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Estimation of antibodies to mutated citrullinated vimentin in Egyptian patients with chronic hepatitis C virus infection associated with arthropathy.

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Abstract

Background: The prevalence of extra hepatic manifestations of chronic HCV infection is more than 74%, among different extra-hepatic manifestations (EHMs) articular involvement is a frequent complication. Clinical picture of HCV related arthropathy varies widely; RA-like HCV related arthropathy can be clinically indistinguishable from recent onset RA, in which articular damage and deformities have not yet occurred. Differentiating patients with HCV related arthropathy from RA patients represents a diagnostic and therapeutic challenge.

Aim of the work: The study aimed to determine the prevalence of anti-MCV antibodies in HCV-infected patients and to assess the utility of anti-MCV antibodies in distinguishing between patients with RA and those with HCV-related arthropathy.

Patients and Methods: This study was conducted on 75 chronic hepatitis C patients who fulfilling the designed inclusion criteria. The study was carried out in outpatient clinics of Tropical Medicine department and Rheumatology departments Al-Azhar University Hospitals (Al-Hussein & Sayed Galal Hospitals), during the period from March to November 2016. The patients enrolled in the study were classified into three groups: Group (I): Included 25 patients of HCV and Rheumatoid Arthritis, Group (II): Included 25 patients of HCV with articular manifestation. and Group (III): Included 25 patients of HCV without articular manifestation.

Results: Seroprevalence of Anti- MCV in GI was positive in 23/25 versus 2/25 seronegative cases while the seroprevalence of Anti- MCV in GII was positive in 2/25 versus 23/25 seronegative cases ($P>0.05$) and the mean titer of Anti-MCV antibodies was 136.26 ± 113.3 , 14.05 ± 5.1 , and 12.89 ± 5.8 in GI, GII, and GIII respectively. The sensitivity and specificity of Anti- MCV was 92% and Diagnostic Accuracy also 92% so Anti-MCV antibodies had higher specificity for diagnosis of RA (p value <0.001). **Conclusions:** Anti-MCV antibodies may help in differentiating patients with RA from those patients with HCV related arthropathy.

Keywords: HCV, RA, anti-MCV

Introduction

HCV associated arthritis in contrast to RA has a benign course, typically not deforming and not associated with articular bony erosions involving predominantly small joints of the hands (metacarpo-phalangeal, proximal interphalangeals and wrists) (Remoroza and Bonkovsky, 2003).

Differentiating patients with HCV related arthropathy from rheumatoid diseased patients represents a diagnostic and therapeutic challenge (Rinera et al., 2000), because the classic clinical picture of RA is not entirely helpful in differential diagnosis, other diagnostic tools, such as the detection of serologic abnormalities in sera of patients with RA, could be helpful in differentiating between these disorders (Olivieri et al., 2003).

The discovery of anticitrullinated protein autoantibodies has led to the development of various new tests, such as anti-cyclic citrullinated peptide (anti CCP) antibodies, and anti-mutated citrullinated vimentin (anti-MCV) antibodies, to diagnose RA, and to distinguish between RA and other causes of arthritis (Al-Shukaili et al., 2012).

Citrullinated proteins are likely to be found in RA synovium. Palmitadyl adenine deaminase (PAD) containing inflammatory cells infiltrate the site of inflammation, at the onset of death of these cells, the intracellular calcium concentration is raised causing activation of PAD and consequently citrullination of proteins (Vossennar et al., 2003).

Aim of the work

The aim of the study was to determine the prevalence of anti-MCV antibodies in HCV-infected Egyptian patients and to assess the utility of anti-MCV antibodies in distinguishing between patients with rheumatoid arthritis and those with HCV-related arthropathy.

Patients and Methods

A cross sectional study was performed to determine the prevalence of anti-MCV antibodies in HCV-infected patients and to assess the utility

of anti MCV antibodies in distinguishing between patients with RA and those with HCV-related arthropathy. The study was conducted on 75 chronic hepatitis C patients who fulfilling the designed inclusion criteria. The study was carried out in outpatient clinics of Tropical Medicine and Rheumatology departments Al-Azhar University Hospitals (Al-Hussein & Sayed Galal Hospitals), during the period from March to November 2016. The study included Egyptian patients 18 years ,Serum positive for both anti HCV antibodies and polymerase chain reaction (PCR) for HCV RNA, either cirrhotic or non-cirrhotic, with or without articular manifestation and RA patients fulfilling the 1987 revised criteria of American College of Rheumatoid (ACR) for RA diagnosis . Patients with liver disease other than chronic hepatitis C, or malignancy, Patients with previous interferon treatment, women who were pregnant or breast-feeding were excluded from the study. The steps of the study were explained to the patients who were met the eligibility criteria and they were asked to sign a consent form. The patients enrolled in the study were classified into three groups: **Group (I):** Included 25 patients of HCV and Rheumatoid Arthritis, (RA patients fulfilling the 1987 revised ACR criteria for RA diagnosis). **Group (II):** Included 25 patients of HCV with articular manifestation. **Group (III):** Included 25 patients of HCV without articular manifestation. All patients were subjected to thorough clinical examination including general and abdominal examination with stressing on the manifestations of chronic liver illness and special emphasis on joint examination. Complete blood count, ESR, CRP, liver biochemical profile including serum bilirubin, liver enzymes (ALT, AST), total proteins, albumin, prothrombin time (PT), and concentration ,fasting blood glucose , and kidney function tests were evaluated to patients groups. Also HBs Ag, HCV antibodies and Quantitative HCV RNA by polymerase chain reaction (PCR). Immunological profile including: RF assay and anti MCV: RF was assayed with a quantitative immunonephelometry test. RF was considered to be positive when the concentration was higher than 15 IU/ml. Anti-MCV was measured using an indirect solid phase ELISA for the quantitative measurement of IgG class autoantibodies against

Mutated Citrullinated Vimentin (MCV) in human serum (using kit from ORGENTEC Diagnostika GmbH, Mainz, Germany). Imaging including Abdominal ultrasonography and Plain ray on affected joints were evaluated.

Results

The present study included 75 patients with chronic HCV infection, they were 26 male (34.7%) and 49 females (65.3%), with their age ranged between 22 and 76 years. The patients were divided into 3 groups according to their joint affection. **Group (I):** included 25 patients of HCV and Rheumatoid Arthritis. RA patients fulfilling the 1987 revised ACR criteria for RA diagnosis. **Group (II):** included 25 patients of HCV with articular manifestation. **Group (III):** included 25 patients of HCV without articular manifestation. Regarding to the demography of the studied groups, Group I included 7 male patients (28%) and 18 females (72%), with mean age of 45.00 ± 10.85 years. Group II included 9

male patients (36%) and 16 females (64%), with mean age of 48.76 ± 10.02 years. Group III included 10 male patients (40%) and 15 females (60%), with mean age of 46.04± 13.63 years. There was no statistical significant difference between groups as regards the age, gender and residence (*p* > 0.05). As regard to history taking, there was a statistical significant difference between groups as regards some symptoms suggestive of hepatic decompensation as hepatic encephalopathy, jaundice, ascites, hematemesis and melena (*p* <0.05) . The articular manifestation among patients in group I and II shows symptoms suggestive of peripheral joint arthropathy (arthralgia and or arthritis). A statistical significant difference is found between group I and II; group I patients showed higher rate of swelling, redness, hotness, limitation of movement, deformity and morning stiffness of peripheral joints when compared to patients of group II =*p* <0.001. (Table 1)

Table (1): Symptoms of articular manifestation among patients in GI &GII

Symptoms		Group I (n = 25)		Group II (n = 25)		p-value
		n	%	n	%	
Number of affected peripheral joints	< 3 joint areas	3	12.0%	18	72.0%	<0.001
	3 joint areas including hand	22	88.0%	7	28.0%	
Arthralgia	+ve	25	100.0%	25	100.0%	<0.001
	-ve	0	0.0%	0	0.0%	
Morning Stiffness more than 1 hour	+ve	25	100.0%	2	8.0%	<0.001
	-ve	0	0.0%	23	92.0%	
Cardinal symptoms of inflammation (arthritis)	+ve	25	100.0%	4	16.0%	<0.001
	-ve	0	0.0%	21	84.0%	
Deformity	+ve	11	44.0%	0	0.0%	<0.001
	-ve	14	56.0%	25	100.0%	
Axial joints affected	+ve	2	8.0%	1	4.0%	0.353

Regarding the number of affected peripheral joints, group I showed higher mean number of affected joint areas than group II ($p < 0.001$). The affection of axial joints is insignificantly different between groups I and II ($p > 0.05$). As regards the distribution of peripheral joint affection among the studied patients, 25 patients in group I (100%) had affection of hand joints (metacarpophalangeal and proximal interphalangeal joints), 13 patients (52%) had wrist affection, 15 patients (60 %) had knee and small joints of feet affection, 11 patients (44 %) had elbow affection and 9 patients (36 %) had shoulder affection. While in group II patients, 18 patients (72 %) had hand joints affection, 11 patients (44 %) had knee affection, 8 patients (32 %) had wrist affection and 6 patients (24 %) had elbow, shoulder, and ankle affection.

The general examination of the studied groups showed that there was statistically significant

difference between groups as regard Jaundice and flapping tremors ($p < 0.05$), while no statistically significant difference between groups as regard mental state, spider naevi, palmar erythema and lower limb edema ($p > 0.05$).

Regarding to joint examination (Table 2) demonstrates peripheral joints examination of affected patients (group I & II): there was a statistical significant difference between both groups as regards the distribution of joints affected ($p < 0.001$). Group I patients had higher rate of affection of 3 or more joint areas while patients of group II showed less number of affected joint areas.

Patients of both groups showed tender joints on examination, group I patients showed higher rate of signs of arthritis including swelling, warmth and deformity when compared to patients of group II ($p < 0.05$). (Table 2)

Table (2): Joints examination of patients in group I and II :

		Group I (n = 25)		Group II (n = 25)		p- value
		n	%	n	%	
Number of affected peripheral joints	< 3 joint areas	3	12.0%	18	72.0%	<0.001
	3 joint areas including hand	22	88.0%	7	28.0%	
Symmetry	+ve	25	100.0%	16	64.0%	0.001
	-ve	0	0.0%	9	36.0%	
Deformity	+ve	11	44.0%	0	0.0%	<0.001
	-ve	14	56.0%	25	100.0%	
Axial joints affected	+ve	2	8.0%	1	4.0%	0.552
	-ve	23	92.0%	24	96.0%	
		(n = 25)		(n = 25)		p- value
Number of tender joints	Mean ± SD	15.28±6.63		9.32±4.15		0.004
		(n = 25)		(n = 4)		p- value
Number of swollen joints	Mean ± SD	15.28±6.63		1.20±3.055		<0.001

Group I patients showed higher mean number of tender and swollen joints when compared to patients of group II, only 4 patients in group II had swollen joints, ($p < 0.001$). On examining the axial joints, there was no statistical significant difference between both groups as regards the axial joints affected ($p > 0.05$) Table (2)

The results of laboratory investigations of the studied groups showed that Group I patients had statistically significant higher mean of acute

phase reactants (ESR, CRP) ($p < 0.001$) than patients Group II & III. There was no statistically significant difference ($p > 0.05$) between groups as regards CBC parameters. There was no statistically significant difference ($p > 0.05$) between groups as regards renal function tests. As regards liver function tests of the studied groups: group II & III patients had lower serum albumin levels, higher bilirubin and INR levels than group I patients ($p < 0.05$). Table (3):

Table (3): Laboratory investigations of the studied groups:

	Group I (n = 25)	Group II (n = 25)	Group III (n = 25)	p-value
	Mean \pm SD	Mean \pm SD	Mean \pm SD	
HGB (gm/dl)	10.38 \pm 1.84	10.11 \pm 1.70	10.18 \pm 2.03	0.139
WBC (x10³/ml)	6.58 \pm 1.35	6.78 \pm 3.19	5.86 \pm 1.15	0.276
PLTs (x10³/ml)	178.12 \pm 72.2	163.36 \pm 63.3	145.0 \pm 86.2	0.295
ESR (mm/hr)	61.88 \pm 28.3	35.32 \pm 18.46	35.00 \pm 13.73	<0.001
CRP (mg/dl)	21.80 \pm 14.4	8.56 \pm 5.20	6.79 \pm 1.19	<0.001
Creatinine (mg/dl)	1.32 \pm .29	1.17 \pm .39	1.21 \pm .33	0.284
BUN (mg/dl)	25.1 \pm 12.35	24.2 \pm 11.91	22.2 \pm 5.44	0.623
ALT (IU/L)	34.0 \pm 20.6	48.3 \pm 35.04	37.6 \pm 20.7	0.144
AST (IU/L)	43.80 \pm 24.6	54.56 \pm 28.8	42.32 \pm 22.46	0.185
Alkaline phosphatase (U/L)	177.24 \pm 63.81	186.04 \pm 77.9	204.28 \pm 71.9	0.399
Total Protein (gm/dl)	6.90 \pm .787	7.07 \pm .88	6.78 \pm .934	0.487
Albumin (gm/dl)	3.54 \pm .59	2.99 \pm .71	2.79 \pm .62	<0.001
Total Bilirubin (mg/dl)	1.76 \pm 1.35	3.24 \pm 2.08	2.82 \pm 1.25	0.005
PT (sec)	15.69 \pm 2.33	18.14 \pm 3.52	17.46 \pm 2.46	0.009
INR	1.37 \pm .204	1.59 \pm .311	1.52 \pm .27	0.012
FBS (mg/dl)	112.08 \pm 29.5	108.32 \pm 30.7	110.8 \pm 30.3	0.905

Radiological findings of the affected joints (in most cases hand joints) were detected by plain X-ray. There was a statistical significant difference between Group I & II patients as regards the

presence of radiological erosions, 16 patients in Group I showed radiological erosions while none of patient in Group II showed radiological erosions ($p < 0.001$). Table (4):

Table (4): Plain X- ray of affected joints of the studied group: (Group I & II)

		Group I (n = 25)		Group II (n = 25)		p-value
		n	%	n	%	
Presence of radiological erosions	+ve	16	64.0%	0	0.0%	<0.001
	-ve	9	36.0%	25	100.0%	

Table (5) showed that the prevalence of +ve RF and Anti-MCV antibodies was high in group I.

		Group I (n = 25)		Group II (n = 25)		Group III (n = 25)		p-value
		n	%	n	%	n	%	
RF	+ve	24	96.0%	13	52.0%	4	16.0%	<0.001
	-ve	1	4.0%	12	48.0%	21	84.0%	
Anti- MCV	+ve	23	92.0%	2	8.0%	1	4.0%	<0.001
	-ve	2	8.0%	23	92.0%	24	96.0%	

There was statistical significant difference between group I patients when compared to group II & III patients ($P < 0.001$), while there was no

statistically significant difference between group II & III patients ($P > 0.05$). Table (5)

Table (6): Comparison between the studied groups as regard the mean titer of RF and Anti-MCV antibodies:

		Group I (n = 25)	Group II (n = 25)	Group III (n = 25)	p-value
		RF	Mean±SD	89.76±55.06	
	Range	12.00-215.0	4.00-42.00	2.00-27.00	
Anti- MCV	Mean±SD	136.26±113.39	14.05±5.14	12.89±5.89	<0.001
	Range	14.60-460.0	6.80-29.50	4.60-34.50	

Table (6) showed that the mean titer of RF and Anti-MCV antibodies was high in group I. There was statistical significant difference between

group I patients when compared to group II & III patients ($P < 0.001$), while there was no statistically significant difference between group II & III patients ($P > 0.05$).

Table (7): Seroprevalence of Anti-MCV in group I regarding to the articular manifestations:

		Group I				p-value
		+ve Anti-MCV (n= 23)		-ve Anti-MCV (n= 2)		
		n	%	n	%	
Peripheral joints affected	<3 joint areas	3	13.0%	0	0.0%	0.586
	>3 joint areas including hand	20	87.0%	2	100.0%	
Swelling (cardinal signs of arthritis)	+ve	23	100.0%	2	100.0%	0.191
	-ve	0	0.0%	0	0.0%	
Symmetry	+ve	23	100.0%	2	100.0%	0.664
	-ve	0	0.0%	0	0.0%	
Deformity	+ve	11	47.8%	0	0.0%	0.664
	-ve	12	52.2%	2	100.0%	
Axial joint affection	+ve	2	8.7%	0	0.0%	0.877
	-ve	21	91.3%	2	100.0%	
Morning Stiffness more than 1 hour	+ve	23	100.0%	2	100.0%	0.877
	-ve	0	0.0%	0	0.0%	
Number of tender joints	Mean ±SD	15.21±6.48		16.0±11.31		0.877
Number of swollen joints	Mean ±SD	15.21±6.48		16.0±11.31		0.877

Table (7) showed that there was no statistical significant difference between positive and

negative Anti-MCV in group I patients as regards articular manifestations ($P>0.05$).

Table (8): Seroprevalence of Anti-MCV in group II regarding to the articular manifestations:

		Group II				p-value
		+ve Anti MCV (n= 2)		-ve Anti MCV (n= 23)		
		n	%	n	%	
Peripheral joints affected	<3 joint areas	2	100.0%	16	69.6%	0.358
	>3 joint areas including hand	0	0.0%	7	30.4%	
Swelling (cardinal signs of arthritis)	+ve	1	50.0%	3	13.0%	0.171
	-ve	1	50.0%	20	87.0%	
Symmetry	+ve	1	50.0%	15	65.2%	0.667
	-ve	1	50.0%	8	34.8%	
Deformity	+ve	0	0.0%	0	0.0%	0.664
	-ve	2	100.0%	23	100.0%	
Morning Stiffness more than 1 hour	+ve	0	0.0%	2	8.7%	0.763
	-ve	2	100.0%	21	91.3%	
Axial joints affected	+ve	0	0.0%	1	4.3%	0.327
	-ve	2	100.0%	22	95.7%	
Number of tender joints	Mean ±SD	6.50±.70		9.56±4.24		0.276
Number of swollen joints	Mean ±SD	3.50±4.95		1.00±2.92		0.276

Discussion

Our aim in the current study was to estimate anti-MCV antibodies in HCV-infected patients and to assess the utility of anti MCV antibodies in distinguishing between patients with RA and patients with HCV-related arthropathy among Egyptian patients. The current study was carried out in Al-Azhar University Hospitals (Al-Hussein and Sayed Galal University Hospitals). A total of 75 patients were included in this study. Included patients were recruited from Tropical Medicine and Rheumatology departments during the period from March to November 2014. They were classified into three groups: **Group (1)** included 25 patients of HCV and Rheumatoid Arthritis, RA patients fulfilling the 1987 revised ACR criteria for RA diagnosis. **Group (2)** included 25 patients of HCV with articular manifestation. **Group (3)** included 25 patients of HCV without articular manifestation.

The current study showed that group I included 7 male patients (28%) and 18 females (72%), with mean age of 45.00 ± 10.85 years. Group II included 9 male patients (36%) and 16 females (64%), with mean age of 48.76 ± 10.02 years. Group III included 10 male patients (40%) and 15 females (60%), with mean age of 46.04 ± 13.63 years. There was no statistical significant difference between groups as regards the age, gender and residence ($p > 0.05$).

Our results regarding the age and gender were close to that of **Elewa et al., (2012)** who found that the mean age was 42.8 ± 16.1 years in RA patients, with 25 (83%) female patients, and the mean age was 50.9 ± 14.8 in HCV infected patients with arthritis, with female percentage of 66%.

Also, our results coincides with that is reported by **Elbordeny et al., (2008)** who studied that the mean age was 45.7 ± 7.47 years in HCV patients with articular manifestation, with 16 (80%) female patients, and the mean age was 49.8 ± 6.58 years in HCV patients without articular manifestation, with 12 (60%) female patients.

Duration of articular manifestation in our study ranged from 1 to 16 years in group I with mean 6.84 ± 2.7 years, and from 1 to 9 years in group II with mean of 5.92 ± 1.8 years. This is in agreement with **Hussein et al., (2015)** who studied that the mean of disease duration was 9.6 ± 2.3 and 9.6 ± 4.3 years in HCV-infected RA patients and HCV patients with articular manifestations respectively.

On studying the articular manifestation among the studied groups, we found that cardinal symptoms and signs of arthritis, morning stiffness, symmetry of polyarthritis and deformity were highly significant in group I compared to group II ($p < 0.05$). On the other hand, the manifestation of hepatic decompensation in the form of hepatic encephalopathy, jaundice, ascites, hematemesis and melena between the studied groups showed lower rate of these manifestations in group I compared to group II and III. Our explanation referring to that the main presentation and concern of such patients in group I were the articular manifestation and most patients ignore about the HCV infection. In our study we found that all patients of group I (100%) had manifestation of arthritis and were presented with morning stiffness of more than one hour, while in group II 4 (16%) patients had manifestation of arthritis and only 2 (8 %) patients were presented with morning stiffness of more than one hour. Moreover, that arthritis was symmetrical in 25 (100%) and in 16 (64%) of group I and group II patients respectively.

This was in agreement with **Zucherman et al., (2001)** who studied 185 HCV infected patients with different rheumatological manifestations. Nearly the same results were reported by **Zehairy et al., (2012)** who found that most patients with RA-like HCV related arthropathy may fulfill some of the ACR criteria for RA diagnosis.

This was in agreement with **Elnadry et al., (2013)** who found that 22 (75.9%) patients of RA infected with HCV were presented with morning stiffness of more than one hour, while 10 (32.3%) patients of HCV with articular manifestation were presented with the same complaint.

Arthritis in the current study was symmetrical in 23 (79.3%) patients and 5 (16.1%) patients of RA patients infected with HCV and HCV patients with articular manifestation respectively. Also, our results coincides with that reported by **Amin and Heidar (2014)** who found that symmetrical polyarthritis detected in 9 (36%) patients among HCV- associated arthropathy patients.

Jadali and Alavian, (2010) reported that HCV related arthritis usually manifests as rheumatoid-like, symmetrical inflammatory polyarthritis. The joints involved in HCV-related arthritis have a similar distribution with that is affected in RA.

Regarding to the number of joint affected, the current study revealed 3 or more joints area affection in 22 patients (88%) among group I compared to 7 patients (28%) in group II, regarding the distribution of peripheral joint affection, we found high prevalence of affection of hand joints (100%) and wrist affection (52%) in group I compared to (72 %) and (32 %) in group II respectively. Our results coincides with **Zuckerman et al., (2000)** who reported that most patients with RA like HCV related arthropathy may fulfill some of the ACR (American College of Rheumatology) criteria for RA diagnosis. The current study showed higher rate of deformity in group I patients corresponding to 11 (44.0%) patients, while none in group II patients had deformity ($p < 0.05$), the results agree with that is reported with **Mahmoud et al., (2011)** who stated that deformity was found in 5 (22.7%) patients in HCV-Ab positive RA patients. As regard laboratory investigation of our patients, there was significant elevation in ESR and CRP in group I compared to group II and III, as these are acute phase reactants and its elevation is associated with active inflammation elsewhere, its elevation was obvious in group I versus group II and III.

The mean of ESR was 61.8 ± 28.3 mm/h, 35.3 ± 18.4 mm/h and 35.0 ± 13.7 mm/h in group I, II and III respectively. This is in agreement with **Ahmed et al., (2012)** who reported that the mean ESR was 76.4 ± 20.3 mm/h, and 56.9 ± 6.4 mm/h in RA patients and HCV related polyarthritis respectively.

This also is concordant with **Elnadry et al., (2013)** who found statistically significant increases in the level of ESR in HCV-infected RA patients with mean of 40.55 ± 12.6 mm/h, compared to HCV patients with and without articular manifestation, with mean of 13.90 ± 3.5 mm/h and 13.19 ± 5.6 mm/h respectively.

The mean of CRP was 21.80 ± 14.4 mm/h, 8.56 ± 5.2 mm/h and 6.79 ± 1.19 mm/h in group I, II and III respectively. This was in agreement with **Elewa et al., (2012)** who reported high CRP level in RA patients compared to HCV patients with arthropathy.

Regarding the radiological finding on the affected joint, the current study showed joint affection in the form of joint erosion in 16 (64%) patients among group I while no positive radiological finding among group II. This was in agreement with **Mahmoud et al., (2011)** who reported that 17 (77.3%) HCV-positive RA patients had joint erosions. Similar results reported by **Elbordeny et al., (2008)** who found 14 (70%) patients with HCV-positive RA had radiological erosions on plain X-ray while none of HCV related arthropathy patients had the same finding. In our study, RF was positive in 24 (96%) patients of group I, compared to 13 (52%) patients and 4 (16%) patients in group II and III respectively, with statistically high significant increase in RF level in group I with mean of 89.76 ± 55.06 compared to 17.12 ± 9.94 and 9.12 ± 6.26 in group II and III respectively. This was in agreement with **Bombardieri et al., (2004)** who found that 66.7% of HCV- positive RA patients were RF positive, while 37.5% were RF positive in HCV patients with articular manifestation. **Kaptanoglu et al., (2010)** also reported that RF was positive in 37.5% of patients with HCV-associated arthropathy. This also, coincides with **Elewa et al., (2012)** who found that The mean titer of RF in patients with early RA (190.75 ± 290.9) was significantly higher than in HCV patients (43.43 ± 110.05) which is statistically significant, and nearly similar results reported by **Elbordeny et al., (2008)**.

However, opposite results were also reported by **Zukeramm et al., (2000)**; **Bassyouni et al. (2009)**; **Ezzat et al. (2011)** and **Zehairy et al., (2012)** who found that RF was positive in patients with HCV- associated arthropathy with percentage of 61%, 60%, 81.8% and 86.7% respectively. **Sene et al., (2006)** detected that RF is not specific tool to distinguish between RA patients and patients with HCV-related arthropathy, as many cases of recent onset RA were seronegative while many cases of rheumatoid like conditions such as HCV infection may be seropositive. **Koga et al., (2007)** also reported that RF can be detected in from 50~80% of RA patients, however, it is also detected in patients with either other autoimmune diseases or HCV infection, as well as even in normal healthy subjects.

In our study, Anti-MCV was positive in 23 (92%) patients of group I, whereas it was positive in 2 (8%) patients and only one (4%) patient in group II and III respectively with highly a statistically significant difference between group I and both groups II and III, while no statistically significant difference between group I and II.

This was in agreement with **Kaptanoglu et al., (2010)** who investigated the role of anti-MCV in HCV patients. They tested the presence of anti-MCV in 34 RA patients and 30 HCV-infected patients. They detected anti MCV positive in 30% of HCV-infected patients compared to 70.6% in RA. This is in accordance with **Zehairy et al., (2012)** who detected anti-MCV positive in 30% of patients with HCV related arthropathy compared to 93.3% in patients with RA. Thus, anti-MCV was statistically higher in RA patients than in HCV patients with arthropathy.

The formation of anti-MCV antibody in patients with chronic hepatitis is not difficult to explain. Hepatic stellate cells contain vimentin; oxidative stress due to liver injury can modify this vimentin so that it becomes immunogenic stimulating the production of anti-MCV (**Niki et al., 1996**; **Dejaco et al., 2006**)

Abdeen et al., (2011) reported the presence of anti-MCV antibody in patients with chronic hepatitis and have demonstrated that it can be used to diagnose liver cirrhosis with 60%

specificity. They showed that significant protein citrullination of vimentin occurs in patients with chronic hepatitis and that the serum concentration of anti-MCV antibody could differentiate patients with no liver fibrosis from those with moderate to severe fibrosis and this supports the theory that hepatic stellate cells play a central role in liver fibrosis. In addition, the level of anti-MCV in our study was statistically significantly higher in group I compared to group II and III, with mean of 136.2 ± 113.3 , 14.0 ± 5.1 and 12.8 ± 5.8 in group I, II and III respectively.

This was in agreement with **Zehairy et al., (2012)** who studied that the mean of anti-MCV was 444.1 ± 374.2 in RA patients compared to 34.3 ± 32.9 and 29.0 ± 20.9 in HCV patients with and without arthropathy respectively.

This also, coincides with **Elewa et al., (2012)** who found that the mean titer of serum anti-MCV in patients with RA (420.9 ± 560.44 U/ml) was significantly higher than in HCV patients (12.97 ± 7.90). Similar results reported by **Elbordeny et al., (2008)** and **Liu et al., (2008)**. Moreover, these results supported with **Xia et al., (2009)** who stated that the mean titer of serum anti-MCV in patients with early RA 523.9 ± 660.45 U/ml was significantly higher than in other patients with other diseases as systemic lupus erythematosus, primary Sjögren's syndrome, systemic sclerosis, ankylosing spondylitis, viral hepatitis type B and tuberculosis, which revealed anti-MCV highly specific for RA. Using an ROC curve analysis to assess the reliability of RF and anti-MCV to distinguish rheumatoid arthritis from HCV associated arthropathy, our study showed that Anti-MCV shows higher specificity (92%), PPV (92%), and diagnostic accuracy (92%) than RF (48%), (64.86%) and (72%) respectively.

Similar results were reported by **Elewa et al., (2012)** with specificity of (92.3%), a PPV of (96.6%), and diagnostic accuracy (93%) for Anti-MCV which is higher than RF (43%), (70%) and (65%) respectively. **Zehairy et al., (2012)** also found the sensitivity of anti-MCV and RF was 93.3 and 86.7% respectively, whereas their specificity was 69.1 and 18.2%, respectively.

Also, this coincides with **Van Steendam et al., (2011)** who reported that the overall sensitivity and specificity profile of anti-MCV has been noted to be the best among available ACPAs (i.e., around 84% and 87%).

So, we can conclude that differentiation between patients with RA and those with HCV related arthropathy has great relevance in clinical practice to establish the aggressive treatment, to prevent joint erosions in patients with true RA and to reduce the risk of immunosuppression therapy in patients with HCV related arthropathy. Our results showed that anti-MCV antibodies levels are high in RA and may be useful in diagnosis of RA. Moreover, anti-MCV could have a role in differentiating RA from chronic HCV- associated arthropathy patients.

Conclusion

Anti-MCV antibodies may help in differentiating patients with RA from those patients with HCV related arthropathy.

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