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Antibodies against hepatitis C virus among renal transplant patients in Greece

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Abstract. To evaluate the prevalence of hepatitis C virus (HCV) infection in Greek renal transplant (RT) patients and its association with abnormal liver function tests (LFTs), serum anti-HCV was determined (Ortho-ELISA test system) in 206 RT and 245 haemodialysis patients (HD) as controls. The prevalence (10.2%) of anti-HCV in RT patients was significantly higher ($P < 0.0001$) than in the Greek general population (0.7%) and lower ($P < 0.0001$) than in the HD patients (23.8%), and was not related to the patients' age, post-transplant time or pre-transplant HD time. None of the anti-HCV RT patients was HBsAg +, whereas 13 (62%) and 12 (57%) of them were anti-HBsAg + and anti-HBc +, respectively. The incidence of abnormal LFTs in anti-HCV + HBsAg – and anti-HCV – HBsAg + RT patients was similar. Our findings indicate that: (a) the prevalence of serum anti-HCV in the Greek RT population is high, although considerably lower than in HD pts; (b) anti-HCV + RT patients have a high incidence of abnormal LFTs, comparable to that seen in HBsAg + RT patients; and (c) in a substantial proportion of anti-HCV + RT patients there is evidence of previous HBV infection.

Key words: Hepatitis C viral infection – Renal transplantation – Abnormal liver function tests

Liver disease is a serious complication of renal transplantation, since death due to liver failure occurs in 8–28% of renal transplant (RT) patients [3, 13]. Although viral hepatitis is one of the most common causes of liver disease complicating renal transplantation [5], until 1989 most cases of acute and chronic HBsAG – viral hepatitis in RT recipients were very loosely attributed to an unidentified hepatitis virus, designated as non-A, non-B virus [1]. In 1989, when an assay for the detection of an antibody against a recombinant viral agent (c100-3) was introduced [4], a diagnostic tool for hepatitis C viral (HCV) infection became available, and the significance of HCV as a major cause of non-A, non-B hepatitis has since emerged [2]. However, the prevalence and clinical implications of HCV infection in RT patients has not been adequately studied. This, as well as the fact that the frequency of infection with HCV has a considerable geographical distribution [9, 11, 14, 17, 18], motivated us to carry out the present study, the purpose of which was to evaluate the prevalence of HCV infection in a number of patients representative of the Greek RT population and its association with abnormal liver function tests (LFTs).

Materials and methods

Included in the study were 206 RT recipients (49 male, 57 female; aged 43.3 ± 13.6 (17–73) years) who visited the outpatient clinic of Laiko General Hospital, Athens, between July and September 1990. Their pre-transplant haemodialysis (HD) time was 2.4 ± 2.1 (0.2–10) years and their post-transplant time was 3.1 ± 2.8 (0.3–17.5) years. Of the study group, 112 had received a cadaveric graft and 49 a graft from a living related donor. The immunosuppressive regimens consisted of: azathioprine (AZA) + cyclosporin (CsA) + methylprednisolone (MP) (151 patients), AZA + MP (27 patients), CsA + MP (27 patients) and MP only (1 patient). The control group comprised 245 HD patients (137 male, 108 female; aged 56.1 ± 15.1 (19–73) years) who had undergone HD for 4.2 ± 4.4 (0.3–18) years.

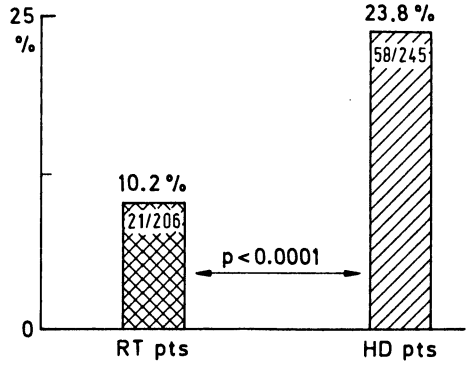

Fig. 1. Prevalence of HCV antibodies in RT and HD patients

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Serum antibody against HCV (anti-HCV) was determined with a first generation enzyme-linked immunosorbent assay (Ortho HCV ELISA Test System, Ortho Diagnostic Systems) which detects antibody to a recombinant antigen of HCV (c100-3). Initially reactive samples were retested twice more, and only samples that were repeatedly reactive were considered as positive. Hepatitis B markers were determined with commercially available kits of ELISA-ORGANON (HBsAg, anti-HBs) and E.I.A.-SORIN (HBeAg, anti-HBe, anti-HBc, anti-HBcIgM). Serial LFT measurements (SGOT/SGPT, alkaline phosphatase, γGT and bilirubin) were routinely performed in all patients. LFT results were arbitrarily defined as abnormal when the mean level of two sequential measurements was 1.5 times above the upper limit of the normal range. This definition was chosen because, in RT patients with liver disease, the LFT results are usually not increased [3, 13].

Statistical analyses were performed with the use of the chi-squared test and Student's *t*-test where applicable.

Table 1. Relation between prevalence of anti-HCV and age in RT patients

Age groups (years)	No. of patients	No. anti-HCV +	%
0–29	29	3	10.3
30–39	49	2	4.1
40–49	57	6	10.5
50–59	58	9	15.5
60–69	12	1	8.3
≥ 70	1	0	0

$P = 0.54$

Table 2. Relation between prevalence of anti-HCV and post-transplant time

Post-transplant time (years)	No. of patients	No. anti-HCV +	%
0–3	131	16	12.2
4–7	61	3	4.9
> 8	14	2	14.2

$P = 0.24$

Table 3. Relation between prevalence of anti-HCV and pre-transplant HD time

Time on HD (years)	No. of patients	No. anti-HCV +	%
0–3	136	13	9.5
4–7	22	3	13.6
> 8	11	0	0

$P = 0.45$

Table 4. HBV markers in the anti-HCV + RT patients

	No. of patients	%
HBsAg +	0	0
anti-HBc + /anti-HBs +	8	39
anti-HBc + /anti-HBs –	4	19
anti-HBc – /anti-HBs +	5	23
All markers –	4	19
Totals	21	100

Results

Antibody against HCV was repeatedly found to be present in the serum of a significantly higher proportion of RT (21/206, 10.2%) than HD (58/245, 23.8%) patients ($P < 0.0001$) (Fig. 1). The prevalence of anti-HCV in the RT population was not significantly affected by sex (M, 14/149; F, 7/57; $P = 0.70$), age ($P = 0.54$, Table 1), post-transplant time ($P = 0.24$, Table 2) or pre-transplant HD time ($P = 0.45$, Table 3). None of the anti-HCV + RT patients were HBsAG + whereas 13 (62%) of them were anti-HBs + and 12 (57%) were anti-HBc + (Table 4). A similar incidence ($P = 0.26$) of abnormal LFT results was noted in anti-HCV + /HBsAG – and HBsAG + /anti-HCV – RT patients and both anti-HCV + and HBsAG + RT patients, had similar serum creatinine levels ($P = 0.30$) and post-transplant time ($P = 0.94$) (Table 5).

Discussion

The prevalence of anti-HCV + RT patients found in the present study (10.2%) was significantly higher than the very low prevalence (0.7%) found in the Greek general population [15] and significantly lower than the prevalence observed in the HD patients (23.8%). This probably reflects the limitation of test sensitivity, especially in immunosuppressed patients [20]. Regarding the relation between the presence of serum anti-HCV and post-transplantation time or time on HD, the available data are restricted and conflicting [10, 16]. In the present study, no relation was observed between the presence of serum anti-HCV and sex, age, post-transplant time or pre-transplant HD time. It must be noted, however, that in the present study no precise data are available regarding the pre- and post-transplant transfusion history of the patients. None of the 21 anti-HCV + RT patients was found to be HBsAG +, whereas 57% had evidence of previous HBV infection (anti-HBc +) and 62% were immune against HBV (anti-HBs +). This finding is in agreement with the proposal that anti-HBc can be regarded as a 'surrogate assay' for HCV [12, 19] and that, in the majority of anti-HCV + HD patients, there is serological evidence of previous HBV infection [8].

Table 5. Abnormal LFT results, post-transplant time and serum creatinine in anti-HCV + and HBsAg + RT patients

	n	Post-transplant time (years)	Serum creatinine (mg%)	Abnormal LFT	
				n	%
anti-HCV +	21	2.9 ± 2.6	2.7 ± 2.4	14	66
HBsAg +	19	2.9 ± 2.8	2.0 ± 1.4	14	73
P value		0.94	0.30		0.26

In contrast to the infection with HBV [6, 7], data concerning the clinical implications of HCV infection in RT patients are not yet available and this is mainly due to: the very recent availability of the first diagnostic test for hepatitis C [4]; the varying incidence of hepatitis C viral infection in renal transplant units, depending on the geographical origin of the population studied [10, 14, 16, 18]; and the fact that the definition of the hepatic status of RT patients necessitates histological examination, since their liver disease often has a latent course, both clinically and biologically [6]. As a very approximate approach to this matter, the incidence of abnormal LFT results in anti-HCV + and HBsAg + /anti-HCV − RT patients was compared. We found that anti-HCV + patients had a high incidence of persistently abnormal LFT results comparable to that found in HBsAg + patients. This finding suggests that, regarding liver disease, anti-HCV + RT patients probably have an unfavourable course, similar to that seen in HBsAg + RT patients [6, 7]. We also observed that both groups of patients have similar serum creatinine levels and post-transplant time.

In conclusion, the results of the present study indicate that: (a) in Greek RT patients the incidence of HCV infections is significantly higher than in the general population and lower than in HD patients; (b) anti-HCV + RT patients have a high incidence of abnormal LFT results, comparable to that seen in HBsAg + RT patients; and (c) in a substantial proportion of anti-HCV + RT patients there is evidence of previous infection with HBV.

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