Prevalence of hepatitis C virus infection in Egyptian patients with rheumatoid arthritis

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ABSTRACT

Aim: Egypt has the highest HCV prevalence in the world; however, there is paucity of data on the prevalence of HCV in Egyptian rheumatoid arthritis (RA) patients. The aim of the current study was to estimate this prevalence.

Methods: The study included 300 Egyptian patients diagnosed with RA according to the ACR/ EULAR 2010 classification criteria. All participants were tested for HCV antibodies using 3rd generation ELISA and positive patients were tested for HCV RNA by Real Time PCR.

Results: HCV antibodies were detected in 15% of patients (45/300), of which 80% were positive for HCV RNA (36/45). Prevalence of HCV antibodies was higher in females than males (15.3% and 12.5%, respectively) and in patients living in rural areas than those living in urban areas (16.7% and 14.6%, respectively). HCV prevalence increased sharply with age to reach 50% in patients older than 60 years (12/24). There was a statistically significant increase ($p<0.001$) in the mean age and RA disease duration in the HCV antibodies positive group (51.1 vs. 41.2 and 11.7 vs. 5.2 years, respectively). HCV was strongly associated with RF (OR = 3.7, P< 0.001). Lower spontaneous clearance of HCV was observed in the studied RA patients compared to population based estimates.

Conclusion: We estimated that the prevalence of HCV antibodies in Egyptian patients with RA is 15%. Given this exceptionally high prevalence, we recommend screening of all RA patients in Egypt for hepatitis C at diagnosis and before starting treatment.

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INTRODUCTION

The unique high endemicity of HCV (genotype 4) in Egypt is well documented[1,2]. Patients with rheumatoid arthritis (RA) are potentially exposed to HCV infection due the increased exposure to healthcare services and related invasive procedures, which carries increased risk in Egypt for HCV transmission[3,4]. Moreover, there is a complex relationship between RA and HCV. Chronic HCV infection alone has been shown to be associated with an increased risk for development of RA[5]. A case report was published presenting a patient who developed RA 9 weeks after treatment of hepatitis C with Peg-IFN and ribavirin[6]. Other diagnostic and therapeutic challenges complicate the relation between the two diseases.

We also have noted that the proportion of patients who are exposed to HCV infection and spontaneously clear the virus can be modified by other selected co-morbidities such as HIV and diabetes mellitus[7].

The aim of the current study was twofold, first to determine the prevalence of HCV infection in Egyptian patients diagnosed with RA and secondly, to provide evidence that RA modifies HCV spontaneous clearance.

PATIENTS AND METHODS

This was a cross sectional study to determine the prevalence of HCV antibodies and HCV RNA in Egyptian patients (≥ 18 years old) diagnosed with rheumatoid arthritis (RA) according to the American College of Rheumatology (ACR)/ European League Against Rheumatism (EULAR) 2010 classification criteria. Patients presenting to the rheumatology outpatient clinics at Ain Shams University Hospitals and Ahmed Maher Teaching Hospital, Cairo, Egypt, during the period from June 2015 until February 2017 and with a confirmed diagnosis of RA were invited to participate. Patients younger than 18 years old, with end stage renal disease, on dialysis, or with other connective tissue diseases were excluded from the study.

After approval of the IRB ethical committee of the Faculty of Medicine, Ain Shams University, an informed written consent was obtained from each participant. Full medical history was obtained from all participants and a thorough clinical examination was performed. Patients' disease activity was determined using the Disease Activity Score (DAS28).

The following laboratory tests were completed on all participants: complete blood count (CBC), erythrocyte sedimentation rate (ESR), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and rheumatoid factor (IgM RF). Anti-cyclic citrullinated peptide (Anti-CCP) was done when clinically indicated.

All participants were tested for HCV antibodies using 3rd generation ELISA and positive patients were tested for HCV RNA by Real Time PCR.

RESULTS

HCV antibodies were detected in 15% of patients (45/300), of which 80% were positive for HCV RNA (36/45). The ratio of RNA to antibody is higher compared to general population (66%). Prevalence of HCV antibodies was higher in females than males (15.3% and 12.5%, respectively) and in patients living in rural areas than those living in urban areas (16.7% and 14.6%, respectively). HCV prevalence increased sharply with age to reach 50% in patients older than 60 years (12/24). There was a statistically highly significant increase ($p<0.001$) in the mean age and RA disease duration in the HCV antibodies positive group (51.1 vs. 41.2 and 11.7 vs. 5.2 years, respectively). According to DAS28; only 33 patients (11%) were in remission. The majority of patients (62.7%) had high disease activity. There was no statistically significant difference ($p>0.05$) in DAS28 between HCV antibodies positive and negative patients **(Table 1)**.

While the majority of the patients used a combination of different DMARDs, 14% used a single drug (42/300). The medications used for treatment of RA in the studied patients are shown in **(Table 2)**. There was a statistically highly significant decrease in the use of NSAIDs and methotrexate ($p<0.001$), while there was a statistically highly significant ($p<0.001$) increase in the use of sulfasalazine in patients positive for HCV antibodies.

Table (1): Characteristics of the total studied RA patients and HCV antibodies positive and negative patients:

Variables	*Total (n=300)*	*HCV Ab + (n=45)*	*HCV Ab – (n=255)*	*p-value*
Sex				
Female	268 (89.3%)	41 (15.2%)	227 (84.7%)	0.68*
Male	32 (10.7%)	4 (12.5%)	28 (87.5%)	
Age (years)				
Range	18 - 89	24–72	18 – 89	<0.001**
Mean ± SD	42.7 ± 12	51.1 ± 12.6	41.2 ± 11.5	
Address				
Urban	240 (80%)	35 (14.6%)	205 (80.4%)	0.69*
Rural	60 (20%)	10 (16.7%)	50 (83.3%)	
RA disease duration (Years)				
Range	1 - 45	0 – 45	0 – 25	<0.001**
Mean ± SD	6.2 ± 7.4	11.7 ± 12.8	5.2 ± 5.5	
DAS28 Score				
Range	0.97 – 9.27	1.85 – 8.96	0.97 – 9.27	0.26**
Mean ± SD	5.6 ± 2	5.3 ± 2.2	5.7 ± 2	
Rheumatoid Factor				
Negative	122 (40.7%)	8 (17.8%)	114 (44.7%)	OR =3.7
Positive	178 (59.3%)	37 (82.2%)	141 (55.3%)	<0.001*

* Chi Square; **Student's *t-test*; Ab: antibodies; SD: standard deviation

Table (2): Associated co-morbidities and medication usage in the total studied RA patients and HCV antibodies positive and negative patients (*by Chi-Square test*):

	Total (n=300)	*HCV Ab + (n=45)*	*HCV Ab – (n=255)*	*p-value*
Associated co-morbidities				
Jaundice	8 (2.7%)	2 (4.4%)	6 (2.4%)	0.43
Diabetes	30 (10%)	6 (13.3%)	24 (9.4%)	0.42
Hypertension	38 (12.7%)	8 (17.8%)	30 (11.8%)	0.26
Cardiac diseases	22 (7.3%)	2 (4.4%)	20 (7.8%)	0.42
Lung diseases	22 (7.3%)	11 (24.4%)	11 (4.3%)	<0.001
Renal diseases	6 (2%)	2 (4.4%)	4 (1.6%)	0.20
Neurologic diseases	4 (1.3%)	0 (0.0%)	4 (1.6%)	0.40
Medications				
NSAIDs†	186 (62%)	13 (28.9%)	173 (67.8%)	<0.001
Corticosteroids	278 (92.7%)	43 (95.6%)	235 (92.2%)	0.42
Methotrexate	170 (56.7%)	14 (31.1%)	156 (61.2%)	<0.001
Leflunomide	122 (40.7%)	19 (42.2%)	103 (40.4%)	0.82
Sulfasalazine	48 (16%)	18 (40.0%)	30 (11.8%)	<0.001
Hydroxychloroquine	264 (88%)	42 (93.3%)	222 (87.1%)	0.23
Biologic DMARDs‡	0 (0%)	0 (0%)	0 (0%)	

†NSAIDs: non steroidal anti-inflammatory drugs; ‡DMARDs: disease modifying anti-rheumatic drugs

Table (3): The ratio of HCV antibodies to HCV RNA in the current study compared to the population based EDHS † 2008[1] and EHIS‡ 2015[8] studies.

Study	*Number*	*HCV Ab +*	*HCV RNA +*	*Ratio*
Current study	300	45 (15%)	36 (12%)	0.8*
EDHS† 2008	11,126	1,636 (14.7%)	1090 (9.8%)	0.666
EHIS‡ 2015	16,003	1,600 (10%)	1121 (7%)	0.7

†EDHS: Egyptian Demographic and Health Survey; ‡EHIS: Egyptian Health Issues Survey;
*P< 0.05: A/B Split Test (one tail)

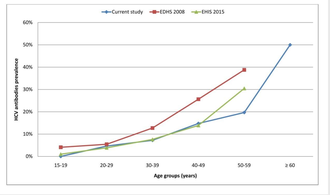

Figure 1. Comparison between HCV antibodies prevalence in the current study, EDHS† 2008[1] and EHIS‡ 2015[8] by age groups.
†EDHS: Egyptian Demographic and Health Survey; ‡EHIS: Egyptian Health Issues Survey

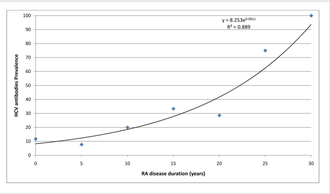

Figure 2. The association between RA disease duration and prevalence of HCV antibodies.

CONCLUSION

We estimated that the prevalence of HCV antibodies in Egyptian patients with RA is 15%. Given this exceptionally high prevalence, we recommend screening of all RA patients in Egypt for hepatitis C at diagnosis and before starting treatment. Our results also suggest that RA patients have a lower spontaneous clearance of the initial HCV infection.

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