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Frequency of Circulating Antibodies to Hepatitis C Virus (HCV): A Follow up Study

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ABSTRACT

The pattern of anti-HCV titer was observed among 24 HCV positive patients for six months in a follow –up study. The study revealed an increase in the titer of HCV antibody of the 24 patients; in the first visit the number of patients with a titer of 1:3, 1:10, 1:100 and 1:300 were 12, 3, 6, 3 respectively, while in the fourth visit the number of patients with the above titers were found in 2,1.9 and 12 patients respectively. This finding reflected the importance of viremia level in the pathogenesis of HCV and its association with the existence of liver disease. The present work also revealed that the changes in the antibody level reflected variation of some liver function tests between first and fourth visit. From this study we can conclud that liver destruction in HCV positive patients can be followed by measuring both anti-HCV titer and variation in liver functions especially ALT level.

مستوى المستضدات لفايروس التهاب الكبد نمط ج: دراسة متابعة

الملخص

جرى تحري عن التغيرات في معيارية المستضد لفايروس التهاب الكبد نمط ج وذلك مـن خـلال متابعة 24 مريضا ولمدة ستة اشهر . اظهرت النتائج زيادة معيار المستضد لدى المرضى حيـث كانـت الزيادة في الزيارة الاولى للمعايير 1:300, 1:100, 1:10, 1:3 هو 3, 6, 3, 12 على التـوالي . بينمـا تغيير في الزيادة الرابعة الى 1, 9, 12, 2 على التوالي وهذه النتيجة تعكس مدى اهمية قيـاس مـستوى الفايروس في الدم في امراضية التهاب الكبد الفايروسي.

كذلك عكست الدراسة تغييرات في مستوى الفحوصات البايوكيمائية التي تخص وضائف الكبد ومن هذا يمكن الاستنتاج بأمكانية متابعة التاف النسيجي الذي يحصل في الكبد لدى المرضى المصابين بألتهاب الكبد الفايروسي نمط ج من خلال قياس معيارية المستضد للفيروس بالطرق السريولوجية مع التغيـرات في مستوى فحوصات وضائف الكبد وخصوصا مستوى الـ ALT.

INTRODUCTION

Hepatitis C virus is an RNA virus responsible for the majority of post-transfusion hepatitis. The HCV is classified into six distinct subtypes, comparing at least 74 different subtypes. Both types and subtypes are subjected to geographical differences in distribution (Amadco and Lawrnce, 1987) (Black, 1997) .

The virus induce a broad spectrum immune response of structural and non-structural antigens. The core and being the most immunogenic, IgG antibodies are the most sensitive marker (Fabrizi and Lunghi, 1996). The IgM antibodies appeares shortly 3-7 weeks after the onset of hepatitis persisted for several months and the disappeared. In contrast the IgG antibodies persisted long-term once it appeared. Thus IgM anti capsid antibodies may serve as a marker indicating acute or active HCV infection (Gordon Kodali, 1994). The aim of the present work was to identify the patterns of anti-HCV titer during six months follow-up of HCV positive patients.

MATERIALS AND METHODS

Twenty-four HCV positive patients were tested by three ELISA test Kits (UBI, Liatek and Bio-ELISA). The anti-HCV positive individuals were followed-up for six months by serological and biological investigations which were done four times. Two months was the period between each visit and blood samples were obtained in each visit.

The serum samples were diluted in to 1:3, 1:10, 1:100 and 1:300 and tested using following to the semi quantitative methods by Lia-Tek third generation (Organon Teknika). The results were read by the Micro–ELISA reader system (Organon Teknika) and interpreted according to the instruction of manufactures. The remaining serum samples used for biohemical investigations which include determination of serum bilrubin, alanin aminotransferase (ALT), asperate aminotransferase (AST) and alkaline phosphatase (ALP)(Irving and Neal, 1994). The results were statistically analyzed (Katsutoshi and Takajii, 1996).

RESULTS

The variation in the pattern of anti-HCV titer during six months follow –up shown in (Fig.1).

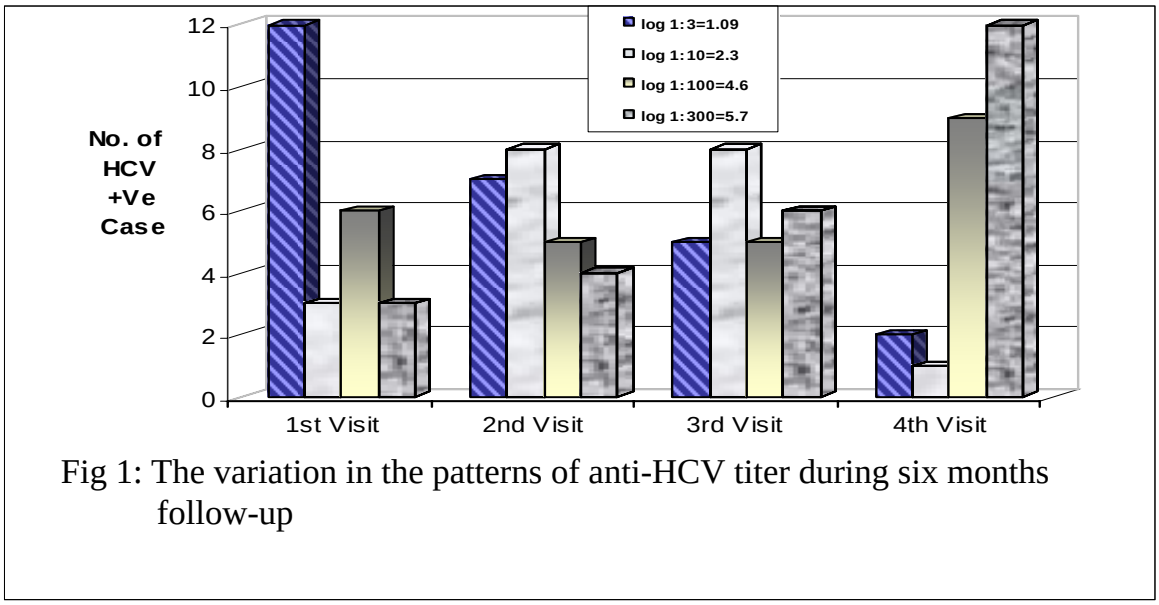

Fig 1: The variation in the patterns of anti-HCV titer during six months follow-up

The results revealed that in the first visit 50% of anti-HCV positive patients have a titer 1:3, While after six months the number decrease to 8.5%.On the other hand the number of patients that have a titer 1:300 was 6.6 in the first visit and increased during follow-up to 50% at the last visit.

The relation between anti-HCV titer and variation in liver function tests and serum albumin during six months follow-up shown in (Fig.2a,2b,2c,2d).

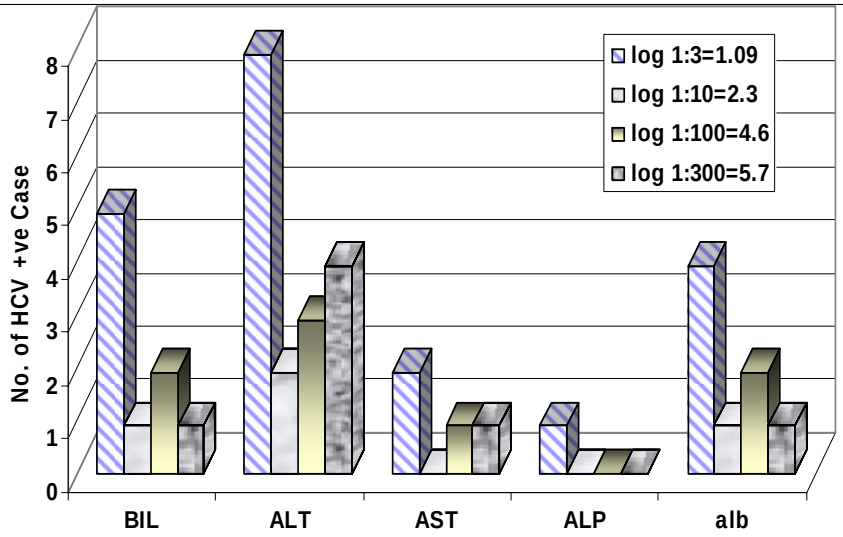

Fig 2a: The alteration of liver function tests and other biochemical test during six months follow-up of 24 anti-HCV positive patients (1st Visit).

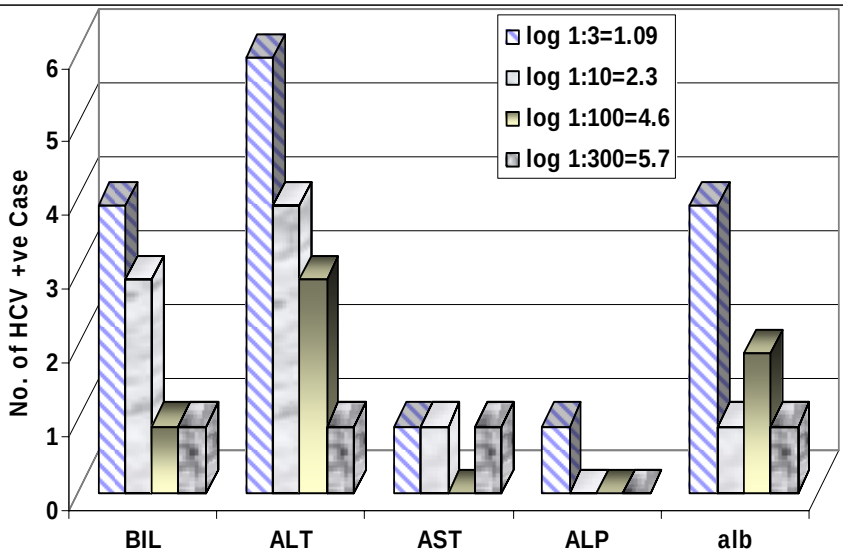

Fig 2b: The alteration of liver function tests and other biochemical test during six months follow-up of 24 anti-HCV positive patients (2nd Visit).

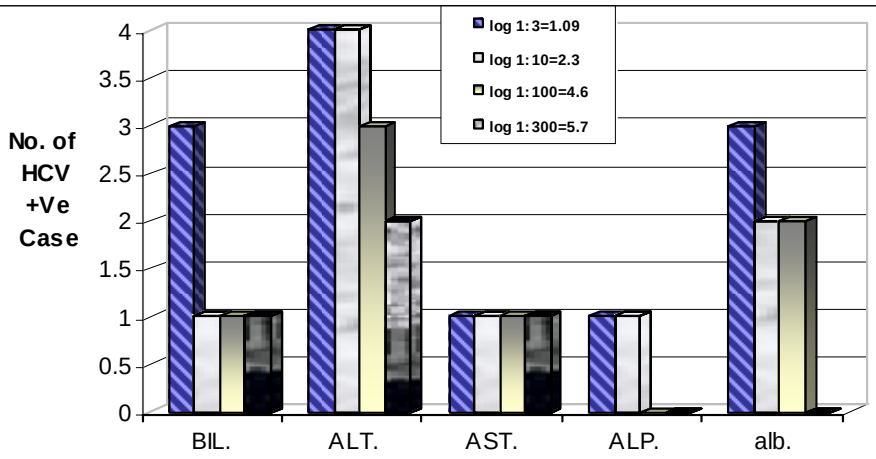

Fig 2c: The alteration of liver function tests and other biochemical test during six months follow-up of 24 anti-HCV positive patients (3rd Visit).

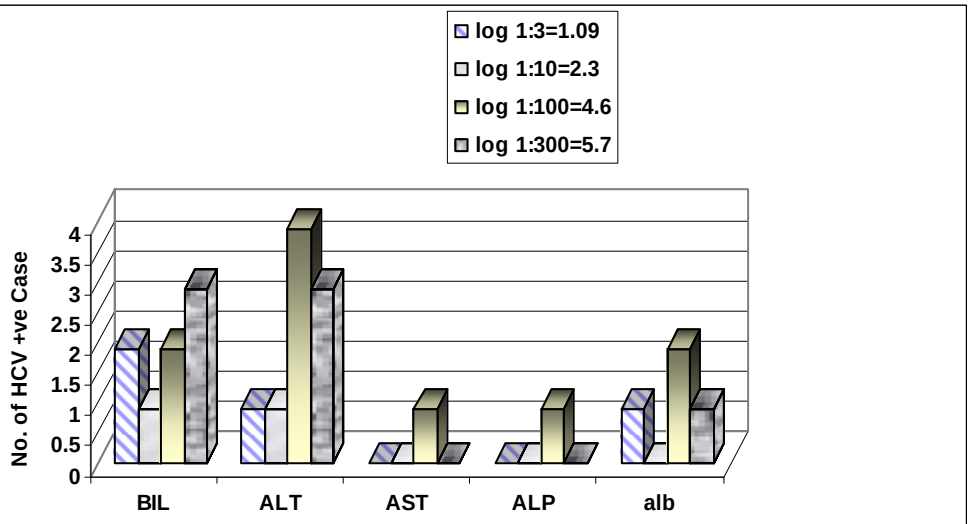

Fig 2d: The alteration of liver function tests and other biochemical test during six months follow-up of 24 anti-HCV positive patients (4th Visit).

In the first visite the number of patients with a titer 1:3, 1:10, 1:100 and 1:300 were 12, 3, 6, 3 respectively. The r-limits between the anti-HCV titer and serum bilrubin, albumin, ALT, AST were 0.75, 0.60, 0.86, 0.45. While, in the fourth visit the number of patiens with the above mentioned titers were found in 6, 13, 4, 2, with r-limits 0.68, 0.75, 0.09 and 0.10 respectively.

The relation between anti-HCV titer and ALT activity during follow up (Table 1).

Table 1: The relationship between the patterns of anti-HCV titer and mean of ALT activity

No **Of patient**	**Risk group**	**Sex**	**1st visit**		**2nd visit**		**3rd visit**		**4th visit**	
			Titer	**ALT I.U/L**	**Titer**	**ALT I.U/L**	**Titer**	**ALT I.U/L**	**Titer**	**ALT I.U/L**
1.	B.d	M	1:3	563	1:3	530	1:3	525	1:3	435
2.	*B.d*	*M*	1:3	586	1:10	341	1:10	340	1:100	160
3.	B.d	M								
4.	B.d	M			1:100	125				
5.	B.d	F					1:300	70		
6.	A.J.C.	M	1:3	427	1:3		1:3	430	1:100	310
7.	A.J.C	F	1:3	442	1:3	425	1:10	435		
8.	H.C.	F	1:100	237			1:100	230		
9.	H.C.	M	1:300	170			1:300	225	1:300	60
10.	Thala	M	1:3	415	1:3	425	1:3	390	1:10	325
11.	Thala	F					1:10	130	1:100	260
12.	Thala	M	1:3	355	1:10	380				
13.	Thala	M	1:10	230	1:10	275				
14.	Thala	F			1:300	239				
15.	Thala	F								
16.	Heam	M	1:3	307	1:3	263	1:3	325		
17.	Heam	M			1:3	325			1:100	180
18.	Heam	M			1:10	215	1:10	230		
19.	Heam	F	1:10	260	1:100	197			1:300	172
20.	Heam	F	1:100	230			1:100	380	1:300	296
21.	T.B.	M	1:3	222						
22.	Dia	M								
23.	Cont.	F								
24.	Cont.	F	1:10	180	1:100	115	1:100	80		
Total			1:1		14		13		9	

The limits of t-test between:1st and 2 nd visit=21.5
1st and 3rd visit =20.5
1st and 4th visit =17.5

**B.d: Blood donors, A.J.C.=Acute jaundice patients, H.C.=Health care, Thala.=Thalassemia patients, Dia.=chronic diabetes patients, Cont.=Relative contact*

In the first visit the number of patients with elevated ALT at a titer 1:3, 1:10, 1:100 and 1:300 were 8, 2, 3, 1 respectively and the mean value of ALT activity in cotrast to this titer were 414.6 /IU, 245/ IU, 215.6 /Iuand 170/IU. In comparsion with the fourth visit the number of patients with elevated ALT activity at the above mentioned titer were 1, 1, 4 and 3 respectively .

DISCUSSION

Several authors mentioned that there was a close relationship between immunoglobulin G HCV antibodies and viremia in HCV infection. Among various antibodies anti-HCV-Core protein has been shown to be a very sensitive marker for HCV infection. In contrast to IgG antibodies IgM antibody response during HCV infection is limited and only a few reports are available about IgM antibodies which serves as an acute-phase marker in HCV infection (Fabrizi and Lunghi, 1996)(Gordon and Kodali, 1994).

In the current study the variation in HCV titer was observed during follow-up. The increase in the titer of HCV antibody of 24 patients during six months follow-up suported by Navascus et al. (Lau and Lesniewski, 1994) who observed 81 anti-HCV positive patients. Also report by Serfaty et al. (Liaw et al., 1998) who mentioned that the viremia level is an important factor in pathogensis of HCV. Other finding by Gordon et al. (Mutimer and Harrison, 1994) showed that the lowest level of HCV titer (viremia) are associated with minimal liver disease.

The hepatic enzyme level were found to be a good indicator for HCV infection (Navascues and Rodrigues, 1994). The present work shows variation in biochemical tests during six months follow-up. In comparison with anti-HCV titer by using (UBI-ELISA kits). The statistical analysis using correlation coefficient test revealed that the r-limits were as follows :-

In the first visit r-limits between anti-HCV titer and serum bilrubin, ALT, AST and serum albumin were 0.75, 0.60, 0.75, 0.00 and 0.10 respectively. A study by Irving and Neal (1994) found that the peak enzymes concentration was correlated with severity scores. The serum enzymatic concentration activity were the most commonly used biochemical markers of hepatocellular necrosis. The ALT is highly specific for liver, whereas AST was less specific for liver injury (Richard and Remington, 1985). The serum alkalin phosphatase may be normal or mildly elevated and the serum albumin concentration may decrease slightly. The prolong elevation of aminotransferase for greater than six months suggests chronic hepatitis (Liaw et al., 1998).

In the present study strong correlation was found between the anti-HCV titer and ALT activity during the follow-up. The study by Okanoue et al. (Smith and Duridson, 1995) on forty-nine individuals with normal liver test and positive anti-HCV found twenty-four cases with chronic persistence acute hepatitis developed an elevated ALT-concentration during 12-months follow-up.

Also Mutimer et al. (Zeuzem and Roth, 1995) reported significant correlation between ALT and portal activity. Other finding reported that the mean ALT level were three time the upper normal value in post-transfusion and community acquired hepatitis(Lau and Lesniewski 1994; Navascues and Rodrigues 1994; Liaw et al., 1998). Thus the ALT testing can be used to identify the HCV window phase, among symptom free persons as well as anti-HCV.

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