March 1994

Serum Alpha 1 Antitrypsin in Liver Diseases

Anjum Shahid
Aga Khan University

Anwar Ali Siddiqui
Aga Khan University, anwar.siddiqui@aku.edu

Sarwar J. Zuberi
Aga Khan University

M A. Waqar
Aga Khan University

Serum Alpha 1 Antitrypsin in Liver Diseases

Anjum Shahid, Anwar Ali Siddiqui*, Sarwar J. Zuberi and M.A. Waqar*
PMRC Research Centre, Jinnah Postgraduate Medical Centre and Department of Biochemistry, The Aga Khan University Hospital*, Karachi.

Introduction

Alpha 1 antitrypsin (α1 AT) deficiency and its association with the pathogenesis of liver disease continues to be controversial. Recent biochemical characterization also indicates that its involvement in liver disease is obscure[1]. The deficiency itself may not be a cause of liver disease as it occurs with almost the same frequency in patients with and without liver disease[2,3]. The present study was conducted to determine the association of serum alpha 1 antitrypsin with various types of acute and chronic liver diseases.

Patients, Methods and Results

Fifty patients suffering from acute viral hepatitis (AVH), 50 biopsy proven cirrhotics and 100 healthy adults were selected. Controls were included on the basis of normal liver function tests whereas liver diseases were classified on clinical examination, biochemical investigations, i.e., liver function tests and liver biopsy. Raised aspartate and alanine transaminase (three times the normal) was the criteria for selecting patients with AVH while all cirrhotics were biopsy proven. Age and sex distribution in controls and patients with liver disease is presented in the accompanying table.

Table. Age and sex distribution in controls and patients with AVH and cirrhosis.

Groups	Sex		Age (years)
	M	F	Mean (range)
Controls (100)	52	48	33 (18-82)
Acute viral hepatitis (50)	37	13	32 (18-60)
Cirrhosis (50)	26	24	42 (18-75)

Quantitative measurement of serum alpha 1 antitrypsin was carried out by single radial immunodiffusion (RID) technique using M. Partigen immunodiffusion plates[4] (Behring Diagnostic) while phenotyping was done by ultra thin layer polyacrylamide gel isoelectric focussing (IEF) and for further confirmation of alpha 1 antitrypsin bands we used immunofixation technique[5].

Mean serum alpha 1 antitrypsin concentration by RID in healthy controls was 2.47±0.08 g/l (range 0.52-5.0 g/l). Any value less than 2.0 g/l was considered lower than normal. In patients with AVH the concentration varied from 0.52-4.7 g/l (mean 3.2±0.11 g/l). With the exception of one patient, all others had values within the normal expected range, while 12% cirrhotics had low concentrations, mean being 2.71±0.11 g/l. IEF profile in controls showed that phenotype MM predominates (70%) followed by M1 M2 (28%) and FM3 (2%). MM is also the most common phenotype in patients with AVH (72%) and cirrhosis (52%) while M1 M2 was found in 28% and 48% of the patients respectively.

Comments

The present findings indicate that almost 98% of the patients with acute viral hepatitis had values within the normal expected range while 12% cirrhotics manifested low levels. These low levels, however, appear to be of no diagnostic significance as not a single sera exhibited total or intermediate deficiency phenotype when subjected to isoelectric focussing. The study therefore supports the notion that phenotypes associated with both total or intermediate deficiencies are less in our local population than in Europeans[6,7] and American caucasians[8].

Phenotype MM overwhelmingly dominates all other types and thus can be regarded as the normal type for our population.

References

1. Propst, T., Propst, A., Dietz, O. et al. High prevalence of viral infection in adults with homozygous and heterozygous alpha 1 antitrypsin deficiency and chronic liver disease. Ann. Intern.Med., 1992;117:641-45.
2. Hodges, J.R., Millward-Sadler, G.H., Barbatis, C. et al. Heterozygous MZ alpha 1 antitrypsin deficiency in adults with chronic active hepatitis and cryptogenic cirrhosis. N.Engl.J.Med., 1981;304:557-60.
3. Fisher, R.L., Taylor, L. and Sherlock, S. Alpha 1 antitrypsin deficiency, the extent of the problem. Gastroent., 1976;71:346- 51.
4. Mancini, G., Carbonarer, A.O. and Hereman, S.J.F. Immunochemical quantitation of antigens by single radial immunodiffusion. Immunochem., 1965;2:235-54.
5. Jeppsson, J.O. and Franzen, B. Typing of genetic variants of alpha 1 antitrypsin by electro focusing. Clin.Chem., 1982;28:219- 25.
6. Carrell, R.W. and Owen, M.C. Alpha 1 antitrypsin, structure, variation and disease. Essays. Med. Biochem., 1979;4:83-119.
7. Sveger, T. Liver disease in alpha 1 - antitrypsin deficiency detected by screening of 200,000 infants. N.Engl.J.Med., 1976;294:1316-21.
8. Perlmutter, D.H. and Pierce, J.A. The alpha 1 antitrypsin gene and emphysema. Amer.J.Physiol., 1989;L147-62.