

Serum IgE levels in liver cirrhosis. Contrasting results in alcoholic and non-alcoholic patients

C. VIDAL†, A. G. QUINTELA§, I. MILLÁN*, F. GUDE† and
V. CUERVAS-MONS

Department of Medicine and *Biostatistics, Clínica Puerta de Hierro, Autonomous University, Madrid; and
†Clinical and Epidemiological Research Unit, Hospital General, Santiago de Compostela, Spain

Summary

Hypergammaglobulinemia is a well-known feature of liver cirrhosis, but studies on serum IgE in this setting are limited. The present study evaluates serum IgE concentration in a group of cirrhotic patients and examines their relationship with aetiological, clinical and analytical parameters (including liver function tests and hepatic phagocytic activity). The presence of specific IgE against common dietary antigens was also investigated. Total serum IgE was determined by enzyme immunoassay (EIA) in 52 cirrhotics (27 alcoholic and 25 non-alcoholic, including eight virus B and seven virus C-related cirrhosis, three primary biliary cirrhosis, three cryptogenic, three haemochromatosis and one Wilson's disease) and 34 healthy subjects (used as controls). Serum IgE (IU/ml) in controls was not significantly different from that of cirrhotic patients (median 42, range 2–726 vs median 86, range 2–> 1000, respectively) ($P = \text{NS}$). However, serum IgE among alcoholics (median 199, range 19–> 1000) was higher than that of controls ($P < 0.001$), virus B-related cirrhotics (median 25, range 3–> 1000) ($P < 0.05$), virus C-related cirrhotics (median 47, range 2–170) ($P < 0.05$), or non-alcoholic cirrhotics as a whole (median 23, range 2–> 1000) ($P < 0.01$). High IgE levels (≥ 170 IU/ml) were detected in 55.5% of alcoholics compared with only 12% of non-alcoholic cirrhotics ($P < 0.01$). Moreover, IgE levels were very high (> 1000 IU/ml) in six patients of the alcoholic group (22.2%) compared with only one non-alcoholic patient (4%). Increased serum IgE levels did not seem to be related to either parameters of liver function (serum bilirubin, albumin, prothrombin or Child-Pugh score), hepatic phagocytic function or other immunoglobulins. Skin-prick tests failed to demonstrate increased sensitization to eight common dietary antigens in the patients studied. On multivariate analysis, only the alcoholic aetiology of the disease correlated with high serum IgE levels. These data suggest that increased serum IgE might be a common and rather specific feature of chronic alcoholic liver disease.

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Introduction

The occurrence of profound alterations in the immunological system of patients with chronic advanced liver diseases and, especially, liver cirrhosis is well known.

Correspondence: Dr C. Vidal, c/ Salvador de Madariaga 68, 7ºF, 15008 La Coruña, Spain.

† Present address: Dr C. Vidal, Allergy Unit, Hospital Médico-Quirúrgico Conxo, Santiago de Compostela; § Dr G. Quintela, Department of Medicine, Hospital General, University of Santiago de Compostela, Spain.

Whether they are either cause or consequence of liver injury is difficult to know in many cases [1–7]. One of these common immunological alterations is hypergammaglobulinemia [7,8], which is present in two-thirds of patients with liver cirrhosis [9]. Variable increases in serum IgG, IgA and IgM have been reported in different liver diseases [7] and they are usually associated with both a worse prognosis and greater severity [10–12].

It has been previously suggested that increase in serum gammaglobulins may be due to the impairment of the phagocytic activity of Kupffer cells [7,13–20]. Under

normal circumstances, Kupffer cells clear the circulation of a number of potentially harmful biological materials [21–25]. In chronic liver diseases, antigens are no longer cleared primarily by the liver but are taken up by other immunological cells elsewhere [16,26,27]. Previous studies in experimental animal models have confirmed that antibody responses to several antigens are increased after the induction of phagocytic blockade of Kupffer cells [28–30]. These data may be relevant to the explanation of the abnormal presence of serum antibodies directed to commensal bacteria in the gut, particularly *Escherichia coli* [13,14], the high incidence of bacterial infections [31–34], and the detection of specific antibodies against food antigens, all of them commonly seen in cirrhotic patients [13,35,36]. The establishment of intrahepatic portosystemic shunting of blood away from the hepatic macrophages, [7,19] together with the numerical and functional defects of damaged Kupffer cells in these patients, [20] may allow dietary antigens and bacteria, among others, to reach more immunocompetent cells, potentiating antibody production. However, the real mechanism and site of production of those serum gamma-globulins remain to be clarified.

Studies on serum IgE levels in this setting are scarce and not well standardized [37–45] so the possible role of this particular immunoglobulin in liver diseases might have been underestimated. In view of the foregoing, the present study was aimed to analyse serum IgE levels in an homogeneous group of patients with advanced liver cirrhosis, evaluating their relationship with several aetiological, clinical and functional parameters (including phagocytic activity of Kupffer cells). The possible role of common dietary antigens in the pathogenesis of the suspected increased serum IgE was also investigated.

Patients, materials and methods

Patients

Fifty-two consecutive cirrhotic patients, 41 men and 11 women (mean age 56.8 ± 12.1 years, range 28–80 years), admitted to our Division due to an episode of decompensation of their liver disease (ascites, hepatic encephalopathy or variceal bleeding) during a 9-month period entered the study. It was performed the day before discharge from the hospital when clinical recovery was achieved. All the patients gave their written permission to the study, which had been previously approved by the Ethics Committee of the Hospital.

Liver cirrhosis was histologically proven in 29 of these 52 patients (55.7%). In the remaining 23, liver biopsy was not performed due to clotting abnormalities, but the presence of ascites, oesophageal varices, low prothrombin indexes and hypergammaglobulinemia strongly sug-

Table 1. Aetiology of liver cirrhosis in the patients studied

Aetiology	Number (%)
Alcohol	27 (51.9%)
Hepatitis virus	
Type B	8 (15.3%)
Type C	7 (13.4%)
Primary biliary cirrhosis	3 (5.7%)
Haemochromatosis	3 (5.7%)
Cryptogenic cirrhosis	3 (5.7%)
Wilson's disease	1 (1.9%)

gested this diagnosis, and the patients were also considered cirrhotic.

The aetiology of the disease was established using standard epidemiological, clinical, biochemical, immunological and histological parameters (Table 1). Alcoholic cirrhosis was diagnosed when chronic daily alcohol intake was greater than 80 and 100 g in women and men, respectively, in the absence of any other cause of liver cirrhosis. Virus B and virus C-related cirrhosis was suspected in the presence of serological evidence of these viral infections and negative history of alcohol or hepatotoxic drug intake. Primary biliary cirrhosis, haemochromatosis and Wilson's disease were histologically documented in all cases. Cirrhosis was cryptogenic in three, all of them biopsied.

Thirty-four healthy age- and sex-matched non-alcoholic volunteers (23 men and 11 women; mean age 57.1 ± 13.1 years, range 26–80 years) were used as controls. Liver function tests were within normal limits in all cases.

Conditions known to be associated with high serum IgE levels, such as personal history of allergy, rhinitis and/or bronchial asthma, occupational diseases, allergic drug reaction in the previous 6 months, IgE myeloma, Hodgkin's disease, parasitic infestation and dermatological entities (allergic contact dermatitis, atopic dermatitis and bullous pemphigoid) [46] were ruled out in both, cirrhotics and healthy controls. Information on cigarette consumption was recorded and intercurrent illness (heart or respiratory disease) excluded.

Liver tests

Liver function tests (serum ALT, albumin and total bilirubin) were assessed using a Hitachi 737 multichannel autoanalyser (Hitachi, Japan). Prothrombin time was calculated following Quick's method. Serum total protein electrophoresis was done with the PARAGON P/N 655,900 method (Beckman Instruments Inc, USA) and

serum IgG, IgA and IgM were quantified by nephelometry. Patients were classified according to the Child-Pugh score (which includes albumin, prothrombin time, bilirubin, presence of ascites and encephalopathy) as class A, B or C, the latter representing poorer hepatic function and thus worse prognosis [47].

Total serum IgE

Sera from patients and control subjects were stored at -20°C until tested all together for total serum IgE. IgE was determined in duplicate by a sensitive enzymeimmunoassay test (Pharmacia Diagnostics AB, Sweden) and calculated by comparison with a standard curve. Upper and lower limits of IgE determination were 1000 and 2 IU/ml, respectively. A total serum IgE level equal or greater than 170 IU/ml was considered elevated according to the previous experience of our laboratory (it also approximated to the 90th percentile limit of control subjects in our study). For further analysis, in some cases, serum IgE levels were expressed as their logarithmic values.

Specific IgE

Skin-prick tests for eight common dietary antigens (ovalbumin, lacto-albumin, β -lactoglobulin, codfish, tuna, peanut, almond and beef) in a glycerinated saline solution yielding a final concentration of 1/10 g/ml (Dome-Hollister-Stier Laboratories, Spain) were performed to detect specific IgE. Saline solution and 0.1% histamine clorhydrate were used as negative and positive controls, respectively.

Skin tests were performed by placing a small drop of each allergen extract and control solutions on the volar surface of the forearm. A lancet was passed through the drop and inserted into the epidermal surface at a low angle. The tip was then gently lifted upward to elevate a small portion of the epidermis without inducing bleeding. Afterwards, the solution was wiped away with paper tissue and reading done 15 min later. The presence of a weal reaction at least 3 mm bigger than that produced by histamine control was considered positive.

Hepatic phagocytic activity: liver scintigraphy

This was carried out using a gamma camera with parallel holes (Diagnost A[R], Philips, Germany) incorporating a low energy resolution collimator in 43 patients. Recording was started 15 min after the intravenous injection of 3 mCi of Amerscan-TM Hepatate II (Amersham International, UK). Anterior, posterior, right and left lateral views were obtained and recorded. Later on, liver scans

were blindly examined and scored on a 0–9 basis, following the criteria of Castell and Johnson [48] recently used by others [19,31]: for liver mottling: 0=none, 1=mild, 2=more marked with scattered defects, and 3=liver only faintly visualized; for splenic uptake: 0=none, 1=less than liver uptake, 2=equal to liver uptake, and 3=greater than liver uptake; for bone marrow: 0=none, 1=faint visualization, 2=more marked but less than liver uptake, and 3=equal to or more than liver uptake. Therefore, the more altered the liver scan, the greater the scan score.

Statistical analysis

Chi-square test with Yates' correction, when necessary, was used to evaluate dichotomous variables. Two-tailed Students' *t*-test and Mann-Whitney *U*-test were used to compare continuous variables depending on their distribution, normal or not, respectively. These continuous variables were expressed as mean $\pm$ two standard deviations or median and range, in each case. Univariate analysis was done using Pearson's rank correlation. Variables that achieved statistical significance ($P < 0.05$) on univariate analysis, were subsequently included in a multivariate analysis using a backward logistic regression expressed as:

$$e^{\alpha + \beta x} / 1 + e^{\alpha + \beta x}$$

where, e =natural logarithmic base, α =constant and βx =linear combination of predictive analytical parameters. The helpfulness of the adjustment was verified by the Hosmer-Lemeshow method.

Results

There were no significant differences between alcoholic and non-alcoholic cirrhotic patients in clinical and biochemical parameters (Table 2) except for serum alanine aminotransferase (smaller in the alcoholic group, $P < 0.05$), IgA and β -globulins (higher in the alcoholic group, $P < 0.001$). Reticulo-endothelial phagocytic activity, measured as described above, was poorer in the alcoholic group ($P < 0.05$).

As can be seen in Fig. 1 and Table 3, serum IgE (IU/ml) levels in controls were not significantly different from those of cirrhotic patients. However, when considering sub-groups of cirrhotic patients, serum IgE was significantly higher in alcoholics than in either controls or non-alcoholic cirrhotics.

According to serum IgE levels, cirrhotic patients were divided into two groups: patients with normal IgE levels (< 170 IU/ml) ($n = 34$) and patients with high IgE levels (≥ 170 IU/ml) ($n = 18$). The two groups were similar with

Table 2. Clinical and analytical characteristics of cirrhotic patients (divided into alcoholic and non-alcoholic)

	Alcoholic (n=27)	Non-alcoholic (n=25)
Age	55.4 ± 10.8	58.4 ± 13.3
Sex	23/4	18/7
Ascites (Y/N)	18/9	13/12
Encephalopathy (Y/N)	4/23	9/16
Esophageal varices (Y/N)	24/3	21/4
Child's class (A/B/C)	(5/10/12)	(8/8/9)
Child's score	8.8 ± 2.0	8.6 ± 3.1
Liver scan score†	5.6 ± 2.0*	4.3 ± 2.1
Albumin (g/l)	3.2 ± 0.5	3.3 ± 0.8
Bilirubin (mg/dl)	2.3 (0.3–22.9)	1.4 (0.4–18.4)
Prothrombin (%)	56.6 ± 15.2	57.9 ± 21.8
ALT (IU/l)	47 (15–590)*	117 (26–587)
α1-globulin (g/l)	0.2 ± 0.08	0.2 ± 0.07
α2-globulin (g/l)	0.5 ± 0.2	0.5 ± 0.1
β-globulin (g/l)	0.8 ± 0.2	0.7 ± 0.2
τ-globulin (g/l)	1.7 ± 0.6	1.6 ± 0.7
Albumin/globulin	1.1 ± 0.3	1.1 ± 0.4
IgG (mg/dl)	1641 ± 573.9	1790.7 ± 766.6
IgA (mg/dl)	603 (209–1400)‡	318 (106–1840)
IgM (mg/dl)	210.1 ± 88.2	216.6 ± 108.9

Data expressed as mean ± SD, except for IgA, ALT and bilirubin which are expressed as median and range (non-normal distribution). (#). † Obtained only in 23 alcoholic and in 20 non-alcoholic cirrhotics. * $P < 0.05$ and ‡ $P < 0.001$ with respect to non-alcoholic cirrhotics.

Table 3. Total serum IgE levels (median and range) expressed in IU/ml in every group

	Median	Range
Healthy controls	42	2–726
Alcoholic cirrhosis	199	19–> 1000*
Non-alcoholic cirrhosis	23	2–> 1000
Hepatitis virus	36	2–> 1000
Type B	25	3–> 1000
Type C	47	2–170
Miscellaneous	18	2–88

* IgE in alcoholic cirrhotics was significantly higher than that of healthy controls ($P < 0.001$), non-alcoholic cirrhotics as a whole ($P < 0.01$), hepatitis B virus-related cirrhotics ($P < 0.05$), hepatitis C virus-related cirrhosis ($P < 0.05$) and miscellaneous group ($P < 0.01$).

respect to age, sex, proportion of smokers, years of evolution of the disease, Child–Pugh score, prothrombin time and serum albumin, α1-globulins, α2-globulins, IgG and IgM levels. Serum IgA was higher in patients with increased IgE levels (median, 659; range 261–1400 mg/dl) than in patients with normal serum IgE (median, 327; range 106–1840 mg/dl) ($P < 0.01$). Betaglobulins followed a similar pattern (0.9 ± 0.2 vs 0.7 ± 0.2) ($P < 0.01$). Liver scan score was significantly higher (this reflecting a poorer reticulo-endothelial function) in the group of patients with high IgE levels (6.1 ± 2.1 vs 4.5 ± 1.9) ($P < 0.05$). Men presented high serum IgE in larger proportion than women (39.0% vs 18.2%) albeit the difference was not significant.

The most prominent differential feature between cirrhotic patients with normal and high IgE levels was based on the aetiology of the disease: 83.3% of patients with serum IgE levels equal or greater than 170 IU/ml belonged to the alcoholic group; while 55.5% of the alcoholic cirrhotic patients presented high serum IgE compared with only 12.0% of non-alcoholic patients ($P < 0.01$) and 8.8% of healthy controls ($P < 0.001$).

Moreover, six patients of the alcoholic group presented very high levels of IgE (>1000 IU/ml) (22.2%) as compared with only one patient in the non-alcoholic group ($P = \text{NS}$) and none among the control subjects ($P < 0.05$). Interestingly, five of these seven patients with very high IgE levels belonged to Child–Pugh class 'C'.

When looking for intercorrelation between immunoglobulins (IgG, IgA, IgM and IgE) and clinical and biochemical parameters reflecting the stage of the disease (Table 4), we found a markedly different behaviour of IgE when compared with IgG and IgA. So, IgG correlated negatively with prothrombin time, serum albumin and

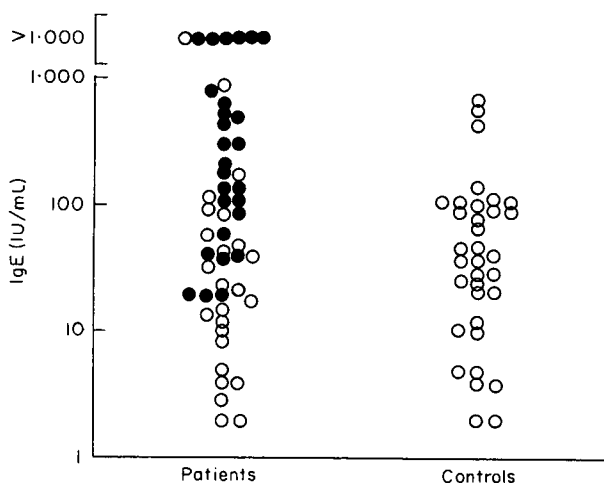
**Fig. 1.** Serum IgE concentrations in cirrhotic patients and controls. ●. Patients with alcoholic cirrhosis. Upper normal limit (170 IU/ml).

Table 4. Univariate analysis: Pearson's rank correlation between different parameters in the group of cirrhotic patients

	Prothrombin		ALT	Alpha-1-globulin	Alpha-2-globulin	Beta-globulin	Gamma-globulin	Child's score	Liver scan score	IgG	IgA	IgM	IgE
	Bilirubin	time											
Bilirubin	1.000		0.153	-0.007	-0.152	0.033	0.079	0.554†	0.282	0.234	0.428†	0.120	0.116
Prothrombin time		-0.461*	0.007	0.199	0.329	0.015	-0.382	-0.682†	-0.265	-0.287@	-0.399*	-0.161	-0.114
Albumin		1.000	-0.192	0.218*	0.434*	0.013	-0.331@	-0.812†	-0.297	-0.410*	-0.496†	-0.245	-0.049
ALT			1.000	-0.054	-0.138	0.133	0.261	0.137	0.021	0.469†	0.163	-0.060	-0.030
Alpha-1-globulin				1.000	0.695†	0.279	-0.061	-0.221	-0.134	-0.231	-0.144	0.004	-0.075
Alpha-2-globulin					1.000	0.276@	-0.019	-0.444*	-0.287	-0.241	-0.334@	0.032	0.015
Beta-globulin						1.000	0.061	-0.004	-0.172	-0.026	0.543†	-0.149	0.393*
Gamma-globulin							1.000	0.303@	0.167	0.530*	0.320@	0.375*	0.053
Child's score								1.000	0.356@	0.330	0.621†	0.186	-0.023
Liver scan score									1.000	0.185	0.209	0.143	0.156
IgG										1.000	0.220	0.189	0.044
IgA											1.000	-0.025	0.328@
IgM												1.000	-0.074
IgE													1.000

@ $P < 0.05$; * $P < 0.01$; † $P < 0.001$.

alanine aminotransferase, whereas IgA did with prothrombin time, serum albumin and total bilirubin and, consequently, with Child-Pugh score. By contrast, neither IgE nor IgM correlated with any of these clinical and biochemical parameters to a statistically significant degree. IgE showed positive correlations with IgA and β -globulins on univariate analysis. However, when introducing parameters for multivariate analysis, only the aetiology (alcoholic or not) appeared as a predictor of high serum IgE level in patients with liver cirrhosis (regression coefficient 2.107, SEM 0.786, $P=0.007$).

The usefulness of serum IgE to determine the aetiology of the cirrhosis in a given patient was evaluated. High serum IgE (≥ 170 IU/ml) had a relatively low sensitivity (55.5%) and negative predictive value (64.4%) in the diagnosis of alcoholic cirrhosis. However, its specificity (88.0%) and positive predictive value were greater than those of high serum IgA (≥ 325 mg/dl), known to be characteristic of alcoholic liver disease (56.0 and 69.4, respectively). On multivariate logistic regression analysis, both IgE and IgA seemed to provide information on the aetiology of the advanced chronic liver disease because of their close relationship with the alcoholic origin of the disease (for IgA: regression coefficient 2.298, SEM 0.868, $P=0.008$; for IgE: regression coefficient 1.628, SEM 0.782, $P=0.037$). Thus, in cases in which serum IgE ≥ 170 IU/ml and serum IgA ≥ 325 mg/dl, the probability of the alcoholic origin of liver injury reached 86% (on the contrary, when both parameters are within normal limits such probability falls to 10.8%).

Only three patients with liver cirrhosis (5.8%) presented detectable cutaneous specific IgE to any of the dietary antigens tested. One alcoholic patient with serum IgE greater than 1000 IU/ml presented detectable specific IgE to three different allergens (ovalbumin, β -lactoglobulin and codfish). The other two patients with positive skin-prick tests showed sensitization to peanut. The remaining 49 cirrhotic patients showed no reaction at all.

Discussion

Our results show a remarkable, frequent and selective increase in total serum IgE in patients with alcoholic liver cirrhosis.

Elevated serum IgE concentrations in patients with liver damage have been previously reported but data on this setting are far from being conclusive since studies mixed patients not only with different aetiologies but also with very different stages of liver disease [37,40-45]. The present study analysed patients with advanced chronic liver disease, meaning that they may be considered homogeneous with regard to the severity of the disease. In that situation, only alcoholic patients seemed to demon-

strate increased IgE levels, particularly when compared with hepatitis virus-related cirrhotics. This finding might be somewhat at odds with those in previous studies. Van Epps *et al.* [37] reported that 26 out of 46 (56.5%) of patients with different stages of alcoholic liver disease presented increased serum IgE levels, a figure similar to that observed in the present study. However, in the same study 52.3% (11/21) of patients with non-alcoholic liver disease also presented raised IgE values so no clear difference was apparent among the various types of liver disorder studied. Nevertheless, the group of non-alcoholic patients investigated by the authors consisted mainly of cases of acute hepatitis (11/21) which are a well-known cause of increased serum IgE levels [37,40-42,45] and only included five cases of liver cirrhosis. Along the same line, Levo and Shalit [41] reported an apparent high prevalence of elevated serum IgE in non-alcoholic liver cirrhosis (15/49 patients, 32.6%) but this figure may be misleading since serum IgE levels higher than 100 IU/ml were considered elevated so that 25% of control subjects had also raised IgE values, the difference being not significant.

According to our data, chronic advanced liver disease *per se* does not seem to be the reason for such an increase in total serum IgE. In fact, in our study, IgE values were not increased in non-alcoholic cirrhotic patients when compared with healthy controls. Moreover, serum IgE concentrations were very low in our three patients with primary biliary cirrhosis, as has been previously reported by others [44]. Furthermore, serum IgE values did not correlate with the degree of liver function impairment as other immunoglobulins do [10,49]. As a matter of fact, serum IgG and IgA (but not IgE) inversely correlated with parameters of liver function included in the Child-Pugh score. Besides, IgE levels were not found to be related to total serum gammaglobulin levels but this is not surprising since it is well-known that IgE represents a minimum fraction of total gammaglobulins [50].

The possible influence of alcohol consumption alone (in absence of liver dysfunction) on IgE production cannot be directly resolved from this study because all the patients had advanced chronic liver disease. Previous studies have focused on this problem with different results. Thus, while Sugerman *et al.* failed to show increases in serum IgE levels after alcohol intake [51], Hallgren and Lundin found elevated IgE levels in alcoholics with supposedly normal liver function [52]. However, the criterion for ruling out liver damage in the latter work was based on the presence of normal plasma concentrations of IgG, IgA, IgM and albumin which are not necessarily altered in all cases of liver disease [9,12]. Given that the absence of liver damage in asymptomatic patients is very difficult to assess without performing liver biopsies, we think the results of that study based on the

isolated influence of alcohol without liver involvement could be misleading. By contrast, excellent work reported by Smith *et al.* showed that elevated serum IgE in alcoholics correlated with the degree of liver fibrosis and cirrhosis [53]. Therefore, alcohol consumption *per se* did not seem to be the only cause of increased serum IgE levels, although the same authors found a decline in IgE values after a few days of abstinence, thus suggesting that acute alcohol intake may also play a role. In the present study, the IgE level was assessed at the end of a period of hospitalization, as has been stated elsewhere, so that a minimum of 10 days of alcohol abstinence was guaranteed; it is not probable that acute alcohol ingestion played an important role in IgE elevation, especially when considering the short half-life of this immunoglobulin (2–7 days in normal subjects) [46].

In our opinion, some specific feature of alcoholic cirrhosis should exist that influences IgE synthesis or catabolism. Our study does not permit to establish the cause of raised serum IgE in alcoholic patients but several hypotheses can be drawn. Taking into account that the IgA level is also found to be selectively elevated in alcoholic cirrhosis [7,49,54,55], a common mechanism for both IgE and IgA could be suggested. Nonetheless, even though univariate analysis revealed a significant correlation between IgE and IgA values, multivariate logistic regression failed to show a direct interdependence. Besides, as mentioned above, IgA but not IgE correlated with parameters of liver dysfunction. Thus, a common pathogenic mechanism for rises in IgE and IgA cannot be affirmed from the results reported here.

At least three factors associated with alcoholic cirrhosis could influence serum IgE levels: hepatic reticulo-endothelial disfunction, malnutrition, and alterations at the T-cell level. First, alcoholic liver cirrhosis may differ from other aetiologic groups in the greater depression of the reticulo-endothelial system commonly associated with it. Chronic exposure to alcohol induces a significant decrease in the phagocytic function of Kupffer cells, both in experimental animal models [56–60] and in humans [61]. In fact, in our study, alcoholic patients had a poorer hepatic phagocytic function (evaluated by Castell and Johnson's semi-quantitative score [48]) than non-alcoholic patients. According to the spillover theory, stimulus for IgE production should arise from antigens in the gastrointestinal tract bypassing the filtering capacity of Kupffer cells. Along this line, we have previously observed that Kupffer cell phagocytosis blockade favours the production of IgE and IgG1 specific antibodies against ovalbumin introduced into the portal vein in an experimental animal model [30]. The finding of a poorer phagocytic activity in cirrhotic patients with high IgE values when compared with those with normal IgE titres

in the present study also supports this idea. The liver will be, as suggested by others, an integral part of the enteric mucosal barrier [62]. However, the incapacity to demonstrate specific IgE to common food antigens in our patients contradicts the proposed mechanism. Nevertheless, the absence of positive skin tests cannot definitively rule out the presence of serum specific IgE even directed to the same antigens.

Secondly, IgE synthesis could be potentiated by malnutrition [63–65] which is usually more marked in alcoholic cirrhotic patients [7,66]. Finally, it is also known that alcohol is particularly toxic for the T-cell limb of the immune system [5,67] which, at the same time, controls the antibody response to T-dependent antigens. Since IgE synthesis depends on T-cell regulation [68], a defect in suppressor T-cells could potentiate IgE synthesis. These two subjects have not been studied here and would require further analysis.

In summary, alcoholic cirrhosis may be considered among the causes of increased total serum IgE. Further studies are needed to clarify the pathogenesis of this phenomenon, as well as its pathologic consequences and clinical significance.

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