

Short communication

## No Evidence of *Hepatitis C* Virus Infection in Individuals with Cardiovascular Disease in Mashhad

Morteza Shakeri Hoseinabad<sup>1,2</sup>, Ehsan Aryan<sup>1</sup>, Majid Ghayour Mobarhan<sup>3,4</sup>, Mohsen Moohebat<sup>5</sup>, Samaneh Abolbashari<sup>1,2</sup>, Aida Gholoobi<sup>6</sup>, Amin Houshyar Chechaklou<sup>1</sup>, Atieh Yaghoubi<sup>1,2</sup>, Mojtaba Meshkat<sup>7</sup>, Zahra Meshkat<sup>1\*</sup>

1. Antimicrobial Resistance Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.
2. Student Research Committee, Mashhad University of Medical Sciences, Mashhad, Iran.
3. Metabolic Syndrome Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.
4. International UNESCO Center for Health-Related Basic Sciences and Human Nutrition, Department of Nutrition, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.
5. Cardiovascular Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.
6. Medical Genetics Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.
7. Mashhad Branch, Islamic Azad University, Mashhad, Iran.

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### Abstract

**Background and Aim:** *Hepatitis C* virus (HCV) infection is one of the leading causes of morbidity and mortality worldwide. It has been hypothesized that a number of bacteria and viruses might be involved in the pathogenesis of cardiovascular disease. The aim of this study was to define the prevalence of HCV in patients with cardiovascular disease in comparison with a control group.

**Methods:** In this study, 281 individuals including 143 cardiovascular patients and 138 healthy controls were assessed for identification of HCV antibodies. The data collection was done between April 2016 and February 2017. The prevalence of HCV antibodies was determined by the enzyme-linked immunosorbent assay (ELISA) method.

**Results:** There was no HCV infection in both patients with or without cardiovascular disease. There was a significant direct correlation between cardiovascular diseases and mean level of FPG (Fasting plasma glucose) ( $p < 0.001$ ). Also the Systolic and Diastolic blood pressures were significantly higher in the patients with cardiovascular disease ( $p < 0.001$  and  $p = 0.005$ , respectively).

**Conclusion:** The results of this study show that no evidence of HCV infection is found among a group of cardiovascular patients in the city of Mashhad.

**Keywords:** *Hepatitis C* Virus; Cardiovascular Disease; Prevalence; Iran; Mashhad.

\*Corresponding Author: Zahra Meshkat; Email: meshkatz@mums.ac.ir

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### Introduction

Cardiovascular diseases (CVD) are described as a range of disorders including the heart or blood vessels diseases. CVD may be related to underlying factors such as smoking, alcohol consumption, diabetes, obesity and high blood cholesterol (1).

Evidence has emerged indicating that infection is also a risk factor of atherosclerosis (2). Many

studies have shown that a wide range of bacteria and viruses can cause cardiovascular disease in humans. The most common viral causes of CVD and myocarditis are *Adenovirus*, *Cytomegalovirus* (CMV), *Coxsackievirus B*, *Human parvovirus B19*, *Hepatitis C virus* (HCV), and *Respiratory syncytial virus* (RSV) (3-6). Additionally, several studies have shown an association between periodontal disease such as *Porphyromonas gingivalis*,

*Actinobacillus actinomycetemcomitans*, *Treponemadenticola*, and *Tannerella forsythia* and CVD (7, 8).

HCV is a small, enveloped positive-stranded RNA virus belonging to the Flaviviridae family and the genus *Hepacivirus* (9). About 2-3% of the world's population is infected with the *Hepatitis C virus* (10, 11). According to the World Health Organization's (WHO) report in 2015, only 20% (14 million) of the 71 million persons living with HCV globally were aware of their disease (12, 13).

HCV can cause both acute and chronic hepatitis (the virus leads to chronic hepatitis in up to 60–80% of infected people). It is also associated with liver steatosis, fibrosis and insulin resistance (14-16).

In April 2017, WHO declared that the prevalence of HCV infection is clearly various in different geographic regions (12). Different studies have stated that Iran is a country with low-frequency of HCV infection (17, 18). The prevalence of HCV infection is less than 1% in the general population of Iran and it is lower than the neighboring countries including Afghanistan (1.1%), Turkey (1%-2.1%), Pakistan (4.7%), Iraq (7.1%), and Qatar (6.3%) (18).

Some of the major risk factors for the incidence of HCV infection are injecting drug addiction, blood product transfusion, organ transplantation, hemodialysis, human activities with potential exposure to blood, sexual transmission, and vertical transmission (17, 19). Up to now, no appropriate vaccine or effective post-exposure prophylaxis for the disease prevention has been available (20).

HCV infection is one of the leading causes of death worldwide. Cirrhosis and liver failure are the two main cause of death in HCV positive patients; additionally, some studies demonstrated that CVD can be another possible cause of the increased mortality rate in these patients (21, 22). Findings which are consistent with this are the results of clinical studies which have shown that HCV-infected patients have a higher prevalence of metabolic disorders, such as type 2 diabetes mellitus, in comparison to non-infected controls (23).

Considering the obtainability of antiviral treatments which might impose an extra risk for CVD due to

their side effects, an updated estimate of the impact of HCV infection on CVD risk seems necessary. To the best of our knowledge, the prevalence of HCV infection among CVD patients has not yet been assessed in any study. Hence, we conducted this study to define the prevalence of HCV infection among a group of individuals with CVD in Mashhad city.

## Methods

In this study, from 2016 to 2017, participants (n=281) underwent physical examinations and medical interviews. All individuals including those with or without CVD were assessed for the presence of HCV infection. Diagnosis of CVD including stable or unstable angina, myocardial infarction or stroke was confirmed by a cardiologist and/or a neurologist after physical examination and para-clinical evaluation. All the subjects were serologically assessed for anti-HCV antibody using HCV ELISA kit (Diapro; Italy). Age, gender, job, history of smoking, systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting glucose and lipid levels were measured. Furthermore, data related to tobacco and alcohol consumption and anthropometric measurements were also collected. The process of the study was explained to the participants before registration. In addition, each item was described individually for the agreement to obtain a written consent for those who agreed to participate in the study. The study was approved by the Ethic Committee of the Mashhad University of Medical Sciences.

## Results

A total of 281 participants (143 CVD patients, and 138 subjects without any sign or symptoms of CVD) aging 36-71 (mean  $51.42 \pm 6.24$ ) were included in our study.

The demographic characteristics of participants are shown in Table 1.

All serum samples were negative for HCV antibody analyzed by ELISA and thus no cases of HCV infection was identified in either the case or control group. The mean fasting plasma glucose (FPG) level in the cardiovascular group was higher than the control group which was statistically significant

( $p < 0.001$ ). Also the mean systolic and diastolic blood pressures were significantly higher in the

cardiovascular group ( $p < 0.001$  and  $p = 0.005$  respectively) (Table 2).

**Table 1.** Demographic characteristics of participants

Variables	subgroups	N (%)
Cardiovascular disease	Yes	143 (41.6)
	No	138 (49.1)
Gender	Male	117 (41.6)
	Female	164 (58.4)
Education Level	Uneducated	28 (10)
	Primary	130 (46.3)
	College	102 (36.3)
	Bachelor	16 (5.7)
	Master	5 (1.8)
Marriage Status	Single	1 (0.4)
	Married	253 (90)
	Divorced	6 (2.1)
	Widow	21 (7.5)
Smoking Status	Non smoker	187 (66.5)
	Current Smoker	53 (18.9)
	Ex-smoker	41 (14.6)
Hypertension diagnosis	Yes	81 (28.83)
	No	200 (71.17)
Diabetes diagnosis	Yes	60 (21.35)
	No	221 (78.65)

**Table 2.** Difference in the mean Fasting Plasma Glucose (FPG) and the mean Systolic/diastolic blood pressure in patients with and without cardiovascular diseases

Variable	Patients with cardiovascular disease	Patients without cardiovascular disease	p-value
FPG (mg/dL)	124.38±62.70	98.56±55.03	<0.001
Systolic Blood pressure (mm Hg)	136.27±22.21	124.98±23.39	<0.001
Diastolic Blood pressure (mm Hg)	84.75±11.15	80.83±12.20	0.005

## Discussion

Numerous studies have shown that the *Hepatitis C virus* (HCV) infection is one of the major causes of morbidity and mortality in the world; with a mortality rate that is currently higher than HIV infections (24-26). Additionally, these studies demonstrate the increasing incidence of both liver disease and cardiovascular disease (CVD) related mortality in HCV patients (27-29).

The incidence rate of hepatitis C has increased worldwide and approximately 2-3% of the world

population is infected with HCV (12). Recently, the relationship between *Hepatitis C* virus and risk of cardiovascular disease has gained interest among researchers (5, 29, 30).

Because HCV infection may interfere with glucose and lipid metabolism and eventually lead to the development of atherogenic disorders (16), and on the other hand, because HCV is reported to prompt pro-inflammatory cytokines, such as interleukin (IL)-6, tumor necrosis factor (TNF)- $\alpha$  and C-reactive protein, which can affect the coronary arteries resulting in CVD (31), it seems necessary

that the risk of CVD in HCV infected individuals be estimated. It would also be beneficial to evaluate the prevalence of HCV infection among those with CVD.

The current study was implemented to both estimate the prevalence of HCV infection in a group of individuals diagnosed with CVD and also to determine any possible association between HCV infection and CVD.

The result of this study showed that no case of HCV infection was present among the study participants; either with or without CVD. Therefore, we could not assess the association between cardiovascular disease and infection with HCV among the studied population. This might be due to the relevantly low prevalence of HCV infection in Mashhad. In a study which was conducted on the general population of Mashhad, the seroprevalence of HCV was as low as 0.2% and HCV infection prevalence was 0.13% (32).

Liao and colleagues performed a population-based cohort to show the relationship between HCV infection and risk of stroke. The result of this study demonstrated that the risk of stroke in people who live with HCV infection was 2.5%, while this risk in people without HCV infection was 1.9%. The adjusted HR (Hazard ratio) of stroke in HCV positive people compared with HCV negative people was 1.27 (95% CI 1.14 to 1.41) (30).

On the other hand, the result of another cohort study showed that there was no significant association between HCV infection and ischemic heart diseases and also the rate of death among ischemic heart diseases with anti-HCV seropositive was too low (29). The somewhat conflicting results of the mentioned studies increase the need for implementing larger cohort studies to evaluate the more precise relationship between HCV and CVD.

Results of the current study confirms that HCV infection in Iran is mostly diagnosed in individuals in high-risk groups such as injecting drug users, patients with hemophilia and thalassemia, and patients undergoing hemodialysis and it more rarely occurs in the general population (33). Thus it is difficult to access the difference between the prevalence of HCV infection in two subgroups of

with and without cardiovascular diseases who are not in any of the mentioned high risk groups.

## Conclusion

This study demonstrated that no evidence of HCV infection is seen among a group of cardiovascular patients in the city of Mashhad and it cannot be concluded from this study if there is or not a relationship between HCV infection and cardiovascular diseases. Our findings can be in favor of the concept of the low prevalence of HCV infection in Mashhad.

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## Ethics

The study was approved by the Ethic Committee of the Mashhad University of Medical Sciences (Ethics code: IR.MUMS.fm.REC.1396.435).

## Conflict of Interest

The authors declared that they have no conflict of interest.

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