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Original article

Effect of HCV Seropositivity on Outcome of Percutaneous Coronary Intervention

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Abstract

Background: The association between HCV infection and atherosclerotic coronary heart disease (CHD) remains unclear. **The aim** of this study was to detect the effect of HCV seropositivity on outcome of percutaneous coronary intervention. **Methods:** This prospective study was conducted on 150-patients in Benha University Hospital and National Heart Institute from April 2021 to March 2022.The participants were classified into three equal groups: Group 1: HCV seropositive not receiving antiviral treatment, group 2: HCV seropositive, receiving antiviral treatment & became –ve PCR and group 3 (control): HCV seronegative. **Results:**There was statistically significant difference between the three studied groups regarding Gensini score which was significantly higher in group1.Patients in group 1 had higher number of diseased vessels and implanted stents , but without statistical significance. The difference between the three studied groups regarding stent length, stent diameter and dilatation pressure was statistically insignificant. Patients in group 1 had higher cumulative incidence of MACEs such as TLR, MI, CVS, major bleeding, non-cardiac death than group 2 and 3 after 1, 3 and 6 months of clinical follow up but, this difference was not statistically significant. **Conclusion:** HCV seropositivity has a slight impact on the cardiovascular outcomes (TLR, TVR, MI, CVS, stent thrombosis, major bleeding, CABG, cardiac or non-cardiac death), or In-stent restenosis following PCI.

Key words: HCV seropositivity - Percutaneous Coronary Intervention – PCI

List of abbreviations

TLR Target Lesion Revascularization

TVR Target Vessel Revascularization

CVS Cerebrovascular Stroke

CABG Coronary Artery Bypass Graft

MI Myocardial Infarction

HCV Hepatitis C virus

CAD Coronary Artery Disease

ISR In Stent Restenosis

MACEs Major Adverse Cardiovascular Events

Introduction:

Many theories suggested infection as a tributary risk factor of CAD; the association between infections and CAD has been explained by different direct and indirect mechanisms (**1)**.

The acquired information shows the recognizable proof of viral genomes in the atherosclerotic plaques and furthermore proatherogenic impacts of viral disease in cells applicable to atherogenesis (smooth muscle cells, monocyte macrophages, T cells, and endothelial cells) **(**2**).**

It is still controversial whether there is an association between HCV infection and CAD or not (**3**, **4)**.

Different studies have shown conflicting results, some studies showed that there is an association between HCV seropositivity and CAD (**5, 6)**, other studies showed that there is no association between HCV infection and CAD, carotid atherosclerosis, or risk of myocardial infarction (**7)**, while Pothineni et al. reported that HCV infected patients had less obstructive CAD on coronary angiography (**8)**.

The main aim of this study was the detection of the effect of HCV seropositivity on outcome of percutaneous coronary intervention in patients with coronary artery disease.

Patients and Methods

This study was a prospective study that was conducted on 150 patients candidate for elective PCI in both Benha University hospital and National Heart Institute from April 2021 to March 2022. Approval was taken from the Ethics Committee of Benha University. The aim of the study was explained to patients ;also, privacy of data was secured. Patients were followed after 1, 3 and 6 months for MACEs and clinical in stent restenosis.

The participants were classified into three equal groups:

- ***Group 1,*** included 50 patients who are seropositive for HCV and did not receive antiviral treatment.

- ***Group 2,*** included 50 patients who are seropositive for HCV and received antiviral treatment & became –ve PCR.
- ***Group 3***(control), included 50 patients who are HCV seronegative patients.

An informed oral and written consent was taken from participants in the study.

Inclusion criteria:

1. Patients with hepatitis C infection and patients without hepatitis C.
2. Patients aged ≥ 18 years who had symptomatic CAD and showed significant de novo stenotic lesions (≥ 70%) of native coronary arteries that were amenable to elective PCI using drug-eluting stents.

Exclusion criteria:

Patients having any of the following criteria were excluded:

- Target lesion in the left main coronary artery
- Patients with chronic total occlusion lesion
- Patients treated by primary PCI
- Patients who needed bifurcation stenting technique
- Patients with previous history of CABG
- Known hypersensitivity to aspirin or P2Y12 inhibitors.
- Decompensated liver and kidney disease
- Congenital heart disease
- Chronic infections other than HCV infection

Patients who met the selection criteria were subjected to the following:

1-History and Clinical Examination

- Full detailed history: Identification of cardiovascular risk factors (age, sex, smoking, hypertension, diabetes mellitus, dyslipidemia, body mass index, and family history of CAD).
- Full clinical examination.

2- ECG

- Resting 12-lead surface electrocardiogram to identify cardiac rhythm and signs of myocardial ischemia (ST segment and T wave abnormalities or pathological Q waves).

3- Laboratory data

- Laboratory testing includes AST, ALT, fasting blood sugar, hemoglobinA1c level, lipid profile (TG, TC , LDL , HDL), HCV antibodies using PCR.

4- Echocardiography

All patients underwent conventional echocardiography to assess left ventricular ejection fraction by modified biplane Simpson's method and degree of MR and 2D

speckle tracking echocardiography (The LV endocardium was traced manually and the software delineate the curve of the LV epicardium automatically. Thereafter, the curves of the endocardium and epicardium were adjusted to ensure consistency with the LV wall thickness to assess global circumferential strain GCS and global longitudinal strain GLS) Normal GCS varied from -20.9% to -27.8% while GLS >-18% is normal, and GLS -16% to -18% is borderline according to last echocardiographic guidelines (***9***).

5-Treadmill stress electrocardiogram testing using Modified Bruce Protocol when indicated.to detect ischemia before angiography.it was used in 32 patients (18 in group 1 , 9 in group 2 and 5 in group 3).

6. **Coronary angiography** was performed by an experienced intervention cardiologists, to assess severity of CAD and revascularization of significant lesions. Coronary angiography was repeated during follow up when indicated. Patients continued on DAPT (ASA and clopidogrel) throughout the six months follow up.

Gensini scoring system (10) was used to assess severity of CAD

- 1 point for 1-25% stenosis
- 2 points for 26-50% stenosis
- 4 points for 51-75 % stenosis
- 8 points for 76-90 % stenosis
- 16 points for 91 -99 % stenosis
- 32 points for total occlusion

The score is then multiplied by factor representing the importance of the lesion location in the coronary arterial system:

- 5 for a left main lesion
- 2.5 for the proximal Left anterior descending(LAD) or left circumflex artery(LCX)
- 1.5 for the mid segment LAD or LCX
- 1 for the distal segment of the LAD, the LCX, first diagonal (D1), first obtuse marginal (OM1) , right coronary artery , posterior descending artery or intermediate artery.
- 0.5 For the D2 or OM2.

Statistical analysis

- The collected data were computerized and statistically analyzed using SPSS program (Statistical Package for Social Science) version 26. ***(11)***
- Quantitative data were expressed as *mean and standard deviation.*
- All statistical comparisons were two tailed with significance Level of P-value< 0.05 indicates significant while, P≥ 0.05 indicates non-significant difference.
- *Analysis of Variance* was used to calculate difference between quantitative variables in three groups for parametric variables.
- Chi square test ($\chi 2$) and Fisher exact was used to calculate difference between qualitative variables as indicated.

Results:

Patients with diabetes mellitus were 40%, 52% and 40% among group 1, group 2 and group 3 respectively(p = 0.439). Patients with hypertension were 34%, 50% and 42% among group 1, group 2 and group 3 respectively (p= 0.089). Smokers were 22%, 34% and 24% among group 1, 2 and 3 respectively (p = 0.349). Patients with dyslipidemia were 22%, 14% and 24% among group 1, group 2, and group 3 respectively (p = 0.535). There was no statistically significant difference between the three studied groups regarding diabetes mellitus, hypertension, smoking and dyslipidemia.

There were 26%, 34% and 40% had past history of CAD among group 1, 2 and 3 respectively (p = 0.208). There was no statistically significant difference between the three studied groups regarding past history of CAD. There were 30%, 16% and 38% had family history of CAD among group 1, 2 and 3 respectively (p= 0.055) (**Table 1).**

The mean serum LDL levels were 136.8± 9.4, 138± 10.1, and 138.2± 12.3 among group 1, 2, and 3 respectively (p = 0.797). The mean HbA1C were 6.6± 1.3, 6.8± 1.4, and 6.6± 1.3 among group 1, 2 and 3 respectively (p=0.689) . There was no statistically significant difference between the three studied groups regarding serum LDL and HbA1C.liver enzymes (AST ,ALT) showed no statistically significant difference among the three studied groups (p = 0.381) (**Table 2).**

Regarding 2D ejection fraction, degree of MR and 2D speckle tracking echocardiography despite no difference regarding ejection fraction, GLS and GCS were slightly lower in

group than other groups but this was statistically insignificant **(Table 3).**

Regarding lesion and procedure characteristics among the three studied groups, patients in group 1 had higher number of diseased vessels and implanted stents but there was no statistically significant difference between the three studied groups. Regarding stent length, diameter, dilatation pressure and TIMI grades there was no statistically significant difference. While regarding Gensini score, it was higher in group 1 and there was statistically significant difference (P =0.001) (**Table 4).**

Cumulative follow up after 6 months , patients in group 1 had higher complications as regard TLR, TVR, MI, CVS, major bleeding, cardiac death, non-cardiac death(acute liver failure and hepatocellular carcinoma), stent thrombosis and ISR than group 2 and 3 but there was statistically insignificant difference between the three studied groups (**Table 5).**

Table 1: Comorbidities among the three studied groups

Variables	Group 1	Group 2	Group 3	P value
DM				
Yes n (%)	20 (40)	26 (52)	20 (40)	0.439
HTN				
Yes n (%)	17 (34)	28 (50)	21 (42)	0.089
Smoking				
Yes n (%)	11 (22)	17 (34)	12 (24)	0.349
Dyslipidemia				
Yes n (%)	11 (22)	7 (14)	12 (24)	0.535
Family history of CAD	15 (30)	8 (16)	19 (38)	0.055
Yes				
History of CAD	13 (26)	17 (34)	20 (40)	0.208
Yes				

Table 2: Baseline laboratory parameters among the three studied groups:

Variables	Group 1	Group 2	Group 3	P value
Serum LDL				
Mean± SD	136.8± 9.4	138.0± 10.1	138.2± 12.3	0.797
AST	36.2±7.5	31.4±4.3	29.2±6.7	0.381
ALT	32.7±5.6	33.8±5.6	30.6±3.8	
HbA1C				
Mean± SD	6.6± 1.3	6.8± 1.4	6.6± 1.3	0.689

ANOVA; *p is significant at <0.05

Table 3: Comparison between the three studied groups regarding Echo findings.

Variables		Group 1 n (%)	Group 2 n (%)	Group 3 n (%)	P value
Ejection fraction Mean± SD		51.8± 6.2	50.1± 6.8	50.6± 6.1	0.384
Degree of MR	No or trivial	40 (80)	35 (70)	43 (86)	0.079
	Grade I	9 (18)	15 (30)	5 (10)	
	Grade II	1 (2)	0 (0)	2 (4)	
2D-STE Mean± SD	Longitudinal	-15.4± 2.5	-17± 2.2	-19.4± 2.2	0.604
	Circumferential	-16.7± 1.9	-17.4± 1.7	-18.6± 2.3	0.762

Chi square test; ANOVA; *p is significant at <0.05

Table 4: Lesion and procedure characteristics among the three studied groups

Variables	Group 1	Group 2	Group 3	P value
No. of diseased vessels				
One vessel n (%)	35 (70)	41 (82)	47 (94)	0.320a
Two vessels n (%)	12 (24)	8 (16)	3 (6)	
Three vessels n (%)	3 (6)	1 (2)	0 (0)	
No. of implanted stents :				
One stent n (%)	35 (70)	41 (82)	47 (94)	
Two stents n (%)	10 (20)	7 (14)	1 (2)	0.627a
Three stents n (%)	5 (10)	2 (4)	2 (4)	
Stent length				
Mean± SD	25± 5	26± 5	25± 4	0.792b
Stent diameter				
Mean± SD	3.25± 0.25	3 ± 0.5	3.25± 0.5	0.607b
Dilatation pressure				
Mean± SD	18± 2	16± 4	18± 2	0.711b
TIMI grades				
Grade 2	1 (2)	0 (0)	1 (2)	
Grade 3	49 (98)	50 (100)	49 (98)	0.211 a
Gensini score	28.0± 17.8	20.40 ± 13.7	15.76± 9.7	**<0.001b**

a Chi square test; b ANOVA; *p is significant at <0.05

Table 5: Outcomes after 6 months follow up period among the three studied groups**.**

Variables	Group 1 n(%)	Group 2 n(%)	Group 3 n(%)	P value
TLR				0.813
	2 (4)	1 (2)	1 (2)	
TVR				0.813
Yes	1 (2)	2 (4)	2 (4)	
MI	1 (2)	0 (0)	0 (0)	0.365
Yes				
CABG	0 (0)	0 (0)	0 (0)	--
Yes				
CVS	1 (2)	0 (0)	0 (0)	0.365
Yes				
Major bleeding	2 (4)	0 (0)	0 (0)	0.132
Yes				
Cardiac death	0 (0)	0 (0)	0 (0)	--
Yes				
Non-cardiac death	2 (4)	0 (0)	0 (0)	0.132
Yes				
Stent thrombosis	1 (2)	1 (2)	0 (0)	0.602
Yes				
ISR				0.813
Yes	2 (4)	1 (2)	1 (2)	

Fisher Exact test; *p is significant at <0.05

Discussion

As regard comorbidities, our results revealed that, patients with Diabetes Mellitus (p=0.439), Hypertension (p=0.089) and smoking (p=0.349) were more in group 2 than the other two groups but with no statistically significant difference. Also, patients with dyslipidemia (p=0.535) and positive family history of CAD (p=0.055) were more in group 3 than the other two groups but with no statistically significant difference.

In agreement with our results , a multi-center prospective cohort study **Hussein et al., (12)** aimed to investigate the impact of HCV seropositivity on the outcomes following percutaneous coronary intervention, the study enrolled 400-patients candidate for elective PCI using drug-eluting stents; group 1 included 200 patients were HCV seropositive and did not receive antiviral treatment, and group 2 included 200 patients were HCV seronegative. revealed that as regards hypertension, diabetes mellitus, dyslipidemia, and family history of coronary artery disease in the studied groups, there was no statistically significant difference.

Also , a study by **Satapathy et al., (13)**, included 63 HCV-infected patients who were compared with 63 age, race, and sex-matched controls without HCV infection undergoing coronary angiography for evaluation of CAD; they found that there was no significant difference between the studied groups as BMI, hypertension, diabetes mellitus, smoking and alcohol abuse.

In contrast with our results**,** a cross-sectional study done by **Ragab et al., (14)** was conducted in Zagazig University hospitals; they including 509 patients scheduled for elective coronary angiography between June 2013 and June 2014 to detect the prevalence and impact of HCV seropositivity among Egyptian patients referred for coronary angiography. They found statistical difference between the two groups regarding hypertension and diabetes mellitus which was higher in HCV positive group while there was no statistical difference regarding dyslipidemia, smoking and positive family history.

Regarding Baseline laboratory parameters among the three studied groups, we found that the mean serum LDL were 136.8± 9.4, 138± 10.1, and 138.2± 12.3 among group 1, 2, and 3 respectively (p=0.797). The mean HbA1C were 6.6±1.3, 6.8±1.4and 6.6±1.3 among group 1, 2 and 3 respectively (P value 0.689). There was no statistically significant difference between the three studied groups regarding serum LDL and HbA1C.

In agreement with our results, **Hussein et al., (12)** revealed that as regards mean of serum LDL (p=0.461) ,hemoglobin A1c (p=0.256) . There was no statistically significant difference between the two studied groups.

In contrast with our results, **Pothineni et al.,(8)** found that patients with HCV had significantly lower levels of total and low-density lipoprotein cholesterol.

Regarding left ventricular ejection fraction, the mean LVEF was 51.8± 6.2, 50.1± 6.8, and 50.6± 6.1 among group 1, 2, and 3 respectively (p=0.384). There was statistically insignificant difference between the three studied groups regarding LVEF.

In agreement with our results**, Hussein et al., (12)** revealed that as regards to the mean LVEF between the two groups (50.70 ± 9.57 vs 49.95 ± 9.30, p value 0.575)

Ragab et al.,(14) who tested the prevalence and impact of HCV seropositivity among Egyptian patients referred for coronary angiography on CAD, revealed that regarding the mean LVEF between the two groups was

55.32 ± 10.31 Vs. 55.24 ± 9.85, with insignificant difference (*p*=0.95).

A retrospective case control study, **Hossam et al.,(15)** using the database in the Qena University Cardiac Catheter Unit, 200 patients were divided into two groups. The first group (case group) involving 100 patients with HCV infection and the second group (control group) involving 100 patients without HCV infection, revealed insignificant difference (*p*=0.495) regarding the mean LVEF between the two groups (58.5 ± 9.2 VS. 59.4 ± 9.2).

Regarding lesion and procedure characteristics among the three studied groups, patients in group 1 had higher number of diseased vessels and implanted stents but there was no statistically significant difference between the three studied groups. Regarding stent length, diameter, dilatation pressure and TIMI grades there was no statistically significant difference. While regarding Gensini score, it was higher in group 1 and there was statistically significant difference **((***p*=**0.001**).

In agreement with our results**, Ragab et al., (14)** showed, that patients who are HCV antibody positive had higher Gensini score and more severe coronary lesions.

Our results were in agreement with the findings of **Hussein et al., (12)** who reported, that patients in group 2 had a statistically significant higher grade TIMI flow on angiography than patients in group 1. Also, the mean length of stents implanted in group 2 was statistically significantly higher than in group 1, while the number of diseased vessels, means percentage of luminal narrowing, number of stents implanted, mean stent diameter, and mean dilation pressure showed no statistically significant difference between both groups.

Hossam et al., (15) found that the severity of the lesion by Gensini score was significantly higher (*p*=0.001) in the cases group (41.4 ± 30.8) than control group (29.7 ± 21.3). Also, number of the coronary vessels involved was significantly higher in the cases group (*p*<0.001).

Satapathy et al.,(13) showed that combined Reardon's severity score was significantly higher among HCV positive group compared to the controls (6.26 ± 5.39 versus 2.6 ± 3.03; respectively). Also, significant multivessel CAD was also noted significantly more commonly in the HCV group compared to controls (57.1% versus 15.9%).

In contrast to our results, **Pothineni et al., (8)** found that angiographic Gensini score was similar in both groups. There was no correlation between HCV RNA titers and Gensini score (p = 0.9).

Our results showed that regarding the clinical outcomes at 1, 3 and 6 months follow-up, patients in group 1 had higher cumulative incidence of MACEs such as TLR,MI, CVS, major bleeding, non- cardiac death than group 2 and 3 but this was statistically insignificant .

Our findings were supported by the findings of **Hussein et al.,(12)** who reported that regarding the clinical outcomes at 12 months follow-up the cumulative incidence of MACEs (the primary end point) in patients of group 1 was slightly higher than that in group 2 (13.5% vs 11%, p = 0.446) but statistically insignificant.

In contrast to our results , **Pothineni et al., (8)** found that patients with active HCV infection have similar angiographic CAD burden as HCV-negative patients. Furthermore, viral load does not appear to correlate with atherosclerosis burden. Patients with HCV have less-obstructive CAD.

Conclusion: It might be concluded that HCV seropositivity has a slight impact on the cardiovascular outcomes (TLR, TVR, MI, CVS, stent thrombosis, major bleeding,cardiac or non-cardiac death), or in-stent restenosis following PCI.

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