Blood Groups and Susceptibility to Hepatitis C Virus Infection Among β- Thalassaemia Patients

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Abstract

Background: Blood groups have revealed associations with a variety of diseases. However, most of these studies concerned general population and only few of them the potential relationship with viral hepatitis.

Objective: To investigate the association of ABO and Rh blood groups with hepatitis C viral infection in β- thalassaemia patients.

Patients and Methods: A retrospective study was conducted during 2014 at Thalassaemia Center. Hepatitis C ELISA test and blood groups of β- thalassaemia patients were recorded. Statistical Package for Social Sciences software, version 20, was used to analyze data.

Results: Total enrolled patients were 215, seropositive hepatitis C was evident in 24 (11.2%). The overall distribution blood groups among thalassaemia patients was compatible with that of general population. Regarding seropositive hepatitis C patients, most (n=20, 83.3%) were A and B blood groups, only 3 patients (12.5%) were O, and 1 patient (4.2%) AB. Therefore, hepatitis C was significantly associated with groups A and B and those who have group O were spared (p value .014). Most of patients were Rh D positive and no significant effect (p value .392) on hepatitis C could be found.

Conclusion:In β- thalassaemia, most of the hepatitis C infected patients were blood groups A and B whereas blood group O patients seemed to be less susceptible or protected against this infection.

Key words: ABO/ Rh blood group, Hepatitis, Thalassaemia.

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Introduction

ABO blood groups are a set of antigens (agglutinogens) that are genetically determined molecules of carbohydrate carried on the red blood cell surface membranes. Anti-A and Anti-B are mostly IgM antibodies formed in the infancy by sensitization to environmental antigens, such as bacteria, viruses, and foods. They are not red blood cell antibodies but usually bacterial

antibodies, cross – reacting with red blood cells [1- 3].

The relationship of ABO blood groups with some hematological and non- hematological disorders has been reported previously. The frequency of blood groups B and O in patients with type 2 diabetes mellitus was significantly higher and lower, respectively [4]. The most significant blood group-disease associations described for non-O versus O subjects is susceptibility to both venous thrombo-embolism (VTE) and arterial (ischemic heart disease) which is possibly due to high level of von Willebrand factor and clotting factor VIII and it was found that patients of group A2 have lower levels of these factors than A1, B, and AB, so they have a lower risk of VTE [5-7]. The ABO blood group phenotype frequencies in patients with lymphoma were comparable to those found in control group. Total serum cholesterol, systolic/diastolic blood pressure and blood glucose were all significantly higher in both male and female patients with O versus non- O blood groups, with a declining trend from A to B then AB group [8]. Regarding ABO blood group association with thalassemia, no significant association was observed [9].

The Rh blood group system is the most polymorphic of the human blood groups, consisting of at least 45 independent antigens, D antigen is the most common and, next to ABO, is the most clinically significant in transfusion medicine [10]. It had been related with many clinical conditions, a significant association of gingivitis/periodontitis with Rh positive blood group individuals as compared with Rh-ve [11]. In Pakistan, a study found that Rh negative blood group is more frequent in diabetic patients [12]. A study carried out on 250 blood donors had shown that the resistance to toxoplasmosis is higher in Rh-positive than in Rh negative subjects [13].

Hepatitis C virus (HCV), since its characterization in 1989, has been shown as a primary cause of post transfusion non-A, non-B chronic hepatitis [14]. Many studies have shown that ABO blood groups are a risk factor for both hepatitis B and C virus infection [15]. In chronic hepatitis C infection, non-O blood group has been related to progression of liver fibrosis [16]. Nevertheless, the exact mechanism underlying these association remains unclear [17]. Although several studies have assessed the association of blood groups with blood-borne infections, most of them were concerning the general population. The aim of this study was to investigate if susceptibility to hepatitis C in thalassaemia patients is associated with certain ABO and Rh blood groups.

Patients and Methods

A retrospective study was conducted from June to September 2014 at Center of β-thalassaemia at Al- Batool teaching Hospital for Maternity and Children in Baquba city-Diyala province/ Iraq. All registered multi-transfused β- thalassaemia patients, whatever their age, were enrolled in the study.

Anti-HCV results and blood typing (ABO and Rh blood type) were retrospectively

recorded. Anti-HCV antibody had been routinely tested every 6 months using Enzyme-Linked Immunosorbant Assay ELISA (BioTeck, USA) per manufacturer's instructions. Every positive result was confirmed by recombinant immunoblot assay.

Matching of ABO blood group distribution in thalassaemia patients was carried out with general population of the neighboring Babylon and Missan provinces, those provinces having the same ethnic Arabic population background as that of the study area.

The International Society of Blood Transfusion (ISBT) numerical terminology for red cell surface antigens was used to express blood groups together with conventional medical terms in tables, as the followings: ABO blood group (001), A blood group (001001), B (001002), AB (001003), O (001005), Rh blood group (004), RhD positive (004001) [18].

Statistical Analysis

Nonparametric chi square test was applied for matching the thalassaemia patient's blood groups with general population; Pearson chi-square test was used to assess the associations between blood groups and results of hepatitis C serology, the level of significance being set at 0.05 level. Statistical Package for Social Sciences (SPSS) software, version 20, was used to analyze data.

Results

The enrolled patients were 215, most of them being under 12 years old (p value .000); male gender was slightly prevailing, p value (0.152) table (1).

Table (1): Distribution of the study group patients according to the age and gender.

Age/ Gender	Male [a] number (%)	Female number (%)	Total number (%)
1year - < 12 yr	71 (33)	55 (25.6)	126 (58.6)**
12 yr-< 18 yr	22 (10.2)	20 (9.3)	42 (19.5)
≥ 18 yr	25 (11.7)	22 (10.2)	47 (21.9)
Total	118 (54.9)	97 (45.1)	215 (100)

** p value (.000)
[a] p value (0.152)

ABO and Rh D blood groups distribution were comparable among thalassaemia patients of this study and general population of both Babylon and Missan provinces, with a trend towards an excess of O blood group, then B and A , and lastly AB group regarding ABO blood group and Rh positive followed Rh negative , regarding Rh D blood group, in the study group and mentioned populations [19,20]. High statistical significant value for predominance of both O and Rh positive blood groups, p value (.000), table(2).

Table (2): ABO (ISBT terminology) blood group distribution in the thalassaemia group versus general population in Babylon and Missan provinces.

Blood group (ISBT terminology)		Study group %	General population in Babylon [a,c] %	General population in Missan [b,d] %
ABO blood groups	A (001001)	30.7	27.7	22.57
	B (001002)	22.8	28.3	33.26
	AB (001003)	7.4	8.3	8.75
	O (001005)	39.1	35.7	35.42
Rh blood groups	Rh D positive (004001)	91.2	90.1	88.66
	Rh D negative	8.8	9.9	11.34

[a,b] Distribution of ABO blood group of the study group versus general population of Babylon (p value = .595) and Missan (p value= .075).
[c,d] Distribution of Rh D blood group of the study group versus general population of Babylon (p value = .809) and Missan (p value= .637).

Twenty four thalassaemia patients(mean age ± standard deviation = 18.3 ± 6.6 years), representing about 11.2 % of the enrolled subjects, were HCV positive. Most of them were thalassaemia major (n=17, 71%) and the remaining having thalassaemia intermedia. Blood groups of most HCV patients were equally distributed between A and B (n=20, 83.3%), 3 patients (12.5%) had blood group O, and 1 patient (4.2%) AB group, whereas group O was strongly dominant in HCV negative patients (n=81, 42.4), thus blood group O was less associated with HCV infection. HCV infection was detected in 11.7% of Rh D positive and in one patient (5.3 %) of Rh D negative patients, this trivial difference was statistically not significant, table(3).

Table (3): Results of Anti- Hepatitis C antibody according to the blood group in whole study group.

Blood group (ISBT terminology)		Anti- Hepatitis C antibody		Total number (%)
		Positive number(%)	Negative number (%)	
ABO blood groups	A (001001)	10 (4.7)	56 (26)	66 (30.7)
	B (001002)	10 (4.7)	39 (18.1)	49 (22.8)
	AB (001003)	1 (0.4)	15 (6)	16 (7.4)
	O * (001005)	3 (1.4)	81 (37.7)	84 (39.1)
	Total	24 (11.2)	191 (88.8)	215 (100)
Rh blood groups [a]	Rh D positive (004001)	23 (11.7)	173 (88.3)	196 (91.2)
	Rh D negative	1 (5.3)	18 (94.7)	19 (8.8)
	Total	24 (11.2)	191 (88.8)	215 (100)

* p value (.014)
[a] P value (.392)

HCV patients with blood group O were thalassaemia major while the remaining were thalassaemia major and intermedia, but the difference was statistically not significant, p value (530).

Discussion

A relationship between host ABO/Rh blood groups and hepatitis remains controversial [21]. In the current study, the multi-transfused β- thalassaemia patients showed a matched distribution of their ABO blood groups with general population; blood group O being the dominant one. HCV infection was detected serologically in 11.2% of the enrolled patients. There were considerable differences regarding distribution of ABO blood groups between seropositive and seronegative hepatitis C, with groups A and B being the most represented, whereas blood groups AB and O were less likely to be infected.

Many studies have been performed concerning hepatitis relationship with blood group, but they considered general populations and not specifically thalassaemia patients. In a study carried out in Thailand, it was observed that blood group O donors were significantly less HCV infected than the A blood group donors, which is in agreement with the present results [22].

Several studies showed different results from ours. A study, done in Al-Ramadi population/ western Iraq [23], did not show an association between hepatitis C virus

infection and blood groups. Another study, performed in apparently healthy blood donors in Port Hartcourt, Nigeria, found that no significant connection between HCV prevalence and blood groups [24]. An Iran studies [1,25] did not note any relationship between ABO/Rh antigens and sero-positivity of HCV or chronic hepatitis C infection, whereas Behal et al. [15] found that blood groups O and AB individuals has higher and lower HCV seroprevalence, respectively. Other study have reported a significant relationship of blood group O with HCV [21]. These discrepancies might be due to possible antigenic differences between the studied populations, including β- thalassaemia patients in the present study who may be different from general population studies, or it might be due different study designs, including sample size.

In the second part of the present work, we investigated the association of HCV with Rh blood group. The percentage of Rh D negative patients was low when weighted against Rh D positive patients in both seropositive and seronegative groups of the study, which is usually expected because of the natural low frequency of Rh D negative blood group in human beings. Even so, Rh D positive blood group in seronegative hepatitis C patients was double as the percentage of seropositive cases, this difference however being statistically not significant. Many previous studies showed no association of hepatitis C with Rh D antigen, in agreement with the current study data, while Omar et al observed that the frequency of hepatitis B and C infected donors were higher among Rh positive donors [1,21,24-26].

Although the precise underlying mechanism of association of certain blood groups with hepatitis C infection remains elusive, many explanations can be evoked, it can be hypothesized that there might be a shared receptor-binding affinity between the enveloped HCV and ABO antigens of blood groups A or B, it also has been suggested that blood group antigens are receptors for several microorganisms [21]. Furthermore, a genome-wide association studies have noted a relationship between genetic variation in the first intron of the ABO genes and many other factors, including circulatory levels of tumor necrosis factor, soluble intracellular adhesion molecule and serum levels of alkaline phosphatase [27-29]. Presence of anti- A and anti- B antibodies in patients with blood group O might be functioning to give combined protective effect against HCV.

Conclusions

In the light of the present results, most of HCV infected β- thalassaemia patients were blood groups A and B whereas group O patients seemed to be less susceptible to this infection. Larger scale studies are however warranted to confirm these data. The mechanism of the association between certain blood groups and HCV infection also needs further studies at the levels of biochemical, molecular, and genetic

analyses. In the meantime, we should pursue information with educational and work programs to prevent HCV transmission, with special emphasis on the likely target groups, including thalassaemia patients.

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