات. ثلاث وثلاثون مريضا(16%) تم نقل الدم لهم اقل من 30 مره،في حين 107 مريضا(84%) تم نقل الدم لهم اكثر من ثلاثين مره. سبع وخمسون مريضا(27.7%)اجريت لهم عملية رفع الطحال مسبقا.ثلاث وثلاثون مريضا (80%) من مجموع 41 من مرضى الثلاسيميا المصابين بالتهاب الكبد الفيروسي نوع (ج) كان قد تم نقل الدم لهم اول مره قبل اجراء الفحص الروتيني لفيروس التهاب الكبد نوع(ج) لدم جميع المتبرعين عام 2005،في حين ان 8 مرضى (20%) قد تم نقل الدم لهم اول مره بعد عام 2005 .النتائج بينت ان خطر الاصابه بالتهاب الكبد الفيروسي نوع (ج) لدى مرضى الثلاسيميا يزداد مع زيادة عمر المريض وعدد مرات نقل الدم في حين لا يوجد تاثير لجنس المريض او رفع الطحال من عدمه.كما اوضحت النتائج اهمية اجراء فحص الكشف عن فيروس التهاب الكبد نوع (ج)بصوره روتينيه لدم المتبرعين في تقليل الاصابه بالمرض.

نستنتج من هذه الدراسه ان مرضى الثلاسيميا المعرضين لنقل الدم بصوره مستمره هم في خطر الاصابه بالتهاب الكبد الفيروسي نوع(ج)،لذا وجب اجراء الفحوص الروتينيه واستخدام الوسائل المتطوره للكشف عن هذا الفيروس ومعالجة المصابين لتقليل خطر الاصابه بامراض الكبد المزمنه.

*Dept. pediatric ,College of Medicine Al-Nahrain University .
**Al-kadhimiya Teaching Hospital

Abstract

Back ground : Beta thalassemia major occurs in the Mediterranean littoral ,characterized by chronic heterolysis and frequent blood transfusion which carry a lot of complication like viral hepatitis

Objective: To evaluate the prevalence of Hepatitis C infection among multitransfused thalassemia major patients.

Methods: A retrospective study was conducted on 206 thalassemia major patients referred to the IBN-ALBALADY Center of Thalassemia and Hemoglobinopathy from May to September 2011,data about age,sex,number of blood transfusion ,history of splenectomy and result of serological viral markers for anti HCV antibody, HBsAg and anti HIV antibody were obtained from the patient files at the hospital. The result were analyzed using Chi-squared distribute to obtain the p-value.

Results: Out of 206 patients, 99 (48.1%) were male and 107 (51.9%) were female.Forty one(19.9%) were seroposative for hepatitis C infection.Forty six patients were < 5 years tow(4.3%) of them were positive , 77 between 5-10 years,16 (20.8%)of them were infected and 83 above 10 years of age23(27.7%) of them were infected . Thirty three (16%) were received < 30 times blood transfusion only one(3%) of them get the infection, while 173 (84%) received ≥ 30 times40 (23.1%)of them get infecton . Fifty seven patients (27.7%) had already undergone splenectomy 11(19.3%) of them get the infection, while30(20.1%) of 149 patients without splenectomy get the infection.

Conclusion: multi transfused thalassemic patients are at a risk for HCV infection. Thus routine screening using more accurate technique is necessary in order to prevent viral infection.

Key words : Thalassemia , hepatitis ,blood transfusion .

Introduction

Thalassemia is an inherited autosomal recessive blood disease that originated in the Mediterranean region. In thalassemia the genetic defect, which could be either mutation or deletion, results in reduced rate of synthesis or no synthesis of one of the globin chains that make up hemoglobin[1]. The type of thalassemia usually carries the name of the underproduced chain or chains. The reduction varies from a slight decrease bto a complete absence of production. The consequences of impaired production of globin chains ultimately result in the deposition of less H into each RBC, leading to hypochromasia. The Hb deficiency causes RBCs to be smaller, leading to the classic hypochromic and microcytic picture of thalassemia[2].Infants with severe beta thalassemia major (BTM) are well at birth, because the production of beta globin is not essential during fetal life or the immediate perinatal period[3].. Symptoms emerge during the second six months of life when gamma globin chain production decreases and is normally replaced with the production of beta globin to form adult hemoglobin (Hb A, alpha2/beta2)[4] . Eighty percent of untreated children will die within the first five years of life, due directly to the consequences of severe anemia, high output heart failure, inanition, and unusual susceptibility to infection[5] . Massive splenomegaly develops early in the course of BTM due increased red cell destruction and the presence of splenic extramedullary hematopoiesis. Before and after splenectomy, children with BTM suffer immune deficits as the result of premature loss of splenic function [1]The mainstays of therapy for beta thalassemia major are chronic hypertransfusion, splenectomy, iron chelation, and supportive measures directed at the complications of the expanded erythron and iron overload . Emerging therapies include the use of allogeneic bone marrow transplantation, pharmacologic manipulation of fetal hemoglobin levels, and, eventually, gene therapy[6].For many years, the hepatitis B virus was the major incubus for patients with thalassemia.The advent of new screening techniques reduced the magnitude of this problem of hepatitis B .After the discovery of hepatitis C virus in 1989,it was found to be the major cause of

transfusion-associated hepatitis in the world (7) .The key problem with hepatitis C virus infection is it propensity to produce chronic liver disease ,cirrhosis and hepatocelluler carcinoma occurring after a number of years(8).

Enzyme immunoassay; The commonly available screening test for anti-HCV is an enzyme immunoassay (EIA, also called enzyme-linked immunosorbent assay or ELISA) that detects HCV antibodies [9]. . The virologic assays for HCV are the polymerase chain reaction (PCR) and the branched-chain DNA (bDNA test), which permit detection of small amounts of HCV RNA in serum and tissue samples within days of infection[10]. Experience with treatment of chronic HCV infection in children is limited. [11] Combination therapy with interferon-alfa and ribavirin was the first established treatment for hepatitis C in children. For most children and adults, pegylated interferon is now preferred[12] There is at present no effective vaccine against HCV infection [13] .

Patients and methods

This retrospective study was performed from May to September 2011 in the thalassemia center in IBN-ALBALADY Children Hospital in Baghdad .The medical records of 206 patients with thalassemia major were surveyed and analyzed and data regarding age, sex, number of blood transfusion, history of splenectomy and serological viral marker for anti-HCV Ab.(which is done by third generation ELISA test),HbsAg and anti HIV antibody were obtained.The units of blood were provided freely by the central blood bank in Baghdad, which introduced routine screening for HCV Ab. for all blood donors in 2005.In this study we exclude

1. Other types of haemoglobinopathy rather than β-Thalassemia major
2. Age above 18 years.

Statistical analysis: The result were analyzed using Chi-square (X2) test and degree of freedom(df) to obtain p-value, p-value of less than o.o5 consider to be significant.

Results

The total number surveyed were 206 , 41 (19.9%) of them were hepatitis C positive ,only 4 patients (1.94%) were hepatitis B positive and no patient was positive for HIV , as shown in table 1 below:

Table 1. Prevalence of viral seromarkers in the study population.

Viral markers	No. of positive cases	Percentage %
HCV antibody	41	19.9 %
HBsAg	4	1.94 %
HIV antibody	0	0

This study show direct relationship between the age and the prevalence of hepatitis C, where 2(4.3%) patients out of 46 of age less than 5 years were positive for hepatitis C, while 16(20.8%) patients out of 77 of age between 5-10 years were positive for hepatitis C, and 23(27.7%) patients of age above 10 years were positive for hepatitis C, as shown in table 2 below.

Table 2 . Association between the age and the prevalence of hepatitis C.

Age * HCV Crosstabulation			HCV		Total
			Negative	Positive	
Age	Less than 5 years	Count	44	2	46
		% within Age	95.7%	4.3%	100.0%
		% within HCV	26.7%	4.9%	22.3%
		% of Total	21.4%	1.0%	22.3%
	5 to 10 years	Count	61	16	77
		% within Age	79.2%	20.8%	100.0%
		% within HCV	37.0%	39.0%	37.4%
		% of Total	29.6%	7.8%	37.4%
	More than 10 years	Count	60	23	83
		% within Age	72.3%	27.7%	100.0%
		% within HCV	36.4%	56.1%	40.3%
		% of Total	29.1%	11.2%	40.3%
Total		Count	165	41	206
		% within Age	80.1%	19.9%	100.0%
		% within HCV	100.0%	100.0%	100.0%
		% of Total	80.1%	19.9%	100.0%

Chi-square=10.193 , d.f. =2 , P-value =0.006(<0.05) (significant)

There is no significant relationship between the sex and the prevalence of hepatitis C ,where 19(19.2%) patients out of 99 male were positive for hepatitis C while 22(20.6%) patients out of 107 female were positive for hepatitisC, as shown in table 3 below.

Table 3. Association between the sex and the prevalence of hepatitis C.

Sex * HCV Crosstabulation			HCV		Total
			NEGATIVE	POSITIVE	
Sex	male	Count	80	19	99
		% within Sex	80.8%	19.2%	100.0%
		% within HCV	48.5%	46.3%	48.1%
		% of Total	38.8%	9.2%	48.1%
	female	Count	85	22	107
		% within Sex	79.4%	20.6%	100.0%
		% within HCV	51.5%	53.7%	51.9%
		% of Total	41.3%	10.7%	51.9%
Total		Count	165	41	206
		% within Sex	80.1%	19.9%	100.0%
		% within HCV	100.0%	100.0%	100.0%
		% of Total	80.1%	19.9%	100.0%

Chi-square=0.06 , d.f. =1 , P-value =0.806(>0.05) (not significant)

There is direct relationship between the number of blood transfusion and the prevalence of hepatitis C, where only 1(3%) patient out of 33 who receive less than 30 times blood transfusion was positive for hepatitis C, while 40 (23.1%) patients out of 173 who receive equal or more than 30 times blood transfusion were positive for hepatitis C, as shown in table 4 below.

Table 4. Association between the number of blood transfusion and the prevalence of hepatitis C.

No. of blood transfusion * HCV Crosstabulation			HCV		Total
			negative	positive	
No. of blood transfusion	Less than 30 times	Count	32	1	33
		% within No. of blood transfusion	97.0%	3.0%	100.0%
		% within HCV	19.4%	2.4%	16.0%
		% of Total	15.5%	.5%	16.0%
	= or more than 30 times	Count	133	40	173
		% within No. of blood transfusion	76.9%	23.1%	100.0%
		% within HCV	80.6%	97.6%	84.0%
		% of Total	64.6%	19.4%	84.0%
Total		Count	165	41	206
		% within No. of blood transfusion	80.1%	19.9%	100.0%
		% within HCV	100.0%	100.0%	100.0%
		% of Total	80.1%	19.9%	100.0%

Chi-square=7.017 , d.f. =1 , P-value =0.008(<0.05) (significant)

There is no significant relationship between the splenectomy and the prevalence of hepatitis C, where 30(20.1%) patients out of 149 not splenectomized patients were positive for hepatitis C, while 11(19.3%) patients out of 57 splenectomized patients were positive for hepatitis, as shown in table 5 below.

Table5.Association between splenectomy and the prevalence of hepatitis C

Splenectomy * HCV Crosstabulation			HCV		Total
			negative	positive	
Splenectomy	No	Count	119	30	149
		% within Splenectomy	79.9%	20.1%	100.0%
		% within HCV	72.1%	73.2%	72.3%
		% of Total	57.8%	14.6%	72.3%
	Yes	Count	46	11	57
		% within Splenectomy	80.7%	19.3%	100.0%
		% within HCV	27.9%	26.8%	27.7%
		% of Total	22.3%	5.3%	27.7%
Total		Count	165	41	206
		% within Splenectomy	80.1%	19.9%	100.0%
		% within HCV	100.0%	100.0%	100.0%
		% of Total	80.1%	19.9%	100.0%

Chi-square=0.018, d.f.=1,P-value=0.893 (>0.05) , (not significant)

This study show 33(80%) out of 41 infected thalassemic patient had received blood transfusion before the start of routine screening of donor blood for HCV in 2005,while 8(20%) patients after 2005.(as shown in figure 1).

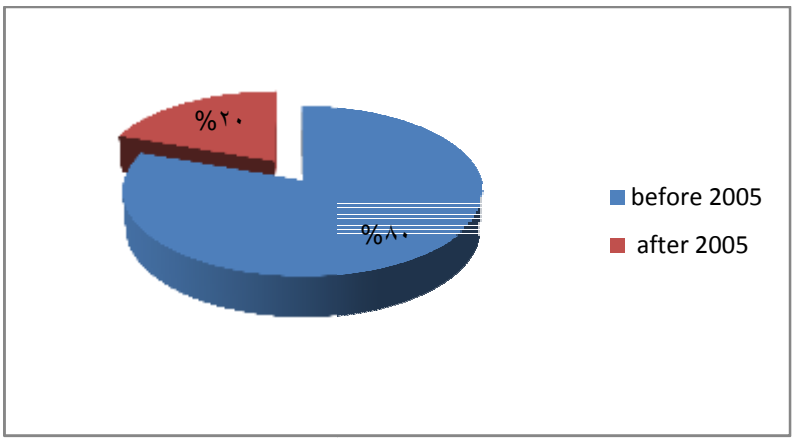

Figure 1. pie chart of time of first blood transfusion for hepatitis C infected patients

Table 6. comparison of our findings with some previous studies

country	Year of study	Number of patients studied	HCV sero-positivity percentage
Bangladesh	2003	259	12.5
India	2002	50	30
Jordan	2001	143	40.5
Britain	1990	73	23.3
Pakistan	2008	180	42
Lebanon	2002	395	14
Libya	2002	250	11
Egypt	1995	18	44
Italy	1994	256	60
Our study	2011	206	19.9

Discussion

In this study, we found a prevalenc of 19.9% for HCV infection. Only 4 patients were positive for HbsAg, which give a prevalence rate of 1.94%, the low prevalence of HBV may be due to the use of hepatitis B vaccine in the immunization schedule,in addition to using third generation ELIZA technique for screening of donated blood,and the strict precautionary measures applied at hospital against spread of HBV infection . None of the patients tested was positive for HIV.(as shown in table 1).

This study showed that the prevalence of HCV infection increases with increasing age of the patients (as shown in table 2) ranging from 4.3% in less than 5 years to 27.7% in more than 10 years. This rising figure has been documented in other studies [14,15,16] this could be explain by increase chance of exposure to infected blood or by increase frequency of admission to hospital with increase possibility to exposure to infected device or material . The patients sex was not a risk factor for HCV infection (as shown in table 3), and this similar to the study from Iran by Ghafourian BoroujerdniaM[16],also splenectomy was not a risk factor for HCV infection (as shown in table 5), which is similar to a report from Italy by Resti and co-workers[17].

There is a clear and evident relationship between the number of blood transfusion and prevalence of HCV infection (as shown in

table 4) as those who received blood ≥ 30 times had a higher prevalence of HCV infection than those who had received <30 times, and this in agreement with other studies [18,19].

Our data showed that 33(80%)out of 41 patients who have anti HCV Ab started receiving blood transfusion before 2005,(as shown in figure 2), suggesting that HCV screening in blood donors is vital in limitation of HCV infection . Our result for prevalence of HCV infection in comparison with studies from other countries(as shown in table 6) that show the prevalence of HCV seropositivity in multitransfused β-thalassemia patients has been observed to vary greatly from 11 to 60%.This extreme degree of variability depends on two major factors, i.e., the prevalence of HCV in the relevant population (and therefore also in the blood donors), and the practice of HCV antibody screening before the transfusion is instituted [20]. The countries with a higher HCV prevalence in general population had a higher prevalence rate among thalassemia patients, too. For Instance, a study in Egypt reported 75% of HCV prevalence among thalassemia patients, considering the fact that the prevalence in their blood donor population was 14.5% [21]. However, in India with a low HCV prevalence among blood donors (1.78%), the prevalence in thalassemics was reported relatively low (25.5%)[22].

Conclusion & Recommendation

1) The prevalence of anti HCV Ab in thalassemia patients is still relatively high, which carries a considerably high risk for development of chronic liver diseases.

2) Screening for blood donors is vital in limitation of HCV infection.

3) Encouragement of bone marrow transplantation in treatment thalassemia patients as advanced method.

4) Recently many countries who had high incidence of thalassemia ,they used preventive methods by doing abortion in prenatally diagnosed patients .

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