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Detection of Hepatitis C Virus among Thalassemic and Hemophilic Patients in Diyala Governorate

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Abstract

Background: Transfusion therapy is now a vital medical to treat patients with different diseases such as anemia, cancer, hemophilia, thalassemia, sickle cell disease and thrombocytopenia to improve the oxygen carrying capacity of blood.

Objective: To determine the frequency of hepatitis C virus in patients with thalassemia and hemophilia in Diyala Governorate.

Patients and methods: Cross sectional study were done in transfusion center in Al-Batool Teaching Hospital for Maternity and Children in Baqubah city during the period from 11th October 2022 till 8th January 2023, the study groups were classified into two groups,14 patients with thalassemia and 11 patients with hemophilia, their age range from 6 to 60 years. All study groups diagnosed using enzyme linked immunosorbant assay for qualitative antibodies detection to HCV in human serum.

Results: The overall frequency of HCV infection was 2% (14 of total 700) in patients with thalassemia, while 11 out of 130 (8.6%) in patients with hemophilia. The anti-HCV seropositivity was highest in males 71.43% and 81.81% than females 28.57 and 18.19% among patient with thalassemia and hemophilic respectively. Regarding of age group, the highest infection rates (50%) was noticed in age group 31-45 years old in-patient with thalassemia while 45.46% show high frequency was noticed in age group 16-30 years Blood group O+ve individuals were commonly infected with HCV 6(42.86%) and 5(45.45%) followed by blood group B+ve 4 (28.58%) and 3(27.28%).

Conclusion: The percentage of HCV infection among β- thalassemia was 2%while 8.6% in patients with hemophilia A was comparable with other Iraqi studies.

Keywords: Blood transfusion; thalassemia, hmophilic, hepatitis C Virus, co-infection.

Introduction

Transfusion with red blood cells is a mainstay in the prevention or treatment of complications associated with the more serious congenital hemolytic anemias. These disorders include hemoglobinopathies, red cell enzyme deficiency disorders, and abnormalities of the red cell membrane. Particular emphasis is devoted to the relatively common hemoglobin disorders, including sickle cell disease and thalassemia syndromes [1].

Hemophilia is a genetic bleeding disorder and categorized into two types hemophilia A and B is treated by recombinant clotting factor VIII or factor IX and immunosuppressives to prevent formation of alloantibodies and inhibitors. Formation of inhibitors to these factors poses a challenge in treating hemophila. Plasma derived activated prothrombin complex concentrate and activated recombinant factor VII are used to treat patients with inhibitors. Treatment also varies with situations such as, pregnancy, surgery, and malignancy, as these trigger increased risk of bleeding [2]. The most common form is factor VIII deficiency, or haemophilia A, which comprises approximately 80% of cases. Factor IX deficiency, or haemophilia B, comprises approximately 20% of cases [3]. Haemophilia is traditionally classified as ‘mild’, ‘moderate’, or ‘severe’, depending on the degree of clotting factor deficit compared with that found in the general population [4].

Thalassemia is one of the most common genetic abnormalities worldwide, affecting approximately 1.5 million of the population and resulting in serious health problems such as increased morbidity and premature death and financial and emotional strain on affected families. Thalassemia is classified into two types: alpha (α) and beta (β). Beta thalassemia is caused by a mutation in the beta-globin gene, whereas alpha thalassemia is caused by a mutation in the alpha-globin gene [5]. Patients with β-thalassemia major who regularly receive transfusions are at risk of developing post-transfusion hepatitis (PTH). Among these infections, hepatitis B virus (HBV) and hepatitis C virus (HCV) are the most common [6].

Hepatitis C virus is a hepatotropic RNA virus that causes progressive liver damage, which might result in liver cirrhosis and hepatocellular carcinoma [7]. Hepatitis C is a global health problem, with an estimated 71·1 million individuals chronically infected worldwide, accounting for 1% (95% uncertainty interval: 0.8-1.1) of the population. Hepatitis C virus transmission is most commonly associated with direct exposure to blood, via blood transfusions, unsafe health-care-related injections and intravenous drug use [8]. Hepatitis C virus infection is one of the most severe side effects of transfusion therapy in people with thalassemia and Sickle Cell Disease (SCD) [91]. It can lead to severe inflammation in liver with long-term problems such as disabling symptoms, cirrhosis, and hepatocellular carcinoma [10].

Many studies done in different Iraqi cities and showed different precentages such as [11][12][13]. The current study design to determine the frequency of hepatitis C virus in patients with thalassemia and hemophilia in Diyala Governorate.

Patents, Materials and Methods

Cross sectional study were done in transfusion center in Al-Batool Teaching Hospital for Maternity and Children in Baqubah city during the period from 11th October 2022 till 8th January 2023, the study groups were classified into two groups, 14 patients with thalassemia (10 males and 4 females) out of 700 patients and 11 patients with hemophilia (9 males and 2 females) out of 130 patients, their age range from 6 to 60 years.

All study groups diagnosed for detection of qualitative antibodies to HCV in human serum using enzyme linked immunosorbant assay.

Statistical analysis

All date analysis using number and percentage.

Results

The present study showed that HCV frequency in thalassemia was 2% (14 out of 700) while 8.46% in patients with hemophilia (11 out of 130) as shown in Figure 1. The infection with hepatitis C virus in relation to type of Beta thalassemia. The highest percentage (71.4 %) thalassemia major patients and positive for HCV antibody in comparison with (28.57 %) in intermediate thalassemia and positive for HCV antibody, while all positive HCV in hemophilia patients belong to type A.

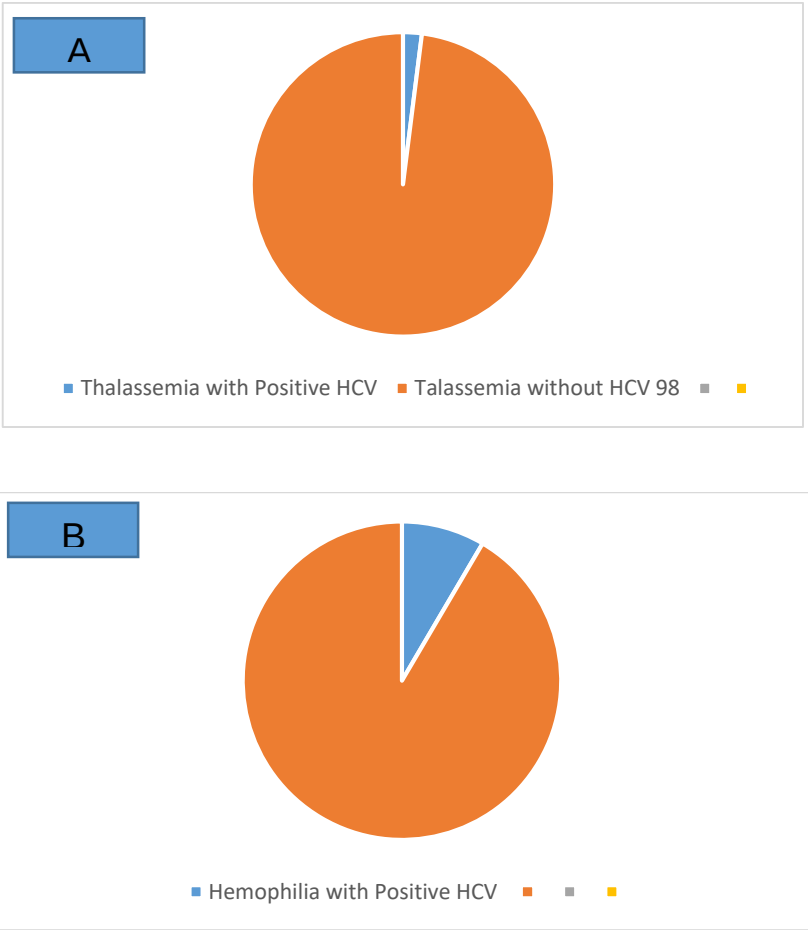

Figure 1: Percentage of HCV infection in patients with Thalassemia and Hemophilia**.**

The percentages of HCV infection was highest in males 71.43% and 81.81% than females 28.57 and 18.19% among patient with thalassemia and hemophilic respectively, as shown in Table 1.

Table 1: Gender Distribution in Study Population.

Name of Disease	Males	Females
Thalassemia	10(71.43%)	4(28.57%)
Hemophilia	9(81.81%)	2(18.19%)

Regarding of age group, the highest infection rates (50%) was noticed in age group 31-45 years old in-patient with thalassemia while 45.46% show high frequency was noticed in age group 16-30 years as shown Table 2.

Table 2: Distribution of Age in Study Population.

Age with years	Thalassemia	Hemophilia
1month-15	3(21.43%)	0
16-30	3(21.43%)	5(45.46%)
31-45	7(50%)	3(27.27%)
46-60	1(7.14%)	3(27.27%)
Total	14(100%)	11(100%)

High percentage of HCV infection among blood group O+ 42.86% and 45.45% followed by B+ 28.58% and 27.28% in patients with thalassemia and hemophilia as shown in Table 3.

Table 3: Distribution ABO Group in Patients with Thalassemia and Hemophilia.

Blood Groups	Thalassemia	Hemophilia
A+	2 (14.28%)	1(9.09%)
A-	1(7.14%)	1(9.09%)
B+	4 (28.58%)	3(27.28%)
B-	1(7.14%)	1(9.09%)
O+	6(42.86%)	5(45.45%)
O-	0	0
AB+	0	0
AB-	0	0
Total	14(100%)	11(100%)

Discussion

The current study demonstrated that, 2% (14 out of 700 patients) of all screened patients with thalassemia had serological evidence of hepatitis C and 8.46% (11 out of 130 patients with hemophilia) had serological evidence of hepatitis C virus. The result of thalassemia goes with other studies done in Iraq and showed different percentages in seropositive for HCV such as 1.59% in Nineveh province [14].3.8% in AD-Diwanya Province, Iraq [15], 7.86 % in Al-Najaf Governorate [16], 12.1% (26 out of 215) in Diyala Governorate using enzyme linked immunosornbant assay [17], 25% in Babylon Governorate [11] and 35% in Duhok Thalassemia Center, Iraqi Kurdistan [18]. The other studies from some neighboring countries reported an HCV infection rate of 19.3% in Iran [19], 4.5% in patients with thalassemia in Turkey [20]. While seropositivity rate was, lower in the present study than that recorded by Al-Fuzae etal. (33%) in Kuwait [21]. This different in prevalence of HCV infection attributed to different epidemiological distribution and risk factors of HCV infection between these countries.

The current study reported 8.46% (11 out of 130 patients with hemophilia) had hepatitis C virus, this result lower than other Iraqi studies like 15.48% in the Hemophilia unit in Children Welfare Teaching Hospital, Medical city in Baghdad [12],25.6% (9 out of 41) were positive for HCV in Al Karama teaching hospital in the city of Al Kut [22]. The prevalence of HCV infection in Iran ranged between 29%-83.3% in different cities. The lowest rate was in Zahedan and the highest in Tehran [23][24]. The rate of HCV infection in one study in Brazil was 42.2% [25]. It was lower in Pakistan 36% [26]. Some studies which was higher or lower than the current study which might be due to number of study population or type of technique use in detection. As well as could be related with lack of effective vaccine and inadequate infection control policies for HCV poses a significant and growing public health problem in low- and middle-income countries [27].

The current study we observed male predominance in both thalacemic and hemophilic patients than females these results were in agreement with the findings of Muhsin and Abdul-Husin in Babylon Governorate who found most of the patients with positive anti-HCV were in males group [11]. Al-Bakaa *et al*., 2020 who reported 15 were males 53.57 % and 13 females 46.42 % [16]. As well as agreed with [14][17][28]. Other study revealed insignificant difference between males and females with HCV infection so both sexes are almost equally infected with hepatitis C virus [29].

In this study showed a highest infection rates (50%) was noticed in age group 31-45 years old in-patient with thalassemia while 45.46% show high frequency was noticed in age group 16-30 years This finding is consistent with other study which reported that 522 (47%) of the cases was the largest group and the age group over the 40 years [30].

Regarding blood group high percentage of HCV infection among blood group O+ 42.86% and 45.45% followed B+ 28.58% and 27.28% in patients with thalassemia and hemophilia. This finding is disagreed with the results of [22]. ABO antibodies can be considered part of the

innate immune system against some bacterial pathogens and enveloped viruses that carry ABO-active antigens. A relation between the liability to develop hepatitis and the ABO blood groups could be related to host factors may be of importance in the genesis and due to geographical distribution, extended tribes and ethnic groups in local population. Also, this could be related with several genetic, developmental, and clinical conditions can affect ABO typing, with implications for epidemiology studies. In many epithelial tissues, ABO expression is heavily dependent on the inheritance of the Secretor/FUT2 gene [28].

In conclusion, the percentage of HCV infection among β- thalassemia was 2%while 8.6% in patients with hemophilia A was comparable with other Iraqi studies.

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References

1. Jefferies LC. Transfusion therapy in autoimmune hemolytic anemia. Hematol Oncol Clin North Am. 1994; 8(6):1053-86.

2. Nikisha GN, Menezes GA. Hemophilia and Its Treatment: Brief Review. International Journal of Pharmaceutical Sciences Review and Research. 2014; 26(14):277-283

3. World Federation of Hemophilia Report on the Annual Global Survey 2009 2011; Montreal: World Federation of Hemophilia. Available from: http://www.wfh.org/2/docs/Publications/Statistics/2009_Global_Survey_Report.pdf.

4. White GC, Rosendaal F, Aledort LM, Lusher JM, Rothschild C, Ingerslev J. Factor VIII and Factor IX Subcommittee Thromb Haemost 2001; 85:560.

5. Surani CC, Shah RV, Sinha M. A study of prevalence of hepatitis-B and hepatitis-C infection in thalassemic patients in a tertiary care hospital, Jamnagar, Gujarat, India. Int J Curr Microbiol App Sci; 2018; 7: 3142-3146.

6. El-Faramawy AA, El-Rashidy OF, Tawfik PH, Hussein GH. Transfusion transmitted hepatitis:Where do we stand now? A one-center study in Upper Egypt. Hepat Mon 2012; 12: 286-91.

7. Manns M, Buti M, Gane E. *et al.* Hepatitis C virus infection. Nat Rev Dis Primers. 2017; 3, 17006.

8. Roudot-Thoraval F. Epidemiology of hepatitis C virus infection. Clin Res Hepatol Gastroenterol. 2021; 45(3):101596.

9. Heit JA. Epidemiology of venous thromboembolism. Nat Rev Cardiol. 2015; 12: 464-474.

10. Ataei B, Hashemipour M, Kassaian N, Hassannejad R, Nokhodian Z, Adibi P. Prevalence of anti HCV infection in patients with Beta-thalassemia in Isfahan-Iran. Int J Prev Med. 2012; 3:S118-23.

11. Muhsin MA and Abdul-Husin IF. Seroprevalence of Hepatitis B and C among Thalassemic, Haemophilic patients in Babylon Governorate-Iraq Medical Journal of Babylon. 2013; 10(2):

12. Abdul Razak MK and Mishlish SM. The Epidemiological Characteristics of Hepatitis C Virus among Patients with Inherited Bleeding Disorders. Journal of Natural Science Research. 2017; 7(2): 53-60.

13. Abdul Razak MK. The prevalence of Hepatitis C Virus infection and potential risk factors among multiply transfused patients. Asian J Pharm Clin Res, 2019; 12(1): 473-477.

14.Dawood AA, Khaleel AM, Hayawi AM. Estimate Viral RNA of Hepatitis C of β-Thalassemia Patients in Nineveh Province. European Journal of Molecular and Clinical Medicine. 2020 7(10):3

15.Jallab HR, Eesa ZM.Prevalence of Hepatitis B and Hepatitis C Viruses in β-thalassemia Major Patient in AD-Diwanya Province, Iraq. Indian Journal of Forensic Medicine & Toxicology, 2A020; 14(2):

16.Al-Bakaa AA, Al-Haris FM, Nasrawi AJM, Al-Saaidy KR. Hepatitis C Genotyping And Viral Titers Among Patients With Beta Thalassemia Major in Al-Najaf Governorate - Iraq. 2020; Supplementary Issue 1

17. Mehdi SH. Al-Zuheiry.The Prevalence and the Quantification of Hepatitis C Virus among Thalassemia Patients using ELISA and PCR in Diyala Province. Diyala Journal of Medicine. 2016 (10):68.

18.Sadullah RK, Atroshi SD and Al-Allawi NA. Complications and Challenges in the Management of Iraqi Patients with β-Thalassemia Major: A Single-center Experience. Oman Medical Journal. 2020; 35(4): e152

19. Shahram M., Moayed A., Behzad H., Jafar K., Babak Y., Mohammad J.,etal."Epidemiology of Hepatitis B, Hepatitis C, and human Immunodeficiency Virus Infections in Patients with Beta-Thalassemia in Iran: A multicenter Study" Iranian Med.J.; 9 (4): 319 – 323, 2006.

20. Sabahattin O., Hasan K., Meryem C., Edip G., Muge O. " Seroprevalence of Hepatitis B

and Hepatitis C in Patients with Thalassemia and Sickle Cell Anemia in a Long-term Follow-up" Archives of Medical Research Mexicano J. 37(7), 895-898, 2006.

21. Al-Fuzae L, Aboolbacker KC, Al-Saleh Q. "Betathalassemia major in Kuwait" J. Trop

Pediatr.; 44: 311 – 312, 1998.

22. Faraj SA, Ansaf A. Frequency of Hepatitis B and C Sero Markers Among Hemophiliacs and Von Willebrand's Disease in Alkut, Iraq. Journal of Global Pharma Technology. 2017; 06(9):109-115.

23. Sharifi MB, Eshghi P, Sanei-Moghaddam E, Hashemi M. Hepatitis B and C virus infections in patients withhemophilia in Zahedan, southeast Iran.Saudi Med J. 2007; 28: 1516–9.

24. Zahedi MJ, Darviesh MS. Assessment of prevalence of hepatitis B and C in hemophilic patients in Kerman in 1383. J Kerman Univ Med Sci.2008; 3:131–5.

25. Silva LK, Souza da Silva MB, Lopes GB, Rodart IF, Costa FQ, Santana LP et al. Prevalence of hepatitis C virus infection and HCV genotypes among hemophiliacs in the State of Bahia, Northeastern Brazil: analysis of serological and virological parameters. Rev. Soc. Bras. Med. Trop. 2005; 38 (6).

26. Naghmi A, Tahira Z, Khalid H, Lubna N. Seroprevalence Anti HCV Antibodies, HCV-RNA and its Genotypes among Patients of Hemophilia, at Hemophilia Treatment Centre Pakistan Institute of Medical Sciences, Islamabad. Int J. 2009;7:84-7.

27. Rezvan H, Abolghassemi H, Kafiabad SA. Transfusion-transmitted infections among multitransfused patients in Iran:A review.Transfus Med 2007;17:425-33.

28. Hussin, A.G. Seroepidem-iological survey of Hepatitis B surface antigen and antibodies of Hepatitis C in Babylon province. MSc .thesis. Babylon University. collag of medicine. 1997.

29. Noaman NG. Prevalence of Hepatitis C Virus Infection among Blood Donors and Certain Risky Groups in Diyala Province. Diyala Journal of Medicine. 2012; 2(1): 46-52.

30. Jafroodi M, Davoudi-Kiakalayeh A, Mohtasham-Amiri Z, Pourfathollah AA, Azade Haghbin.Trend in Prevalence of Hepatitis C Virus Infection among β-thalassemia Major Patients: 10 Years of Experience in Iran. International Journal of Preventive Medicine.2015

31. Cooling L. Blood Groups in Infection and Host Susceptibility. Clin Microbiol Rev. 2015; 28(3):801- 870.