

Transfusion-Related Infections in Thalassemia Major Patients: Kirkuk Thalassemia Center Experience

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Abstract:

Introduction: Thalassemia Major is one of the commonest causes of hereditary anemia in Iraq. Patients usually require frequent blood transfusion. This study tried to estimate the problem of transfusion-related infections among β -thalassemia major patients in Kirkuk governorate-Iraq.

Patients and Methods: The study involved 254 multi-transfused thalassemia major patients attending the Thalassemia Center at Kirkuk governorate over two years period starting from January 2010 to January 2012. Blood samples were tested for HBsAg, anti HCV antibodies, and HIV antibody using an enzyme-linked immunosorbent assay. A control group of 150 Thalassemia minor with nearly matched age and sex to thalassemia major patients was included.

Results: Anti-HCV antibody was positive in 85 out of 254 thalassemia major patients (33.5%), while HBsAg was positive in only one out of 254 patients (0.4%). HIV infection was not found in any thalassemia major patients. The rate of positive anti-HCV antibodies was significantly higher in comparison with the control group (P value <0.000) while it was not significant for HBsAg (P value=0.9). Age categorization for thalassemia major patients with positive HCV test shows that more than three quarters of them are above 10 years old.

Conclusion: HCV is the current major problem in multi-transfused children with thalassemia major and more careful pre-transfusion screening of blood for anti-HCV must be introduced in blood bank centers.

Keywords: Thalassemia Major TM, Transfusion related infection TRI, HCV, HBV, HIV, Kirkuk, Iraq.

Introduction:

Thalassemia or "Cooley's anemia" is an inherited red blood cells disease that is characterized by deficient in the synthesis of one or more globin subunits of the hemoglobin. Iraq is one of the countries in which (6-10%) of the population has hemoglobinopathy. Thalassemia major (TM) is the predominant type of hemoglobinopathy especially in the northern Iraq governorates like Suliamanya, Erbil and Kirkuk⁽¹⁻³⁾.

Conventional treatment of β TM patients consists of frequent blood transfusions and iron chelating therapies to decrease the effect of iron accumulation on different body organs. The rationale for regular transfusion program started in 1960s to achieve higher levels of hemoglobin, prevent the ineffective erythropoiesis, increase oxygen delivery to tissues, promote growth, and improve the general well-being^(4, 5). Current guidelines recommend a pretransfusion threshold not exceeding (9.0%) g/dl, which seems

to be associated with adequate marrow inhibition and a relatively low iron burden⁽⁶⁾. Furthermore, Piomelli *et al*, have recommended a hyper transfusion regimen, with pretransfusion hemoglobin level of 10 g/dl⁽⁷⁾. Thus, they contribute to a group of patients called multi-transfused patients. These transfusions programs would certainly have many drawbacks especially the transfusion-related infections (TRI).

The natural course of the disease is dramatically altered by transfusion side effects, which need to be monitored and treated throughout life. Iron overload resulting in end-organ damage and (TRI) still represent the principal causes of morbidity and mortality. Blood transfusion exposes the patient to a number of risks, adverse events associated with transfusions such as non-hemolytic febrile reactions, allergic reactions, delayed transfusion reactions, transfusion-related lung injury, graft-versus-host disease, red cell alloimmunization and transfusion of infectious agents including viruses, bacteria and parasites^(5,8). The transfusion-associated diseases are overcome by safe donor selection and application of better screening methods. This study was designed to determine the burden of transfusion-TRI in TM patients at Kirkuk governorate.

Materials and Methods:

This study was conducted in the Thalassemia Center at Azadi Teaching Hospital, Kirkuk, Iraq over two years' time period, starting from January 2010 to January 2012. As part of the center policy, screening of TM patients by testing for the viral panel (HBsAg, HCV, and HIV) every 3 months is done. Each time, five to seven milliliter of blood is collected in plain tube and serum is separated and tested for

Hepatitis C Virus (anti-HCV), Human Immunodeficiency Virus (anti-HIV) antibody, and Hepatitis B surface Antigen (HBsAg) using the Enzyme Linked Immunosorbent Assays (ELISA) tests. At the same time, the three viral screening testing panel done on the serum samples of 150 thalassemia minor patients control group selected from our center with nearly similar age and sex character. Data had been gathered, at the end of study period, including age, sex in addition to their viral screen results and analysis was performed using SPSS version 16. Ethical approval for the study was taken from the ethical committee of scientific researchers at Kirkuk health institute.

Results:

It is clear that nearly one third of TM patients have got Anti HCV positive (33.5%; 85/254), which was significantly higher than the control group (1.3%; 2/150), P value <0.001.

Table 2 illustrates that just one out of 254 (0.4%) TM patient have got positive test result for HBsAg and none in the control group is infected with HBV, which is non-significant if compared statistically with P value=0.9. Neither TM nor control group had been infected with HIV virus as shown in (table 3).

Age categorization for TM patients was done and patients were divided into three categories including: less than 5 years old, 5-10 years old and more than 10 years. Figure 1 shows age categories against HCV test result. It is clear that positivity increased significantly with increasing the age and nearly two third of the thalassemia patients (n=65, 76.5%) harboring HCV are more than 10 years old age patients. While the remaining 20 patients are lower than 10 years old; precisely 16 patients (18.8%)

are 5-10 years old and just 4 patients (4.7%) are less than 5 years old.
Figure 2 demonstrates slight female predominance over male in TM patients

in both HCV positive (48 vs. 37) and HCV negative test results (86 vs. 83).

Table (1): HCV status in both TM and control group.

Group	Number	Anti HCV +		Anti HCV –	
		No.	%	No.	%
Thalassemia major	254	85	33.5%	169	66.5%
Control	150	2	1.3%	148	98.7%
Total	404	87	21.5%	317	78.5%
P-value=0.000		Highly Significant			

Table (2): HBV status in both TM and control group.

Group	Number	HBsAg +		HBsAg –	
		No.	%	No.	%
Thalassemia major	254	1	0.4%	253	99.6%
Control	150	0	0%	150	100%
Total	404	1	0.3%	403	99.7%
P-value=0.9		Non-Significant			

Table (3): HIV status in both TM and control group.

Group	Number	HIV Elisa +		HIV Elisa –	
		No.	%	No.	%
Thalassemia	254	0	0%	254	100%
Control	150	0	0%	150	100%
Total	404	0	0%	404	100%
Non-Significant					

Table (4): TRI in TM patients at other Iraqi governorates in miscellaneous time periods.

Governorate	Patient No.	period	HCV + No. (%)	HBV +No. (%)	HIV +No. (%)
Diyala ^(10,11)	110	Jan.1999- Dec. 2000	29/110 (26.4%)	7/110(6.4%)	0(0%)
Basra ⁽¹²⁾	200(including sickle cell)	Nov.1998-May 1999	19(9.5%)	N/A	N/A
Mosul ⁽¹³⁾ IBN AL Alatheer children hospital	626	Aug. 2003-Aug.2004	164(26.2%) Note:12(1.92%) had both HCV&HBV	23 (3.67%)	N/A
Mosul ⁽¹⁴⁾	200	2011	34 (17%)	N/A	N/A
Baghdad 1-Ibn Al Balady teaching hospital, Baghdad ⁽¹⁵⁾	559	1998 Published 2006	376 (67.3%)	N/A	N/A
Baghdad 2-Ibn- AlBalady hospital center and Al-Karamh Hospital ⁽¹⁶⁾	100	Oct.2010- May 2011	21%	2.5%	0(0%)
Babylon ⁽¹⁷⁾	56	Nov.2011 - June 2012	16/56 (25%)	0(0%)	N/A
Kirkuk(Our study)	254	Jan.2010 - Jan. 2012	85/254(33%)	1/254(0.35%)	0(0%)

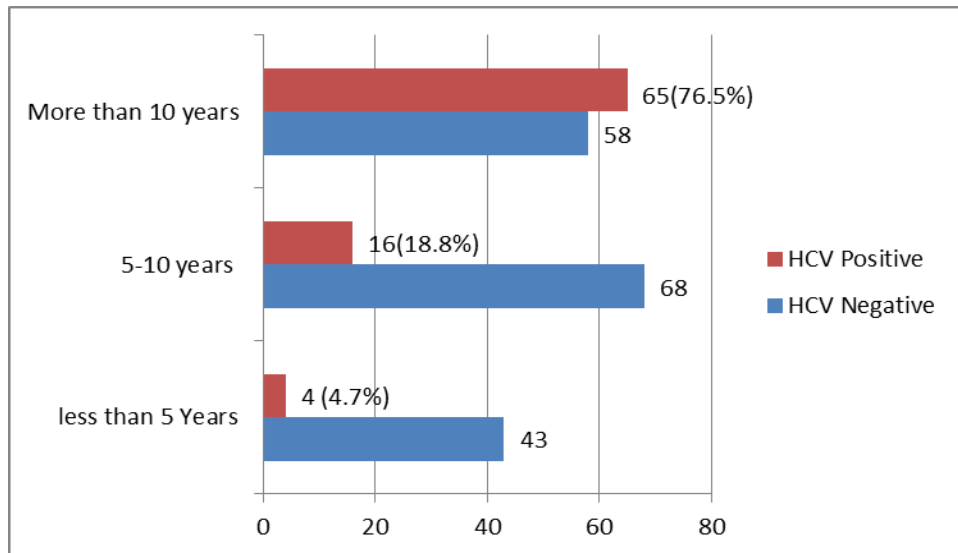
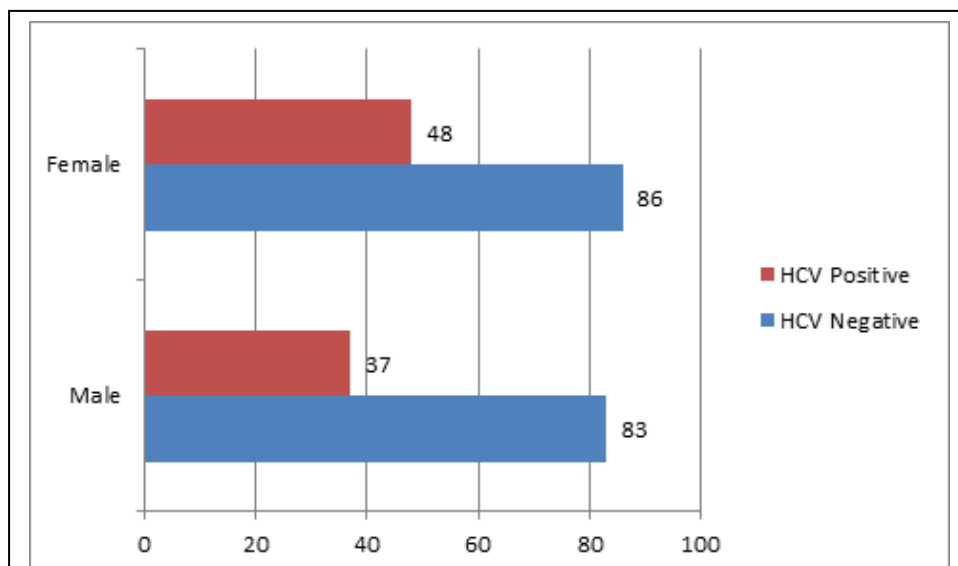


Figure (1):HCV status in TM patients according their age categories.

Note: Quantities shown are the exact patient numbers in each bar line.



Figure(2):Sex exact number bar chart according to HCV test result.

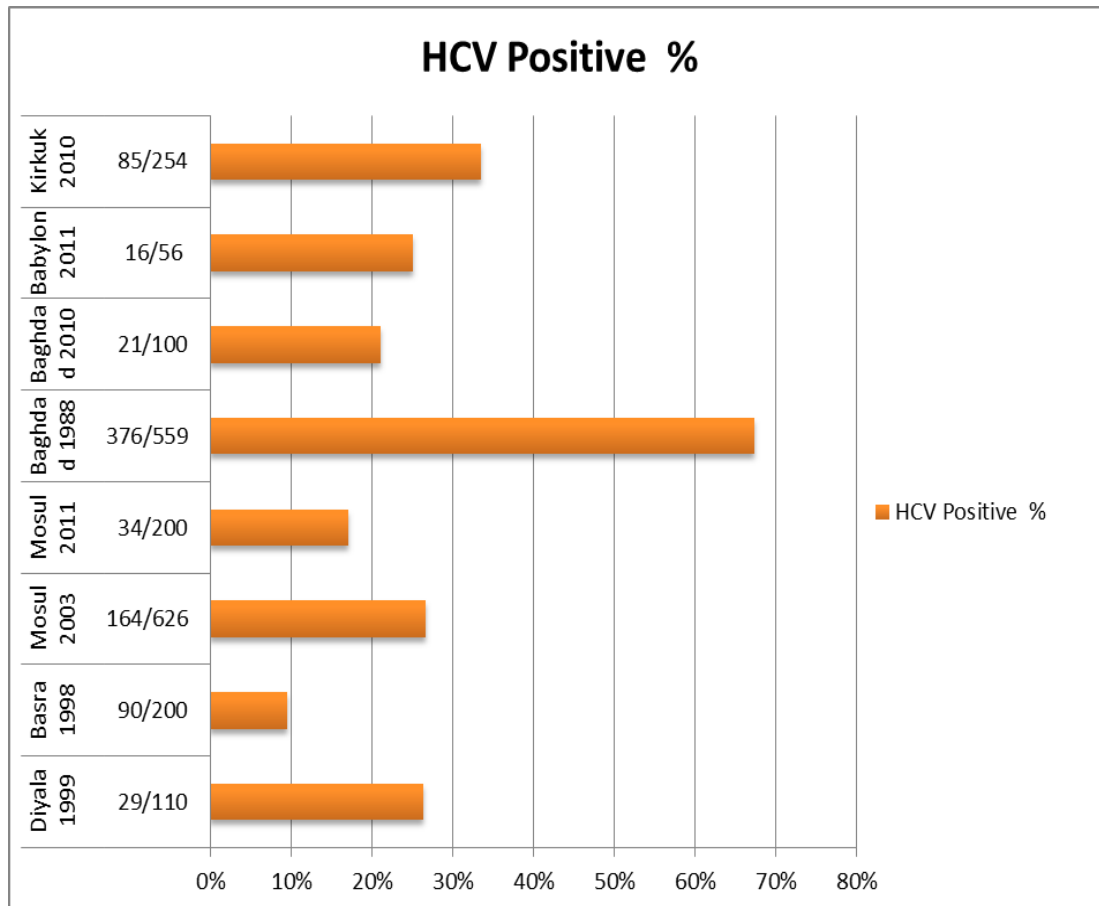


Figure (3):Bar chart for HCV test results in TM patients at different Iraqi governorates.

Discussion:

The feared consequences of transfusions in thalassemia patients include (TRI) such as HBV, HCV, and HIV, as these infections can result in long-term morbidity and mortality. This probability depends on the prevalence of carriers among the blood donors in the population and the number of units transfused. Thus, the infection rate of (TRI) increases with age in subsequent years. In Kirkuk, it had become a policy to screen donated blood for HCV and

HIV since 2004, while HBV screening program started since nineties. This residual risk of (TRI) transmission from screened blood depends on the safety of donor population, sensitivity of the screening tests used, window-period donations and the mutant strains⁽⁹⁾.

Literature on the rates of HCV infections among TM patients in other Iraqi governorates shows nearly similar values. This is summarized in table 4 and figure 3.

From the bar chart it is clear that 1988 Baghdad study that was done in Ibn Elbalady Hospital had the highest registration rates for positive HCV among TM patients by nearly two-third (67%). The existence of hepatitis C (that was originally identifiable non-A non-B hepatitis) was postulated in the 1970s and proven in 1989⁽¹⁸⁾. Before the introduction of screening of blood donors for hepatitis C virus, the risk of acquiring HCV infection as a result of transfusion was (10%)⁽¹⁹⁾. Ten years later, two similar studies were done in Basra 1998 and Diyala 1999 and showed that around one quarter of TM

patients had positive HCV test. Similarly, Mosul study 2003 recorded positivity in (23%) of patients. Lastly, our study reveals around one third (33%) of TM patients have HCV positive test result. Parallel to Kirkuk study, two other studies in Babylon 2011 and Baghdad 2010 demonstrate HCV infection in TM to be around one quarter and one fifth, consecutively. The percentages of TM with HCV test positive in different Iraqi governorates is considered high especially if we know that Iraq is considered a country of low endemicity (<2%) for HBV and HCV, as the prevalence of HBs Ag was (1.6%) and that of Anti HCV Ab was (0.4%) in general population according to the World Hepatitis Alliance, 2010.

In comparison with other countries, many similar studies are available. For example, Alavian et al conducted a literature review on 8554 TM patients recorded in 40 studies in four countries: Iran, Pakistan, Saudi Arabia and Egypt. The review found that HCV seropositivity were (18%), (45%), (63%) and (69%), respectively⁽²⁰⁾. This may be a reflection of the high prevalence of HCV in citizens of these countries. In addition to that, a three-year prospective study was done in India by Choudhury et al⁽²¹⁾, shows increasing rates on three consecutive years at (23%), (30.7%), and (35.9%). While in a recent study done in UAE on 102 patients with hereditary anemia just (3%) of the patients had HCV and 2/102 had HIV, while none of them had Hepatitis B Virus⁽²²⁾.

An important finding in the present study regarding age category is that three quarter (76.5%) of TM patients with positive HCV test were above 10 years old. This is understandable as the number of

exposure to blood units increases with advancing age. Secondly, screening of HCV and HIV started in Kirkuk blood bank in 2004. This means that many blood donations done from carriers without being recognized.

On the other hand, comparing HBV status of TM patients in our center with other Iraqi governorates reveals only one positive Hepatitis B among TM patients in our study. In contrast, it was (6.7%) in DIALA^(10,11), (3.7%) in Mosul⁽¹³⁾, (2.5%) in Baghdad⁽¹⁶⁾ and zero in Babylon⁽¹⁷⁾. Internationally, many prevalence studies for HBV infection among TM patients range from (0.53%) to (7.4%)^(23,24).

Lastly, HIV has neither been detected in TM patients nor in the control group. This could be a reflection of extremely rare registration of HIV among Iraqi citizens.

Conclusion:

This study revealed that of the 254 multi-transfused thalassemia patients, (33.5%) were reactive for anti-HCV, (0.4%) patient was reactive for HBV, and no patient was reactive for HIV. It is concluded that HCV is the current major problem in multi-transfused children with TM and more careful pretransfusion screening of blood for anti-HCV must be introduced in our blood banks.

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