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Association Between ABO Blood/ Rhesus Grouping and Hepatitis B and C: A Case-control Study

Abolfazl Pourhassan

Department of Tropical and Infectious Diseases, Tabriz University of Medical Sciences,
Iman Reza Hospital, Tabriz, Iran

Abstract: During past decades, a connection between hepatitis and the host ABO/Rh blood groups has been always under dispute, with no appropriately designed study yet. This study aimed to investigate possible association between ABO blood/Rh groups with both hepatitis B and C. In this case-control setting, 200 healthy individuals (controls), 200 patients with chronic Hepatitis-B infection (HB) and 200 patients with chronic Hepatitis-C infection (HC) were recruited from 2010 to 2013 in Tabriz Sina Hospital. ABO blood and Rh grouping was performed and the results were compared between the case and control groups. Both pair of the control and HB groups and the control and HC groups were matched for their subjects' age and sex. In the control group, 178 subjects (89%) were Rh+ and 22 subjects (11%) were Rh-. In the HB group, there were 180 Rh+(90%) and 20 Rh-(10%) patients. In the HC group there were 168 Rh+(84%) and 32 Rh-negative (16%) patients. Both pair of the control and HB groups ($p = 0.74$), as well as the control and HC groups ($p = 0.14$) were comparable for the status of Rh. In the control group there were 84 (42%), 32 (16%), 66 (33%) and 18 (9%) subjects with A, B, O and AB blood groups, respectively. The corresponding figures were 84 (42%), 34 (17%), 58 (29%) and 24 (12%) for the HB patients; and 80 (40%), 29 (14.5%), 85 (42.5%) and 6 (3%) for the HC patients. Comparing between the control and HB groups showed no significant difference in terms of the frequency of ABO blood groups ($p = 0.70$). However, with comparing the control and HC groups, the rate of O blood group was significantly higher in the HC group and concomitantly, the rate of AB blood group was significantly higher in the control group ($p = 0.04$). Although, there is not a significant association between ABO blood groups and HB, this association is significant between certain ABO blood groups and HC.

Keywords: Hepatitis C, hepatitis B, ABO blood groups, Rh

INTRODUCTION

Two major forms of hepatitis, B (HB) and C (HC), are among the most serious and very prevalent diseases. These two viral infectious diseases are among the major health problems, especially in developing countries (Rifat-uz-Zaman, 2006; Hejazi *et al.*, 2007; Bidgoli *et al.*, 2007; Hemeida *et al.*, 2011; Sohail *et al.*, 2011; Kilic *et al.*, 2012; Barakat *et al.*, 2012; Abo Elmagd *et al.*, 2011).

It is estimated that approximately 2 billion people are infected with HB virus worldwide, among them 350 million are chronic carriers of the virus. HB infection is the 10th cause of death (Kao and Chen, 2002; Lavanchy, 2004; Shepard *et al.*, 2006).

HC virus is the main cause of transfusion-related non-A, non-B hepatitis. According to official reports, over 200 million individuals suffer from chronic HC infection all over the world. Its prevalence varies between 0.1% in western countries to over 18% in developing regions. It is believed that the most efficient transmission of HC virus is via blood transfusion (Barth *et al.*, 2006; Zeisel *et al.*, 2009).

The connection between various infectious diseases and blood groups has been discussed enthusiastically during recent decades. It has been proposed that this connection is possibly due to interaction between microorganisms and red blood cell membrane, which can be justified by antigenic similarity, affinity toward common receptors or deregulation of antibody response (Mandell, 2009).

This association has been hypothesized in both hepatitis B and C, as well (Behal *et al.*, 2008, 2010). However, to the best of our knowledge, there has not been yet a well-designed case-control study in this regard in the literature. The present study aimed to investigate a possible association between ABO/rhesus (Rh) blood groups and hepatitis B/C infections in an apt-designed setting.

MATERIALS AND METHODS

In this case-control setting, 200 healthy individuals (the control group), 200 patients with chronic hepatitis-B

infection (the case group number 1, HB) and 200 patients with chronic hepatitis-C infection (the case group number 2, HC) were recruited from 2010 to 2013. This study was carried out in Tabriz Sina Teaching Hospital, Department of Infectious Diseases. The controls were selected randomly from blood donors (repeat donors were not included).

The hepatitis-C infection was diagnosed by detection of anti Hepatitis C Virus (HCV) antibody using Enzyme Linked immunosorbent Assay (ELISA) technique (Ortho Clinical diagnostics, Inc. 3rd generation, New Jersey, USA) and confirmed by immunoblot assay.

Similar process was done for detection of hepatitis-B surface antigen (HBsAg) and confirmation of hepatitis-B infection. These methods were also employed for rolling out infections in the controls. No patient was infected simultaneously with HB and HC viruses.

A thorough clinical history taking and medical examination were carried out in all participants.

ABO blood and rhesus (Rh) grouping was performed based on conventional methods. Accordingly, subjects were categorized as ABO blood group A, B, O, or AB and Rh-positive (Rh+) or Rh-negative (Rh-).

This study was confirmed by the ethics committee of Tabriz Azad University and informed consents were obtained from the participants.

Statistical analysis: Data were shown as Mean±Standard Deviation or number (%). The SPSS software for Windows (ver.16) was used. Independent samples t test (for age) and the Chi-square test (for sex and the status of ABO blood groups and Rh) were employed for analyzing. All comparisons were performed in two pairs: Control group vs. HB group and control group vs. HC group. $p = 0.05$ was considered statistically significant.

RESULTS

In the control group, there were 120 males (60%) and 80 females (40%) with a mean age of 37.9 ± 11.0 (range: 18-68) years.

In the HB group, there were 114 males (57%) and 86 females (43%) with a mean age of 35.6 ± 12.2 (range: 23-71) years. In the HC group, there were 130 males (65%) and 70 females (35%) with a mean age of 38.9 ± 10.3 (range: 25-64) years.

Both pair of the control and HB groups (age: $p = 0.49$, sex: $p = 0.54$) and the control and HC groups (age: $p = 0.37$, sex: $p = 0.30$) were matched for their subjects' age and sex.

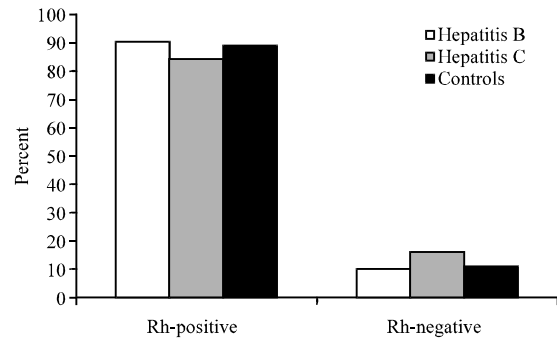


Fig. 1: Rate of Rh-positive and Rh-negative subjects in three studied groups

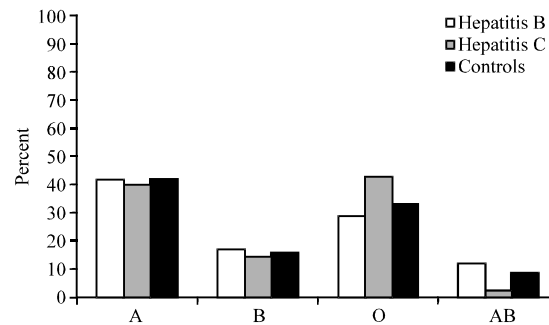


Fig. 2: Rate of ABO blood groups in healthy controls, hepatitis-B positive patients and hepatitis-C positive patients

The Rh status in the studied three groups is summarized in Fig. 1. Accordingly, 178 subjects (89%) in the control group were Rh+ and 22 subjects (11%) were Rh-. In the HB group, there were 180 patients (90%) with Rh+ and 20 patients (10%) with Rh-. In the HC group, Rh was positive in 168 patients (84%) and negative in 32 patients (16%). Both pair of the control and HB groups ($p = 0.74$) and the control and HC groups ($p = 0.14$) were comparable for the status of Rh.

The rate of ABO blood groups in the studied subjects are shown in Fig. 2. Based on this figure, in the control group there were 84 (42%), 32 (16%), 66 (33%) and 18 (9%) subjects with A, B, O and AB blood groups, respectively. The corresponding figures were 84 (42%), 34 (17%), 58 (29%) and 24 (12%) for the HB patients; and 80 (40%), 29 (14.5%), 85 (42.5%) and 6 (3%) for the HC patients.

Comparing between the control and HB groups showed no significant difference in terms of the frequency of ABO blood groups ($p = 0.70$). However, with comparing

the control and HC groups, the rate of O group was significantly higher in the HC group and concomitantly, the rate of AB group was significantly higher in the control group ($p = 0.04$).

DISCUSSION

The notion of the association between hepatitis-B infection and blood groups dates back to a rather old study by Zuckerman and McDonald, 1963 who proposed that A blood group is a risk factor for HB infection, while O blood group was a protective factor in this regard. Since then, some investigators have reported certain roles for ABO blood group in patients with hepatitis-B. For example, in a recent study, Li *et al.* (2012) proposed that ABO blood group may contribute to increased risk of hepatocellular carcinoma in patients with HB infection. In another example, Wang *et al.* (2012) showed that there might be an association between A blood type and increased risk of pancreatic cancer in HB-positive case.

Despite these very important reports, hitherto there has not been any well-designed, case-control study for determining a definite association between ABO blood groups and HB infection; one of the main purposes of the current study. According to our findings, there was not a significant association between ABO blood groups, or Rh status, with chronic HB infection.

This finding is in conformity with the results of a study by Behal *et al.* (2008), who showed that although HBsAg was more frequently seen in B blood group donors and less frequently in AB blood group donors, there was not a significant association between ABO blood groups and hepatitis-B. They also did not confirm a significant connection between the status of Rh and HB infection.

It should be born in mind that the mentioned study, unlike ours, was not a case-control study and only performed on a population of blood donors in India. Nevertheless, their findings support our results.

In another similar report in Egypt, Eissa *et al.* (2007) confirmed that there was not a significant association between ABO blood groups and HB infection. This study was again a screening one on a group of blood groups and was not aimed to investigate a specific connection between blood groups and hepatitis B. This study also confirmed our findings in this regard.

Alaoddolehei *et al.* (2007) in a small study on Iranian blood donors did not report a significant connection between ABO blood groups or Rh status with HB infection. These results are also in line with the findings of the present investigation.

Although, modern studies have denied the first notion of Zuckerman and McDonald (1963), what is the main reason underlying this controversy? This might be justified by possible changes of HB virus in this long period of time, or defected accuracy of old equipments or methods in that era which possible might have led to wrong consequences which does not happen anymore by modern approaches at the current time.

In the second part of the present work, we investigated a possible association between ABO blood groups and Rh with hepatitis C infection. This association is corroborated by the results of some articles. For example, in a very recent study, Woo *et al.* (2013) showed that certain ABO blood groups may increase the risk of pancreatic cancer in patients with hepatitis C.

Surprisingly, unlike the results in the previous section, the findings revealed a significant association between certain blood groups with HC infections. These findings indicated that while O blood group was a factor of susceptibility toward HC infection, AB blood group was a protective factor in this regard. No significant role for Rh status was determined.

In line with our findings, Behal *et al.* (2010) showed that there might be an association between ABO blood groups and HC infection in a study among a population of Indian blood donors. They reported that seroprevalence of HC virus was higher in O blood group individuals and lowest in AB blood group persons. There was not a significant association between Rh group and HC infection.

Although, the mentioned study is not a well-designed case-control study, the results are completely in conformity with our findings.

Caspari *et al.* (1997) also did not find a positive correlation between Rh groups and HC infection. This is also in accordance with our finding.

Although, exact underlying mechanism of association between HC infection and certain blood groups is not well-known, it can be hypothesized that there might be a shared receptor-binding affinity between the enveloped hepatitis C virus and various cells in the body. Furthermore, it has been suggested that blood group antigens are receptors for several microorganisms (Kallenius *et al.*, 1981).

CONCLUSION

In conclusion, this case-control study showed that while there was not an association between blood groups and HB infections, this connection is possibly present between certain ABO groups (O and AB) and HC infection.

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