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Original Article

Hepatitis C (HCV) Viremic Rate and its Correlation to Demographic Factors among HCV Confirmed Iranian Blood Donors

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Abstract

Background: Hepatitis C virus (HCV) viremia is described as persistent HCV RNA among HCV exposed individuals. HCV viremic rate is defined as the proportion of anti-HCV positive and HCV RNA positive individuals to total anti-HCV positive individuals. Knowledge about HCV viremic rate increases understanding HCV epidemiology and provides the likelihood of HCV viremia infection in a given population. The aim of this study was to evaluate HCV viremic rate and demographic parameter correlations among HCV confirmed Iranian blood donors.

Methods: In this analytical, cross-sectional study, serologically confirmed HCV positive blood donors, who were referred to the Iranian blood transfusion centers around the country from November 2015 to September 2017, were included. HCV RNA RT-PCR was carried out by an in-house qualitative assay. Penalized logistic regression was performed for data analysis. STATA software version 13 was used for statistical analysis.

Results: Out of 239 subjects, HCV RNA was amplified in 161 (67.36%, 95% CI 61.21% -73.51%). No statistical associations were found between age, gender, education and marriage status with HCV viremic rate. First time donation was found to be associated with HCV viremia status (adjusted odds ratio [AOR]: 3.26; 95% CI 1.07-9.87).

Conclusion: The results of this study show the likelihood of active HCV infection occurrence among HCV confirmed Iranian blood donors, as the majority are in the active phase of HCV infection. The viremic rate was associated with first time donation. More effective donor selection process and paying special attention to maintenance of non-infected first time donors as a resource of regular donations are needed to improve blood safety. Follow-up studies on viremic first time blood donors are recommended to clarify impact of factors on the occurrence of HCV viremia.

Keywords: Blood donors, Hepatitis C, Viremia

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Introduction

Hepatitis C virus (HCV) is a major cause of liver disease worldwide, leading to cirrhosis and hepatocellular carcinoma. HCV infected individuals initially demonstrate an acute phase of infection and within 6 months, 15% to 45% are spontaneously cleared from infection with the anti HCV positive and HCV RNA negative profile. Remaining individuals progress to chronic infection and continue to be anti-HCV positive and HCV RNA positive. Detectable HCV RNA represents active HCV infection. Patients with active infection are prone to hepatocellular carcinoma and liver-related mortality.^{1,2} Approximately 71 million people are chronically infected around the world. According to the World Health Organization (WHO), European countries with 2.3% and Eastern Mediterranean countries with 1.5%, have the highest prevalence of HCV viremia

and in other regions, prevalence ranges from 0.5% to 1%.³ Based on a comprehensive study, in Iran, prevalence of viremia was 0.4% in the general population.⁴

HCV is a blood borne virus. WHO reported HCV prevalence of 0 to 0.5% in blood donors in 2013.⁵ HCV seroprevalence in Iranian blood donors has been 0.04% in 2014.⁶ High rate of HCV transmission was reported from donations with detectable HCV RNA.⁷ Knowledge about HCV viremia predicts rate of HCV clearance and provides probability of being an active carrier of the infection in a given population.⁸ Seropositivity rate of blood borne viruses such as HCV is higher among male, lower educated, married and first time Iranian blood donors.⁹ However, lack of published data exists about HCV viremia status and related donor characteristics among Iranian blood donors. In this analytical cross sectional study, HCV viremia and

associated donor characteristics were investigated among HCV confirmed Iranian blood donors.

Materials and Methods

Study Population

In this analytical cross sectional study, HCV positive blood donors from all over the country who were referred to blood transfusion centers and consented to participate in this study from May 2015 to September 2017 were included.

Blood Sample Collection

At the same time as the donors' return to blood transfusion centers, a total of 9 ml of whole blood collected in vacutainer tubes with gel separator was obtained from each subject and immediately centrifuged at 3000 RPM for 10 minutes and stored at -70°C until transfer to the central laboratory. Serum in all samples was separated in 1.5 mL micro tubes and stored in -70°C until further processing.

HCV RNA Testing

Viral RNA was extracted by the Tri-Pure method (Roche, the Netherlands) according to manufacturer's instructions. The extracted RNA was dissolved in 20 μL TE buffer and used as the template for further testing. If the further testing was not carried out immediately, the extracted RNA was stored at -70°C . A qualitative assay was performed for HCV RNA RT-PCR by an in-house assay using primers to the highly conserved 5' non-coding region (5' NCR) of the HCV genome as described elsewhere.¹⁰ Briefly, for the reverse transcription polymerase chain reaction (RT PCR) PCR, 5 μL of each extracted RNA sample was added to 5.3 μL of RT-PCR mixture containing random hexamer, dNTP, Reverse Transcriptase (200 U/ μL , Invitrogen, USA), and RNasin (40 U/ μL , Promega, USA). The cDNA was synthesized after 60 minutes at 40°C . Synthesized cDNA was amplified using Taq DNA polymerase (Promega, USA). For cDNA amplification, 10 μL of PCR Mix was added to each micro tube containing synthesized cDNA. The following program of thermal cycling was performed: 95°C for 5 minutes followed by 43 cycles of 95°C for 50 seconds, 60°C for 50 seconds, and 72°C for 50 seconds followed by a cycle of 72°C for 4 minutes.

Statistical Analysis

Descriptive results were expressed in means \pm SD or percentages. The association between demographic characteristics and HCV RNA status was performed using penalized logistic regression model via data augmentation. Weakly informative prior with log-F(1,1) was used to reduce sparse data bias.¹¹⁻¹³ We first screened the variables for univariate association between exposures and outcome. All variables with p value less than 0.2 were used to be included in the backward selection algorithm. Odds ratio (OR) with 95% confidence interval (CI) was calculated

for significant variables with alpha level of 0.05. STATA statistics software (Stata 13 Corp. College Station, Texas) was used for data analysis.

Results

During the study period, a total of 239 confirmed HCV positive blood donors were included in this study. Demographic characteristics of participants are shown in Table 1. The mean age of subjects was 37.58 ± 8.74 . Age was categorized into 2 groups: ≤ 40 and > 40 years old. The majority of subjects were male, < 40 years old, married, with education less than high school diploma and first time donors.

HCV RNA were amplified in 161 subjects (67.36 %, 95% CI 61.02%–73.27%). HCV viremia status and demographic characteristics of participants are shown in Table 2. In univariate analysis, all variables but one had a p value more than 0.2. First time donation was found to be associated with HCV viremia (OR 3.26; 95% CI 1.07 – 9.8, $P = 0.03$). No association was found between gender, age group, marital status and educational status with HCV viremia status (Table 3).

Discussion

According to the present study, approximately two-thirds of confirmed HCV positive Iranian blood donors were viremic (67.36 %, 95% CI, 61.21%–73.51%). The result is in line with the results of a recent comprehensive study on viremic rate of HCV in the Middle East and North Africa; showing that the pooled mean HCV viremic rate was 76.3%, 95% CI: 68.6–84.0% among blood donors.⁸ A study conducted on blood donors in Ahvaz; a city in southwest of Iran; revealed an HCV viremic rate of 81.8% in confirmed HCV positive subjects.¹⁴ Difference in donor characteristics across the studies could be explained by the variation between results. It has been shown that donations

Table 1. Demographic Characteristics of 239 Confirmed HCV Positive Blood Donors, 2015–2017

Characteristic	Anti HCV positive, (N = 239)
Age (y), Mean \pm SD	
Age group (y)	37.58 \pm 8.74
<40	152 (63.60)
≥ 40	87 (36.40)
Gender, No. (%)	
Male	233 (97.49)
Female	6 (3.92.51)
Marital status, ^a No. (%)	
Single	59 (23.11)
Get married	183 (76.89)
Education status, No. (%)	
Under diploma	145 (60.67)
Upper Diploma	94 (39.33)
Donation status, No. (%)	
First time	226 (94.56)
Not-first time	13 (5.44)

^a The sum of numbers is not exactly the total number of subjects because of missing values.

Table 2. Presentation of Demographic Characteristics of 239 Confirmed HCV Positive Blood Donors in Relation to HCV Viremia Status, 2015-2017

Characteristics	HCV RNA Negative (n = 78)	HCV RNA Positive (n = 161)
Prevalence, 95% CI	32.64	
Age (y), Mean ± SD	37.17 ± 9.24	37.78 ± 8.5
Age group (y)		
<40	51 (65.38)	101 (62.73)
≥40	27 (34.62)	60 (37.27)
Gender, No. (%)		
Female	3 (3.85)	3 (1.86)
Male	75 (96.15)	158 (98.14)
Marital status, No. (%)		
Single	21 (26.92)	38 (23.75)
Married	57 (73.08)	122 (76.25)
Education status, No. (%)		
Under diploma	45 (57.69)	100 (62.11)
Upper diploma	33 (42.31)	61 (37.89)
Donation status, ^a No. (%)		
First time	70 (89.74)	156 (96.89)
Not- First time	8 (10.26)	5 (3.11)

^a The sum of numbers is not exactly the total number of subjects because of missing values.

Table 3. Odds Ratios and 95% Confidence Intervals of Independent Variables among Iranian Blood Donors, 2015–2017

Variables	OR (95% CI)	P Value
≥40 (y)	1.12 (0.64–1.96)	0.69
Male gender	1.89 (0.42–8.59)	0.41
Get married	1.11 (0.59–2.07)	0.76
Under diploma	0.83 (0.48–1.44)	0.52
First time donation	3.26 (1.07–9.87)	0.03

with detectable HCV RNA at all levels of viremia would result in HCV transmission via blood transfusion.⁷

In this study, the viremic rate of HCV infection did not differ by gender, age, marital status and educational status. The results are comparable with a study conducted on US first time blood donors.¹⁵ However, the viremic rate was significantly correlated with first time donation. Our results are in accordance with the results of previous studies on blood donors revealing that HCV seropositivity rate is significantly correlated with first time donation.^{9-10,16-18} Moreover, first time donation was reported as a primary risk factor of HCV infection among blood donors.^{9,19-20} HCV seropositivity and viremic rate are lower in regular donors as a result of being less likely to have high risk behaviors. In addition, regular donors have passed the regulated donor selection process and donor screening tests. According to the WHO “Global status report on blood safety and availability 2016”, universally, whole blood donation given by regular donors varies from lower than 0.1% to 100%. Due to increased safety of blood donated by regular donors, in many European countries, blood obtained from first time donors is just used for testing and thus 100% of

blood donations are collected from regular donors.⁵

In Iran, HCV screening of blood donations is performed by serological testing and not by nucleic acid testing. Therefore, the study population was limited to HCV confirmed blood donors (described in text) and accepted to participate in the study during the study period, which resulted in a low sample size. Statistical analysis could be affected by low sample size for evaluation of small effect sizes of variables. To overcome this effect, a special statistical method (described in text) was performed. However, the viremia and demographic profile of participants may not be the same as non-participants and, as a result, the subjects may not be representative of HCV confirmed blood donors that could create bias in assessing viremic rate and related demographic factors.

In conclusion, this study shows that the majority of HCV confirmed Iranian blood donors are in viremic state and consequently are infectious. In addition, the study reveals that HCV viremia is associated with first time donation. The policy makers of Iranian Blood Transfusion Organization (IBTO) may attempt to increase collection from regular blood donors and return of healthy first time blood donors.^{21,22} The results of the presented study emphasize the role of more effective implementation of both blood donor selection and maintenance of healthy first time donors, as a resource of regular donors, for improving blood safety.

Authors' Contribution

FRK performed the bulk of the study and manuscript preparation. KMH and SAKA supervised the study. MM and ZS contributed to the study design, interpretation of the data, and drafting of the manuscript. MAM contributed to the statistical analyses. All authors revised and approved the final manuscript.

Conflict of Interest Disclosures

The authors have no conflicts of interest.

Ethical Statement

The Ethics Committee of High Institute for Research and Education in Transfusion Medicine, Tehran, Iran approved the present study (code No: IR.TMI.REC.1394.1800).

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