



## RHEUMATOID FACTOR ANTIBODY IN ASSOCIATION WITH CHRONIC HEPATITIS PATIENTS TYPE B (HBV) AND C (HCV)

Azhar Emran Lateif Al-Thahab

Department of Biology, College of Science, University of Babylon, Hilla, Iraq

### ABSTRACT

Twenty four hepatitis C patients, and 20 hepatitis B patients were selected for determination of rheumatoid factor in their sera, and 10 healthy persons as a control sample, arranged in male and female groups. The possible role of rheumatoid factor assessment represent as a biomarker for chronic hepatitis C. The disease is being reported while there are no significant differences in RF of hepatitis B patients after comparison with control as well as male and female patients. It was found that RF can discriminate between male, female and total HCV patients as concentration means are taken in consideration. Since there was a range of individual variations in HCV patients and controls, this may reflect variation in genetic backgrounds of the best control groups. All of the aforementioned forms of HCV disease in man were rise up the levels of RF concentration than women in the present study, while hepatitis B patients have no differences due to gender. On the other hand, there is a highly significant increase in RF concentration in HCV patients compared with control, as well as no significant increase in RF of hepatitis B patients.

**KEYWORDS:** hepatitis C, rheumatoid factor, HCV *etc.*

### INTRODUCTION

Hepatitis C virus (HCV) is an RNA enveloped virus in the flaviviridae family, it has very simple positive – sense single stranded RNA genome. HCV antibodies have been implicated in tissue damage because of immune complex formation; example of such tissue damage is antinuclear antibodies and antibodies that work against the liver and kidney. The immune complexes are also deposited in other tissues and cause some of the other extra hepatic problem, including vasculitis, arthritis, glomerulonephritis and others (Kenneth *et al.*, 2010). Rheumatoid factor (RF) is the common serological marker which is used for the diagnosis of rheumatoid arthritis, but it is non-specific and can also be positive in other autoimmune and inflammatory diseases. Patients with Hep. C. may also develop for distinguishing the cause of arthritis, Ant CCP appears to be more specific for rheumatoid arthritis than RF in patients with Hep. B and C. (Lei *et al.*, 2007). The presence of IgM rheumatoid factor (RF) in the serum is the sole serological indicator of criteria for diagnosis of RA. RFs are a subset of antiglobulins directed against the FC region of IgG. RFs are present in the serum of 70 % - 80% of patients with rheumatoid arthritis (RA) at some time during the disease course. However, RFs are also found in the serum of patients with infectious and autoimmune diseases, hyperglobulinemias, B-cell lymphoproliferative disorders and in aged population. This suggests that RF may be a finding associated with B-cell hyperactivity. RFs which have been found among the IgM, IgG and IgA classes of immunoglobulins, reacting only with xenogeny Fc are not auto antibodies and are unlikely to be of pathological significance (Immunchem, 2011). Infectious agents such as viruses and bacteria have also been suggested to trigger RF antibody. However, no relationship between infectious agents and the development of RA has been found by Cacoub *et*

*al.*,(2000). There is a correlation between higher RF concentrations and more-severe disease and poor prognosis, but the use of RF in monitoring disease activity is unclear ( Shmerling *et al.*, 1992). Various viruses have been implicated in the cause and pathogenesis of rheumatoid arthritis (RA). Hepatitis C virus (HCV) infection, which has been recognized as a cause of some autoimmune diseases, and which has been described as sometimes presenting with rheumatic manifestations indistinguishable from RA, might be a candidate (Csepregi *et al.*, 2001) . Various viruses have been implicated in the cause and pathogenesis of rheumatoid arthritis (RA) .Hepatitis C virus ( HCV) infection, which has been recognized as a cause of some autoimmune diseases, and which has been described as sometimes presenting with rheumatic manifestations indistinguishable from RA, might be a candidate ( Maillefert *et al.*, 2002 ).

### MATERIAL AND METHODS

Twenty four hepatitis C patients, and 20 hepatitis B patients, were selected for determination of rheumatoid factor in patient sera using ELISA technique in accordance with a manual procedure of Immunochem, (2011), as well as (10) healthy person as a control sample. All patients are clinically and laboratory diagnosed as hepatitis C or B in Babylon public health laboratory at the period between January and February 2012. Statistical analysis for data was conducted by using SPSS programs.

### RESULTS & DISCUSSION

The controls (C), total chronic hepatitis C, male and female, total hepatitis B, male and female patients, were showing rheumatoid factor concentration means of ; 30.01pg/ml, 73.64 pg/ml, 76.00pg/ml, 70.33pg/ml, 43.7079 pg/ml, 44.0806 pg/ml, 42.8382 pg/ml, respectively. Both of male and female patients of hepatitis

C were of higher concentration means than the control, but, male group was slightly higher than the female group, as showing in table (1). While hepatitis B patient have no difference in male and female as shown in table (3). The table (1) shows a highly significant increasing ( $P < 0.01$ ) of rheumatoid factor in hepatitis C patients after comparison

with control, as well as male and female compared with control samples. This result might be refer to infectious activity of virus against the host tissue to cause tissue damage and activate the immune system to produce different antibodies to and immune complex to regulation the effect of such as an activity .

**TABLE 1:** Rheumatoid factor and hepatitis –C- patients

Group	Control Mean± SD N=10	Hepatitis C. patients Mean ± SD N=24	P. value
Total	30.01± 8.03	*73.64± 50.67	0.001
Male	30.01± 8.03	*76.00± 51.54	0.000
Female	30.01± 8.03	*70.33± 52.01	0.007

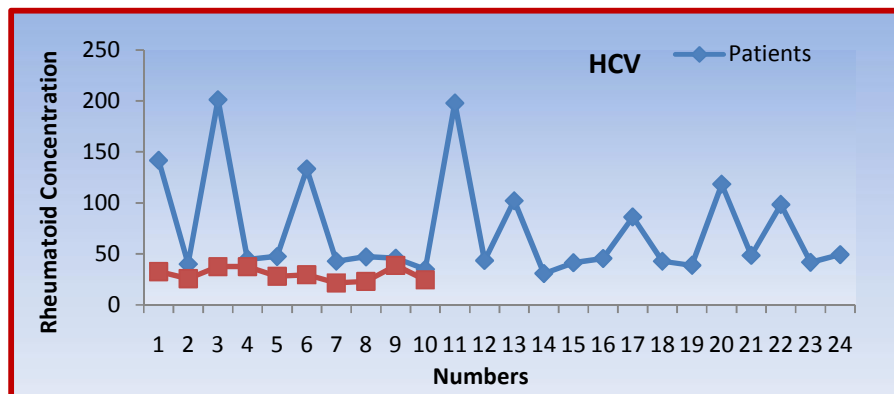
Comparison between hep. C male and female patients show no significant difference ( $P > 0.05$ ) of rheumatoid factor result in male patients compared with female (table 2), although there is a high incidence rate of autoimmune antibodies in the female more than male, but in this study

the increasing of rheumatoid factor might be due to virus activity rather than autoimmunity because the RFs can bind IgG from many species when immobilized on surfaces.

**TABLE 2:** Rheumatoid factor of male and female hepatitis C patients

Group	Male hepatitis C. patients Mean ± S.D N=14	Female Hepatitis C. patients Mean ± S.D N=10	P. value
	76.00± 51.54	70.33± 52.01	0.737
			N.S

Normal distribution of rheumatoid factor among hepatitis C. can see clearly in figure ( 1)



**FIGURE 1:** The normal distribution of rheumatoid factor result among hepatitis C patients and control reflecting the extent of individual variations . (Series 1= Patients data, Series 2= Control.).

In patients of hepatitis B the relationship of rheumatoid factor shows no significant increase in RF concentration of hepatitis B patients in comparison with control as well as male and female as shown in table ( 3). This result might

be show that there is a difference between RF in hepatitis B and C patients, because a difference in the type of tissue damage and virus mechanism for invasion and escape in liver tissue .

**TABLE 3:** Rheumatoid factor and hepatitis –B- patients

Group	Control Mean±S.D N=10	Hepatitis B. patients Mean ±S.D N=20	P. value
Total group	30.01± 8.03	43.7079 ± 4.178	0.106
Male	30.01± 8.03	44.0806±5.222	0.117
Female	30.01± 8.03	42.8382±3.812	0.219
	N=100	N=6	N.S

Result shows no significant difference between male and female patients as shown in table (4).Both results of

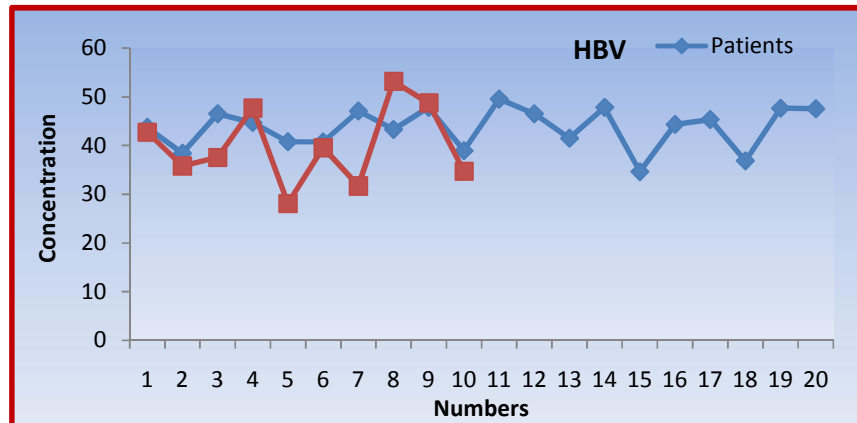
hepatitis B and C have no difference in male compared with female, this result might be refer to the same genetic

background of exposed tissue for viral antigen at both male and female.

**TABLE 4:** Rheumatoid factor of male and female hepatitis B patients

Group	Male hepatitis patients Mean $\pm$ S.D.	Female hepatitis B. patients Mean $\pm$ S.D.	P. value
	44.0806 $\pm$ 5.222	42.8382 $\pm$ 3.812	0.557
	N= 14	N=6	N.S

Normal distribution of rheumatoid factor among hepatitis B. patients can seen clearly in figure (2)



**FIGURE 2:** The normal distribution of rheumatoid factor result among hepatitis B patients and control reflecting the extent of individual variations. (Series 1= Patients data. Series 2= Control.).

RFs frequently occur in a variety of other diseases, such as SLE, endocarditic, tuberculosis, syphilis, sarcoidosis, cancer, viral infection, Sjogren's syndrome and diseases affecting the liver, lung or kidney. The result was normally higher in older patients and in those who have received multiple vaccination and transfusion. (Frances *et al.*, 2009). Most viral infections induce cellular and humoral immune response that act in concert to limit viral spread, clear infection and provide protective immunity against re infection with the same virus (Symmons *et al.*, 1993). Hepatocellular injuries due to immune attack by cytotoxic (CD 8) T- cells are well explained. Serological testing to detects antibody to HCV using ELISA methods confirmatory test using Line Immunoassay and PCR – based assay for viral load can be used to evaluate whether active is present. (Dubois *et al.*, 1997). Immune escape through mutations introduced by the error prone HCV RNA – dependent polymerase, broadly directed cellular responses during acute infection are associated with HCV clearance, while narrow qualitative impaired anti-HCV responses occur in chronic infection. (King *et al.*, 1994). Different cytokine profiles of T-cells within the liver in chronic HBV and HCV infections illustrate a different behavior of local immune response in these two infections that may have pathogenic implications (Cacoub *et al.*, 2000). Arthritis is present in up to 20 percent of HCV patients. In two thirds of the cases, the arthritis mimics a rheumatoid arthritis. Most likely, the arthritis in this setting is due to immune complex formation between the hepatitis C virus and anti-hepatitis C antibodies. Accordingly, the arthritis may occur when the antigen /antibody reach a particular ratio leading to immune complex formation, and this may occur early, late or chronically. (Rosener *et al.*, 2010). In conclusion, the possible role of rheumatoid factor assessment as a biomarker for chronic hepatitis C. The disease is being

reported as well as anti-hepatitis C antibody, but less uses because it not specific for such diseases.

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