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HCV co-infection is related to acute ischemic severity and outcome

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Abstract

Background and aim: HCV infection is associated with increased risk of ischemic cerebral stroke. HCV stroked patients are younger with a lower burden of classical risk factors and higher levels of systemic inflammation. The present study aimed to discover the association between HCV infection functional outcome of stroke.

Patients and methods: The present prospective study included 60 patients with acute ischemic stroke. All patients were subjected to careful history taking and through clinical and neurological examination. Stroke severity at presentation was assessed using National Institute of Health Stroke Scale (NIHSS). Quantitative HCV RNA test was used to diagnose HCV infection. The prognosis of the studied patients was 3 months after treatment using modified Rankin scale (mRS) for neurologic disability.

Results: The present study was conducted on 60 patients with ischemic stroke. They comprised 13 patients (21.7%) with HCV and 47 patients without. Stroke patients with HCV had significantly higher frequency of carotid artery stenosis, higher NIHSS (17.9 ± 6.9 versus 9.9 ± 5.3, $p < 0.001$) and higher frequency of severe stroke (46.1% versus 4.3%, $p = 0.001$) when compared with patients without HCV. Logistic regression analysis identified patients' sex, NIHSS and HCV as significant predictors of outcome in univariate analysis. However, in multivariate analysis, only NIHSS proved to be significant.

Conclusions: The present study suggests a significant link between chronic HCV infection and ischemic stroke severity and poor outcome. This is probably related to the pathogenic effects of the chronic inflammatory state induced by HCV infection on the cerebral microvasculature.

Keywords: Acute ischemic stroke, Hepatitis C, NIHSS score, mRS score

Introduction

Cerebrovascular stroke is the second most common cause of death after cardiovascular ischemia and the third most common cause of disability worldwide [1]. According to the American Heart Association, 87% of strokes are classified as ischemic [2]. Different modifiable and non-modifiable risk factors have been recognized for stroke. Non-modifiable risk factors are gender, age, ethnicity, heredity, and race. Modifiable risk factors include, but are not limited to, hypertension, dyslipidemia, diabetes mellitus, atrial fibrillation, smoking, drug abuse, and alcoholic intake [3].

Approximately 120 million people are chronically infected with the hepatitis C virus (HCV), and before the era of directly acting viral agents, Egypt had the highest world HCV infection prevalence (20–30%) [4]. HCV infection is associated with increased risk of ischemic cerebral stroke. HCV stroked patients are younger with a lower burden of classical risk factors and higher levels of systemic inflammation [5]. It was also noted that HCV infection is associated with an increased risk of cerebrovascular mortality, particularly for those with elevated serum HCV RNA levels [6]. Moreover, it was shown that stroke patients of HCV positive showed a significantly

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higher prevalence of carotid atherosclerosis than that observed in the stroke patients and negative HCV [7].

Interestingly, antiviral treatment led to a significant decrease in the risk of stroke after adjusting for known prognostic factors. The beneficial effect of treatment is particularly intriguing, as it provides strong evidence in favor of a pathogenic role for HCV in cerebral vascular diseases [8].

The present study aimed to discover the association between HCV and infection functional outcome of stroke.

Materials and methods

The present prospective study was conducted at Beni-Suef University Hospitals in the period from August 2019 through April 2020. The study protocol was approved the local ethical committee of Beni-Suef Faculty of Medicine and all patients gave informed consent to participate in the study. The study included 60 patients with acute ischemic stroke. Patients were excluded from the study if they have another disabling neurological or systemic disease e.g. epilepsy, malignancy, etc.

All patients were subjected to careful history taking and thorough clinical and neurological examination. Stroke severity at presentation was assessed using National Institute of Health Stroke Scale (NIHSS). Radiological assessment included brain computed tomography (CT) and carotid and vertebrobasilar duplex. Performed laboratory investigations included complete blood count, liver functions, kidney functions, fasting and postprandial blood sugar, HbA1c and lipid profile. Quantitative HCV RNA test was used to diagnose HCV infection. Other performed investigations were ECG and echocardiography. The prognosis of the studied patients was 3 months after treatment using modified Rankin scale (mRS) for neurologic disability.

Data obtained from the present study were statistically analyzed using SPSS 25 (IBM, USA). Numerical variables were presented as mean and standard deviation (SD) while categorical variables were presented as number and percent. Student t test was used to compare numerical variables while chi-square test or Fisher's exact test were used to compare categorical variables as appropriate. Binary logistic regression was used to identify predictors of the study outcome. *P* value less than 0.05 was considered statistically significant.

Results

The present study was conducted on 60 patients with ischemic stroke. They comprised 13 patients (21.7%) with HCV and 47 patients without. Comparison between the studied groups regarding the clinical and laboratory data showed that stroke patients with HCV had significantly higher frequency of carotid artery stenosis, higher NIHSS (17.9 ± 6.9 versus 9.9 ± 5.3, $p < 0.001$) and higher frequency of severe stroke (46.1% versus 4.3%, $p = 0.001$) when compared with patients without HCV. Moreover, it was shown that HCV + ve patients had significantly higher mRS score (3.6 ± 1.3 versus 2.1 ± 1.3, $p = 0.001$) and higher frequency of cases with unfavorable outcome (76.9% versus 36.2%, $p = 0.005$) when compared with patients without HCV (Table 1).

Logistic regression analysis identified patients' sex [OR (95% CI): 3.6 (1.1–11.5), $p = 0.031$], NIHSS [OR (95% CI): 2.5 (1.4–4.3), $p = 0.001$] and HCV [OR (95% CI): 5.9 (1.4–24.4), $p = 0.015$] as significant predictors of outcome in univariate analysis. However, in multivariate analysis, only NIHSS proved to be significant [OR (95% CI): 2.8 (1.4–5.5), $p = 0.002$] (Table 2).

Table 1 Demographic, clinical and outcome parameters in the studies patients ($n = 60$)

	All patients $N = 60$	**HCV + ve** $n = 13$	**HCV-ve** $n = 47$	***p* value**
Age	55.8 ± 16.1	52.2 ± 18.9	56.8 ± 15.4	0.37
Male/female	42/18	7/6	35/12	0.45
Risk factors n (%)				
Hypertension	24 (40.0)	5 (38.5)	19 (40.04)	0.9
Diabetes	22 (36.7)	7 (53.9)	15 (31.9)	0.15
Heart disease	13 (21.7)	4 (30.8)	9 (19.2)	0.37
Smoking	21 (35.0)	3 (23.1)	18 (38.3)	0.31
Dyslipidemia	10 (16.7)	4 (30.8)	12 (25.5)	0.71
Family history of stroke	6 (10.0)	2 (15.4)	4 (8.5)	0.6
Stroke subtype				
Large artery disease	25 (41.7)	5 (38.5)	20 (42.7)	0.62
Small artery disease	15 (25.0)	3 (23.1)	12 (25.5)	
Cardio-embolic stroke	20 (33.3)	5 (38.5)	15 (31.9)	
Carotid artery state n (%)				
Normal	45 (75.0)	4 (30.8)	41 (87.2)	< 0.001
Stenosis < 50%	11 (18.3)	6 (46.1)	5 (10.6)	
Stenosis ≥50%	4 (6.7)	3 (23.1)	1 (2.1)	
NIHSS	11.6 ± 6.5	17.9 ± 6.9	9.9 ± 5.3	< 0.001
Stroke severity n (%)				
Minor	7 (11.7)	–	7 (14.9)	0.001
Moderate	38 (63.3)	5 (38.5)	33 (70.2)	
Moderate-to-severe	7 (11.7)	2 (15.4)	5 (10.6)	
Severe	8 (13.3)	6 (46.1)	2 (4.3)	
MRS	2.5 ± 1.4	3.6 ± 1.3	2.1 ± 1.3	0.001
Outcome n (%)				
Favorable	33 (55.0)	3 (23.1)	30 (63.8)	0.005
Unfavorable	27 (45.0)	10 (76.9)	17 (36.2)	

Table 2 Predictors of unfavorable outcome in the studied patients

	Univariate analysis			Multivariate analysis		
	OR	95% CI	p	OR	95% CI	p
Age	1.01	0.98–1.05	0.47	–	–	–
Sex	3.6	1.1–11.5	0.031	1.8	0.11–31.3	0.67
NIHSS	2.5	1.4–4.3	0.001	2.8	1.4–5.5	0.002
HCV	5.9	1.4–24.4	0.015	0.1	0.0–4.2	0.22

Discussion

The aim of this work to study the possible relation between HCV infection and ischemic stroke severity and outcome. Among the studied patients, there were 13 patients (21.7%) with HCV. Comparative analysis revealed that HCV patients had significantly higher frequency of carotid artery stenosis. This agreed with El-Azab et al., [7] who showed that stroke patients of HCV showed a significantly higher prevalence of carotid atherosclerosis than that observed in the stroke patients without HCV. Similar conclusions were reported by other studies [9–11]. Interestingly, a meta-analysis found that compared with individuals without HCV, patients with HCV had a higher risk for carotid atherosclerosis, cerebrocardiovascular events such as ischemic stroke and myocardial infarction, and death resulting from cardiovascular disease [12].

In the present study, HCV patients had significantly higher NIHSS and higher frequency of severe stroke when compared with their counterparts without HCV. The association between HCV and severity of ischemic stroke is a novel finding. Infectious agents may play as a stimulus for atherothrombosis [13, 14] by triggering a cascade of immune responses and inflammatory stimuli either locally within vascular tissue or systemically through inflammatory mediators [15].

In addition, the present study noted that HCV patients had significantly higher prevalence of unfavorable outcome. While HCV was considered a significant predictor of stroke outcome in univariate analysis, only NIHSS remained significant in multivariate analysis. Patients with persistent HCV infection had increased circulating levels of inflammation markers such as C-reactive protein and endothelial progenitor cells. This may provide insights on the mechanisms involved in the link between HCV infection and cerebrovascular disease [16, 17].

In conclusion, the present study suggests a significant link between chronic HCV infection and ischemic stroke severity and poor outcome. This is probably related to the pathogenic effects of the chronic inflammatory state induced by HCV infection on the cerebral microvasculature.

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None.

Authors' contributions
Mohammed M. Masoud, has contributed to the research by designing and supervision. Hany A. Sayed, has contributed to the research by writing and data collection. Hatem A. El Masry, has contributed to the research by reviewing. Shaimaa A Abdelkareem, has contributed to the research by data collection and reviewing. All authors read and approved the final manuscript.

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Availability of data and materials
Data of this research will be available upon reasonable request.

Declarations

Ethics approval and consent to participate
The present study was approved by the ethical committee of Beni-Suef Faculty of medicine (Approval number: 208/11) at March, 1, 2019.

Consent for publication
All patients or their legal guardians gave informed consent to participate in the study.

Competing interests
The authors declare no conflict of interest, financial or otherwise.

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