

# To Determine the Frequency of Hepatitis C Virus Infection in Confirmed Cases of Ischemic Heart Disease

ASIM KHAN<sup>1</sup>, FAISAL AMIN BAIG<sup>2</sup>, TAHIR ULLAH KHAN<sup>3</sup>, ATIF MASOOD<sup>4</sup>, ARSALAN NAWAZ<sup>5</sup>, NAFID ULLAH KHAN<sup>6</sup>

<sup>1</sup>Senior Registrar Medicine, University of Lahore Teaching Hospital Lahore, The University of Lahore

<sup>2,4</sup>Associate Professor Medicine University of Lahore Teaching Hospital Lahore, The University of Lahore

<sup>3,5</sup>Assistant Professor Medicine University of Lahore Teaching Hospital Lahore, The University of Lahore

<sup>6</sup>Senior Registrar, Medicine Department, District Headquarter Hospital Bannu.

Correspondence to: Tahir Ullah Khan, Email: [tahirnur69@gmail.com](mailto:tahirnur69@gmail.com), Cell: 03329930269

## ABSTRACT

**Aim:** To determine the frequency of Hepatitis C virus infection in confirmed cases of ischemic heart disease.

**Material and Methods:**

**Study design:** Cross sectional descriptive study.

**Study Place and Duration:** The study was done at department of medicine, Services hospital Lahore over a period of 6 months after approval of Synopsis (December 7, 2017 till June 7, 2108). This descriptive cross sectional study was conducted from 15 June to December 2019 in the Radiology Department of Avicenna Medical College. A total of 90 ultrasounds undertaken at the Gynecological Ultrasound Unit. A total of 32 patients with functioning ovarian cysts were included. A total of 46 individuals with benign tumors and 9 patients with malignant cysts were included in the control group. The remaining patients were not followed up on and were treated at a different center. The majority of the patients had issues with their menstrual cycle and pain.

**Data Collection Procedure:** All 291 patients meeting selection criteria were taken after approval of synopsis in this study. All data was taken from medical departments of SIMS after written informed consent along with their biodata like name, age, along with contact details. A sample of appropriate size of blood was drawn out with help of senior staff nurse in aseptic / sterilized container and was sent out to hospital laboratory for the analysis of HCV. The diagnosis of HCV was done as per operational definition.

**Results:** The mean age of cases was  $53.36 \pm 15.21$  with minimum and maximum age as 28 and 80 years. There were 200(68.7%) male and 91(31.3%) female cases with 2.20:1 male to female ratio. There were 100(34.4%) cases who belonged to lower, 116(39.9%) belonged to middle and 75(25.8%) cases belonged to upper class. According to operational definition, 80(27.5%) of the cases had Hepatitis C while in 211(72.5%) cases Hepatitis C was negative.

**Conclusion:** It is concluded that the prevalence of Hepatitis C virus was positive in 27.5% that's too high, so it must be ensure in all cases IHD to screen and diagnosis of HCV. If they remained undiagnosed then they may develop related complications such as severe coronary lesions that can further elevate the risk of cardiac morbidity and mortality.

**Keywords:** Cardiovascular disease, ischemia heart diseases, risk factor, extra hepatic manifestations

## INTRODUCTION

Coronary artery disease is one of the largest contributors to mortality and morbidity worldwide irrespective of gender. It causes about 33% of all deaths occurring in 35 years plus age group. In developed world, the mortality due to IHD has declined. 1, 2 IHD is significant in terms of morbidity and mortality throughout the world. It could be asymptomatic or present with acute cardiac event. The prevalence of IHD has increased significantly in Southeast Asia, including Pakistan.<sup>3</sup> Aziz et al., reported that prevalence of ischemic heart disease in Pakistan is 4.4 per 100.1 A recent study on local population reported that the most prevalent risk factor was hyperlipidemia constituting about 91.2% cases, hypertension about 70.4%, diabetes about 51.2%, family history of IHD about 40.0% and smoking about 29.2%.<sup>3</sup>

Chronic hepatitis c infection is a major health hazard in terms of causing chronic liver disease and extrahepatic complications including coronary artery disease.<sup>4</sup> Very Recently, chronic hepatitis c infection has been identified as a risk factor for atherosclerosis, which can cause significant mortality.<sup>5,6</sup> Replication of HCV occurs within carotid plaques and brain endothelium; moreover, HCV

patients are prone to higher levels of inflammation as compared to non-hepatitis c effected ones.<sup>7, 8</sup>

Prevalence of HCV in Pakistan is increasing primarily due to the overwhelming unsafe medical practices in our society. HCV seroprevalence among the general adult Pakistani population is 6.8%, while active HCV infection was found in approximately 6% of the population.<sup>9</sup>

There have been few studies done to see the effects of HCV infection on cardiovascular risk, but these have produced no results, 10 in this regard, a study reported high frequency of HCV in diagnosed cases of IHD as 25.3%.<sup>11</sup>

This study is designed to confirm the high statistics of HCV in IHD of local population. The available study reported high frequency of HCV in these cases.<sup>11</sup> This study can help us to find burden of HCV in cases of IHD, if high frequency is found then in future IHD cases was undergone of HCV screening and in future further exploration can be done to prove HCV as a risk factor for IHD. In perspective of treatment, IHD cases was started to cure HCV to minimize the cumulative risk of further morbidity and mortality.

**MATERIAL AND METHODS**

This cross-sectional observational study was performed at medicine unit 1, Services institute of medical sciences, services hospital Lahore over a period of 6 months from December 7, 2017 to June 7, 2108 after synopsis approval applying non-probability sampling technique. About 291 patients were selected using confidence levels of 95%, margin of error at 5% and prevalence of hepatitis C in IHD cases around 25.3% 11 Cases of either gender aged 16- 80 years, patients with Diabetes (BSR > 200 mg/dl, BSF > 126 mg/dl), Known cases of HBV, HCV or HIV, Cases having non-cardiac chest pain, patients with positive family history of HCV or HBV, Congenital heart disease, history of hepatotoxic drugs administration, diagnosed rheumatic heart disease, Sever renal failure (RFT) [creatinine > 1.3 mg/dl), known cases of liver disease were included in the study. All 291 patients meeting selection criteria were taken after approval of synopsis in this study. All data was taken from medical departments of SIMS after written informed consent was taken along with their demographic data like name, age long with contact details. A sample of appropriate size of blood was drawn out with help of senior staff nurse in aseptic / sterilized container and was sent out to hospital laboratory for the analysis of HCV. The diagnosis of HCV was done as per operational definition. All related information and related data was gathered by research himself on attached proforma.

SPSS version 22 was used to enter and analyze data. Mean ± S.D was used for quantitative data like age (years) and duration of IHD (months). For qualitative data like gender, socioeconomic status and HCV, frequency and percentages were used. To address effect modifiers data was stratified for age, gender and socioeconomic class and duration of disease. After stratification Chi-square test was applied taking p-value ≤ 0.05 was significant.

**RESULTS**

The mean age of cases was 53.36 ± 15.21 with minimum and maximum age as 28 and 80 years. Table -1. A total of 76(26.1%) cases were 16-40 years old and 215(73.9%) of the cases were 41-80 years old. Fig-1. There were 200(68.7%) male and 91(31.3%) female cases with 2.20:1 male to female ratio. Fig-2. There were 100(34.4%) cases who belonged to lower, 116(39.9%) belonged to middle and 75(25.8%) cases belonged to upper class. Fig-3. One hundred and fifty five (53.3%) cases had < 6 months of duration while 136(46.7%) cases had IHD since ≥ 6 months. Fig-4. According to operational definition, 80(27.5%) of the cases had Hepatitis C while in 211(72.5%) cases Hepatitis C was negative. Fig-5. In age group of 16-40 years and 40-80 years of age the frequency of Hepatitis C virus was statistically same i.e. 22.4% versus 29.3%, p-value > 0.05. Table -2. In male and female the frequency of Hepatitis C virus was also statistically same i.e. 26.5% and 29.7%, p-value > 0.05. Table -3. In lower, middle and upper socioeconomic class the frequency of Hepatitis C virus was 34%, 27.6% and 18.7% respectively. The frequency of Hepatitis C virus was statistically same in all socioeconomic class, p-value > 0.05. Table -4. The frequency of Hepatitis C virus was also statistically same in cases who had duration of IHD as < 6 months i.e. 29.7%

and in those who had duration of IHD as ≥ 6 months i.e. 25%, p-value > 0.05. Table -5.

Table 1: Descriptive Statistics of age (years)

Mean	53.36
Std. Deviation	15.21
Range	52.00
Minimum	28.00
Maximum	80.00

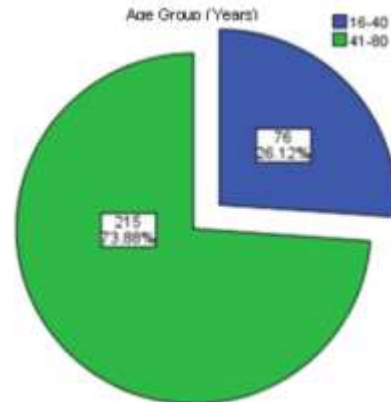


Fig-1: Frequency distribution of Age groups (years)

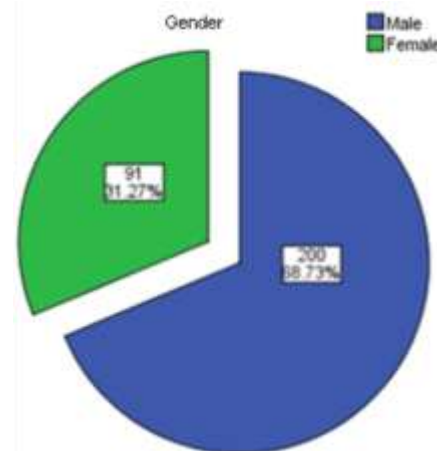


Fig-2: Frequency distribution of gender

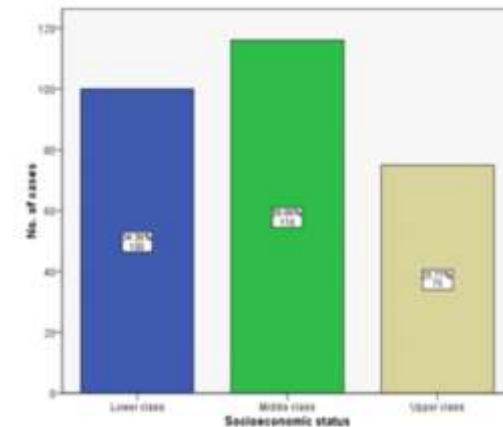


Fig-3: Frequency distribution of socioeconomic status

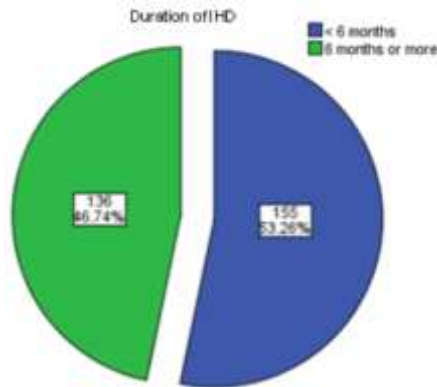


Fig-4: Frequency distribution of duration of IHD

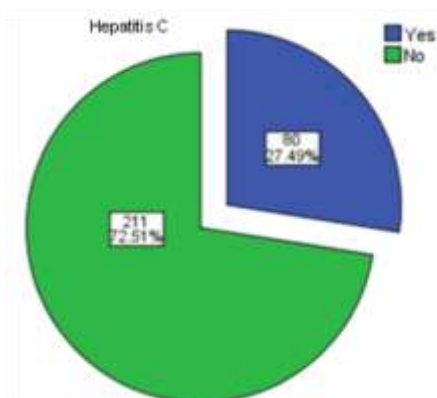


Fig-5: Frequency of hepatitis C virus infection in IHD cases

Table -2: Frequency of Hepatitis C with respect to age (years)

		Hepatitis C		Total
		Yes	No	
Age Groups (Years)	16-40	17(22.4%)	59(77.6%)	76(100.0%)
	41-80	63(29.3%)	152(70.7%)	215(100.0%)
Total		80(27.5%)	211(72.5%)	291(100.0%)

Chi-square = 1.35 p-value = 0.245

Table -3: Frequency of Hepatitis C with respect to Gender

		Hepatitis C		Total
		Yes	No	
Gender	Male	53(26.5%)	147(73.5%)	200(100.0%)
	Female	27(29.7%)	64(70.3%)	91(100.0%)
Total		80(27.5%)	211(72.5%)	291(100.0%)

Chi-square = 0.315 p-value = 0.574

Table 4: Frequency of Hepatitis C with respect to socioeconomic status

		Hepatitis C		Total
		Yes	No	
Socio-economic class	Lower	34(34%)	66(66%)	100(100.0%)
	Middle	32(27.6%)	84(72.4%)	116(100.0%)
	Upper	14(18.7%)	61(81.3%)	75(100%)
Total		80(27.5%)	211(72.5%)	291(100.0%)

Chi-square = 5.05 p-value = 0.080

Table 5: Frequency of Hepatitis C with respect to duration of disease

		Hepatitis C		Total
		Yes	No	
Duration	<6 months	46(29.7%)	109(70.3%)	155(100.0%)
	>6 months	34(25%)	102(75%)	136(100.0%)
Total		80(27.5%)	211(72.5%)	291(100.0%)

Chi-square = 0.795 p-value = 0.373

## DISCUSSION

Ischemic heart disease is among the most frequent cause of more than half the deaths worldwide in recent years. Moreover, more than 20 million people worldwide suffer coronary or cerebrovascular and survive the acute insult.<sup>12,13,14</sup> The incidence of coronary heart disease in Pakistan is not well established. Interview based clinical data shows that the prevalence of coronary events was 4.5% in males and 8.2% in women.<sup>1</sup> Resting electrocardiogram can be used to detect manifestations of ischemic heart disease, since some electrocardiographic abnormalities are indicative of coronary disease in asymptomatic subjects. Ischemic heart disease been shown to enhance atherogenicity. However, the association between chronic hepatitis C (HCV) and IHD remains controversial.<sup>15</sup>

The current cross-sectional study was designed to determine the frequency of HCV in confirmed cases of ischemic heart disease that was found in 27.5% of the cases. A study reported almost similar statistics i.e. 25.3%.<sup>11</sup> A study, conducted by Vassalle et al<sup>16</sup>, showed that the % of HCV infection in control subjects was 2% while it was 6.3% in the Coronary artery disease patients. ( $p < 0.05$ ). Association of HCV positivity and CAD was significant (OR 3.2,  $p < 0.05$ ). After removing the bias of other confounders, the multivariate logistic regression analysis revealed that HCV infection remains independent CAD predictor (OR 4.2,  $p < 0.05$ )<sup>16</sup>.

Several infectious agents have been implicated in the cellular and molecular changes leading to the development of atherosclerosis. Further studies revealed that atherosclerotic process is greatly accelerated by some infectious agents. Hepatic steatosis has been observed more frequently in Persons with HCV infection.<sup>17</sup> Also, inflammatory markers and endothelial dysfunction are more frequently associated with Hepatic steatosis<sup>18</sup>. All these factors contribute to the possibly increased risk of coronary artery disease in HCV-infected persons. A study showed that hepatitis c infected patients, when compared with normal population, had a higher risk of acquiring CAD, even after removal of traditional cardiovascular disease risk factors. A number of mechanisms has been postulated leading to this increased risk. HCV infection itself or other undetermined factors might be contributing to the increased CAD risk in HCV infected patients.<sup>19</sup> According to some studies, there is a possible role of inflammation in the pathogenesis of CAD<sup>20, 21</sup>. There is a complex interplay of cytokines in the whole process. The fine balance between pro-inflammatory and anti-inflammatory cytokines determines the initiation of the atherosclerotic process, its propagation and rupture. Some authors are of the opinion

that markers of inflammation like tumor necrosis factor, c reactive protein and interleukin-6 are high in hepatitis c infected patients that might be contributing to the increased CAD risk<sup>22,23</sup>. This complex cascade of inflammation and thrombosis plays a vital role in the genesis of CAD as HCV infected patients have raised inflammatory markers too. Also, severity of CAD is closely associated with thrombosis and inflammation. HCV infected patients have raised malnutrition inflammation scores compared with normal population. In addition, HCV infected patients have been observed to have higher prevalence of diabetes mellitus, an important CVD risk factor. Another possibility in HCV affected patients is the late diagnosis of diabetes mellitus in these patients. Poor follow-up and hence poor compliance to treatment were the two common pitfalls noted in HCV infected patients<sup>24</sup>.

## CONCLUSION

It is concluded that the prevalence of Hepatitis C virus was positive in 27.5% that's too high, so it must be ensure in all cases IHD to screen and diagnosis of HCV. If they remained undiagnosed then they may develop related complications such as severe coronary lesions that can further elevate the risk of cardiac morbidity and mortality.

## REFERNCES

1. Aziz KU, Faruqi A, Patel N, Jaffery H. Prevalence and awareness of cardiovascular disease including life styles in a lower middle class urban community in an asian country. *Pak Heart J* 2012;41(3):11-20.
2. Hassan AU, Nazir S. Ischemic heart disease: Trend of cardiovascular risk factors in women. *Professional Med J*. 2016;23(12):1442-8.
3. Adam AM, Rehan A, Waseem N, Iqbal U, Saleem H, Ali MA, et al. Prevalence of Conventional Risk Factors and Evaluation of Baseline Indices Among Young and Elderly Patients with Coronary Artery Disease. *J Clin Diagn Res*. 2017;11(7):OC34-OC9.
4. Adinolfi LE, Zampino R, Restivo L, Lonardo A, Guerrera B, Marrone A, et al. Chronic hepatitis C virus infection and atherosclerosis: clinical impact and mechanisms. *World journal of gastroenterology*. 2014;20(13):3410-7.
5. Boddi M, Abbate R, Chellini B, Giusti B, Giannini C, Pratesi G, et al. Hepatitis C virus RNA localization in human carotid plaques. *J Clin Virol*. 2010;47(1):72-5.
6. Wong RJ, Kanwal F, Younossi ZM, Ahmed A. Hepatitis C virus infection and coronary artery disease risk: a systematic review of the literature. *Digest Dis Sc*. 2014;59(7):1586-93.
7. Adinolfi LE, Restivo L, Guerrera B, Sellitto A, Ciervo A, Iuliano N, et al. Chronic HCV infection is a risk factor of ischemic stroke. *Atherosclerosis*. 2013;231(1):22-6.
8. Bassendine MF, Nielsen SU, Bridge SH, Felmler DJ, Sheridan DA, Packard CJ, et al. Hepatitis C virus and atherosclerosis: A legacy after virologic cure? *Clinics and research in hepatology and gastroenterology*. 2017;41(1):25-30.
9. Umer M, Iqbal M. Hepatitis C virus prevalence and genotype distribution in Pakistan: Comprehensive review of recent data. *World journal of gastroenterology*. 2016;22(4):1684-700.
10. Petta S, Maida M, Macaluso FS, Barbara M, Licata A, Craxi A, et al. Hepatitis C Virus Infection Is Associated With Increased Cardiovascular Mortality: A Meta-Analysis of Observational Studies. *Gastroenterol*. 2016;150(1):145-55.
11. Lin M-S, Guo S-E, Chen M-Y, Huang T-J, Huang J-C, Hu J-H, et al. The impact of hepatitis C infection on ischemic heart disease via ischemic electrocardiogram. *Am J Med Sci*. 2014;347(6):478-84.
12. Abbas S, Kitchlew A, Abbas S. Disease burden of ischemic heart disease in Pakistan and its risk factors. *Ann Pak Inst Med Sci*. 2009;5(3):145-50.
13. Sharif S, Anwar N, Farasat T, Naz S. ABO blood group frequency in Ischemic heart disease patients in Pakistani population. *Pakistan journal of medical sciences*. 2014;30(3):593.
14. Sulo G, Iglund J, Vollset SE, Nygård O, Ebbing M, Sulo E, et al. Heart Failure Complicating Acute Myocardial Infarction; Burden and Timing of Occurrence: A Nation-wide Analysis Including 86 771 Patients From the Cardiovascular Disease in Norway (CVDNOR) Project. *J Am Heart Assoc*. 2016;5(1):e002667.
15. Pothineni NV, Delongchamp R, Vallurupalli S, Ding Z, Dai Y, Hagedorn CH, et al. Impact of hepatitis C seropositivity on the risk of coronary heart disease events. *Am J Cardiol*. 2014;114(12):1841-5.
16. Vassalle C, Masini S, Bianchi F, Zucchelli G. Evidence for association between hepatitis C virus seropositivity and coronary artery disease. *Heart*. 2004;90(5):565-6.
17. Sanyal A. non-alcoholic fatty liver disease and hepatitis C–risk factors and clinical implications. *Alimentary pharmacology & therapeutics*. 2005;22(s2):48-51.
18. Targher G, Bertolini L, Scala L, Zoppini G, Zenari L, Falezza G. Non-alcoholic hepatic steatosis and its relation to increased plasma biomarkers of inflammation and endothelial dysfunction in non-diabetic men. Role of visceral adipose tissue. *Diabetic medicine*. 2005;22(10):1354-8.
19. Butt AA, Xiaoqiang W, Budoff M, Leaf D, Kuller LH, Justice AC. Hepatitis C virus infection and the risk of coronary disease. *Clinical Infectious Diseases*. 2009;49(2):225-32.
20. van Leuven SI, Franssen R, Kastelein J, Levi M, Stroes ES, Tak PP. Systemic inflammation as a risk factor for atherothrombosis. *Rheumatology*. 2007;47(1):3-7.
21. Hansson GK, Libby P. The immune response in atherosclerosis: a double-edged sword. *Nature Reviews Immunology*. 2006;6(7):508.
22. Nascimento M, Bruchfeld A, Suliman ME, Hayashi SY, Pecoits-Filho R, Manfro RC, et al. Effect of hepatitis C serology on C-reactive protein in a cohort of Brazilian hemodialysis patients. *Brazilian Journal of Medical and Biological Research*. 2005;38(5):783-8.
23. Riordan S, Skinner N, Kurtovic J, Locarnini S, McIver C, Williams R, et al. Toll-like receptor expression in chronic hepatitis C: correlation with pro-inflammatory cytokine levels and liver injury. *Inflammation research*. 2006;55(7):279-85.