

## ANTIBODIES TO HEPATITIS C VIRUS IN THALASSEMIA

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### ABSTRACT

**The presence of anti-HCV antibodies has been examined in a group of 256 consecutive thalassemic patients who received blood transfusions in several countries around the world. Overall 60% were found to be anti-HCV positive. A higher incidence of anti-HCV antibodies was noted in Italian patients with respect to patients living in Eastern countries, and in southern Italy with respect to northern Italy. Because these patients received a large portion of their transfusions before the anti-HCV test became available, these data indicate a higher anti-HCV seroprevalence among Italian blood donors and confirm published data indicating a higher seroprevalence in southern Italy. The anti-seropositivity correlated highly with serum transaminase elevation and with histological diagnoses of chronic active hepatitis.**

*Key words: HCV, thalassemia*

Hepatitis C virus (HCV) infection is one of the most important problems in transfusion-dependent patients, particularly for those who were transfused before HCV tests became available.<sup>1,2</sup>

### *Patients and methods*

From May 1990 to December 1993 two hundred and fifty-six consecutive multiple-transfused thalassemia patients were tested for anti-HCV antibodies at the Pesaro Bone Marrow Transplant Unit. These patients were born between October 1958 and June 1991 (median February 1980), and had started transfusional therapy between the first and the 144th (median the 11th) month of life. Anti-HCV antibodies were detected with an enzyme-linked immunosorbent assay (ELISA) based on the HCV C100-3 antigen (first generation) from May 1990 to June 1991 (40 patients), and with a second generation ELISA test thereafter (216 patients) (Ortho Diagnostic System, USA). Mean patient age was 12.5 years (2-32) and mean number of pure red blood cell transfu-

sions received was 191 (4-600). One hundred and sixty-one patients were from Italy while 95 were from other countries mainly from the Mediterranean area (24 from Iran, 10 from India/Pakistan, 15 from the Gulf Area, 34 from Greece, 1 from Tunisia, 2 from Turkey and 9 from eastern Europe). An evaluable liver biopsy was available in 244 cases (8 patients aged less than 4 years were not submitted to biopsy, and in 4 cases the liver specimen was considered non evaluable), and was examined for chronic persistent (CPH) and active (CAH) hepatitis.<sup>3,4</sup> The number of transfusions was ascertained from family interviews or from hospital files where possible.

Statistical analysis was performed using the chi-square test to compare differences between populations and the Student's t-test to compare differences between mean values.

### *Results*

Overall 153 patients (60%) were anti-HCV positive. Figure 1 shows anti-HCV seropositivity according to the number of transfusions received.

One hundred and eighteen out of 161 (73.3%) patients who received blood from volunteer donors in Italy were anti-HCV positive, while anti-HCV antibodies were detected in 36/95 (37.9%) of those transfused in other countries. However, mean age ( $13\pm 6$  vs  $10\pm 6$  years;  $p=0.00007$ ) and number of transfusions received ( $218\pm 132$  versus  $145\pm 114$ ;  $p=0.00001$ ) were different in the two groups. Comparing patients who had received the same number of blood transfusions, no difference was noted in the ones who had received less than 100 transfusions, while a significant difference was reported over this limit (Table 1). In these same groups a lower incidence of hepatitis B virus antibodies was observed in Italian patients (the difference is statistically significant only under the limit of 100 transfusions received) (data not shown).

Higher anti-HCV seroprevalence in southern Italy as compared with the northern regions has been reported.<sup>5</sup> In those patients who came to Pesaro we noted the same incidence (73.2% South vs 73.3% North), but also in this case the two populations were different with respect to age ( $13\pm 6$  vs  $16.6\pm 5$ ;  $p=0.003$ ) and number of transfusions received ( $204\pm 124$  vs  $286\pm 168$ ;  $p=0.01$ ). Comparing patients who had received less than 200 transfusions (mean  $118\pm 57$  North,  $118\pm 54$  South;  $p=0.97$ ), a statistical difference was noted ( $4/11$  vs  $47/74$ ;  $p=0.008$ ), while no difference was registered over this limit ( $18/19$  vs  $49/57$ ;  $p=0.3$ ) (mean transfusions  $382\pm 129$  North;  $317\pm 95$  South;  $p=0.06$ ).

The average alanine aminotransferase (ALT) value was  $106\pm 98$  U/L (normal value 2-41) in the seropositive patients and  $68\pm 77$  U/L in the

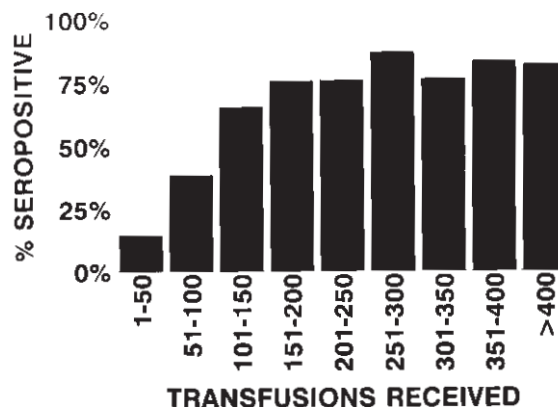


Figure 1. Anti-HCV seropositivity according to the number of transfusions received.

seronegative ones ( $p=0.00038$ ). Among the seropositive patients, 43 out of 148 biopsies (29%) presented histological features consistent with CPH and 63 (43%) were consistent with CAH (33 mild, 26 moderate and four severe). In seronegative patients, 37 out of 96 evaluable biopsies (38%) presented CPH and 22 (23%) CAH (11 mild, 11 moderate and none severe) ( $p=0.09$  comparing the incidences of chronic hepatitis, and  $p=0.0016$  comparing the incidences of CAH).

### Discussion

The data reported confirm that HCV infection is one of the major clinical problems for those patients who required transfusional ther-

Table 1. HCV seropositivity.

Transfusions received	1-100*	101-200**	>200***
Italy	13/37 (35%)	38/48 (78%)	66/75 (88%)
Other Countries	14/48 (29%)	10/26 (38%)	11/21 (52%)
p (chi-squared)	0.4	<0.00001	0.00017

\*mean number of transfusions  $66\pm 30$  Italy,  $61\pm 25$  other countries ( $p=0.4$ ); \*\*mean number of transfusions  $158\pm 29$  Italy,  $154\pm 28$  other countries ( $p=0.5$ ); \*\*\*mean number of transfusions  $333\pm 108$  Italy,  $329\pm 85$  other countries ( $p=0.8$ ).

apy before the HCV screening tests became available. In these patients the probability of being seropositive is proportionally related to the number of transfusions received.

Because these patients had received the majority of their blood transfusions in the *pre HCV era*, the data on Italian patients are in close agreement with the 0.87% anti-HCV seroprevalence reported in volunteer blood donors in Italy.<sup>5</sup> Furthermore, the data indicate a higher HCV seroprevalence in Italy than in Eastern Countries. The observations on Italian patients corroborate the data reported by Sirchia, who indicated a higher anti-HCV seroprevalence in southern Italy.

Analysis of serum ALT and of liver biopsies indicates a strong correlation between HCV infection and inflammatory liver damage,

although other causes like iron deposition and/or other hepatotropic viruses can play an additional role in determining liver damage.

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