

Prealbumin rather than albumin is a more sensitive indicator of acute liver disease

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Abstract

The changes in serum prealbumin (transthyretin) and serum albumin in acute and chronic liver diseases were investigated. Albumin has long been used as a useful indicator of liver function but serum prealbumin has recently been noted for its clinical significance in acute liver diseases. Serum prealbumin concentrations and liver function tests (albumin, bilirubin, alanine aminotransferase) were determined on blood obtained from normal donors (n=148) and from patients suffering from liver diseases (n=78) such as acute viral hepatitis, chronic active hepatitis, cirrhosis and hepatoma. The mean serum prealbumin concentration in normal subjects was 29.6 ± 4.82 mg/dl while the mean serum prealbumin concentration in patients with liver disease was greatly reduced (acute viral hepatitis = 15.3 ± 7.4 mg/dl; chronic active hepatitis = 10.2 ± 6.6 mg/dl; cirrhosis = 9.9 ± 6.4 mg/dl and hepatoma = 10.7 ± 4.2). Albumin concentrations dropped slightly (13% compared to control) in acute viral hepatitis but dropped markedly (28% compared to control) in chronic liver diseases. The study suggests that serum prealbumin concentration might be a more sensitive indicator than albumin in assessing liver dysfunction in acute liver diseases.

Key words: Prealbumin, albumin, hepatitis, liver.

INTRODUCTION

The common biochemical investigations when liver disorders are suspected are: total protein, albumin, bilirubin and enzymes level such as aspartate aminotransferase (AST), alkaline phosphatase (ALP) and alanine aminotransferase (ALT). The enzyme tests indicate the degree of hepatocellular damage but do not necessarily indicate the degree of impairment of liver function.

The liver plays an important role in the synthesis and catabolism of plasma proteins. Thus the study of serum proteins profile provides a useful and true estimation of the pathological condition and the severity of acute liver inflammation. Albumin has been used as one of the indices of liver function but because of its long half life of 20 days: it remains within the normal range in acute hepatic disease.^{1,2}

More recently, the clinical usefulness of prealbumin as a general index of liver function has been noted.²⁻⁵ Prealbumin or transthyretin (TTR), has a molecular weight of 54,000 and is a tetramer which is composed of four tryptophan rich identical subunits of 127 amino acids each. It is a plasma transport protein for retinol and

thyroxine. The name prealbumin derives from its electrophoretic mobility relative to albumin i.e. it migrates faster than albumin on electrophoresis at pH 8.6. Prealbumin has a short half life of 1.9-3.6 days,³ thus its level in plasma is currently the most sensitive indicator of any changes affecting its synthesis and catabolism. Teppo and Maury⁴ evaluated the use of prealbumin in the differential diagnosis of liver disease and concluded that prealbumin reflects the severity of acute liver injury more closely than albumin.

MATERIALS AND METHODS

Subjects

A total of 148 normal individuals (blood donors of Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia who were assessed clinically to be healthy) aged 21-45 years old were randomly picked for the estimation of normal serum prealbumin levels.

100 patients (from the outpatient clinic and from the wards) aged 4-83 years old with clinical and biochemical evidence of liver disease were chosen for this study. 50 patients had acute viral hepatitis while the other 50 patients suffered

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TABLE 1: Biochemical parameters in patients with liver diseases

Disease	n	PA	Albumin	ALT	Bilirubin
Normal	148	29.6 ± 4.8	47.2 ± 4.6	35.0 ± 26.1	8.7 ± 11.1
Acute viral hepatitis	48	15.3 ± 7.4*	41.2 ± 4.0*	835.3 ± 612.6"	106.8 ± 71.6*
CAH	15	10.2 ± 6.6*	33.9 ± 6.5*	155.1 ± 114.5*	94.4 ± 90.6*
Cirrhosis	16	9.9 ± 6.4*	28.1 ± 8.0*	79.7 ± 65.6#	86.3 ± 111.9#
Hepatoma	9	10.7 ± 4.2*	32.8 ± 5.0	90.7 ± 110.8@	101.3 ± 163.4^

PA = Prealbumin

ALT = Alanine aminotransferase

CAH = Chronic active hepatitis

*p < 0.001, #p < 0.01, @p < 0.5, ^p < 0.1 as compared to respective normal values

from chronic liver diseases.

Due to incomplete data from some of the patients, only 47 patients with acute viral hepatitis within 1 month from the onset of clinical symptoms and 30 patients with chronic liver diseases (chronic active hepatitis; cirrhosis; hepatoma) were finally selected from the study.

Biochemical investigation

Serum total protein, albumin, bilirubin and ALT levels were determined using a Hitachi 705 Automatic Analyser (Boehringer Mannheim), while serum prealbumin levels were determined by rocket immunoelectrophoresis.

Rocket immunoelectrophoresis

Gel slides (84 x 94 x 1 mm) containing 0.00583% prealbumin antiserum (Behring, FRG) in 1% agarose in barbitone buffer, pH 8.6, were used. A row of 15 wells were punched at the lower margin of the gel slide. Appropriate control (31 mg/dl) and standard sera (30 mg/dl) were diluted serially and tested along with the test sample. After electrophoresis for 5 hours at 250 volts, the slide was dried and washed with saline. The slide was then stained with Coomassie Brilliant Blue R-250 and the rockets were measured to draw a standard curve and the unknown samples read against the curve.⁶

RESULTS

The serum prealbumin concentrations in healthy blood donors was 19.96-39.2 mg/dl with a mean of 29.6 ± 4.82. This is comparable to the study by Sawant *et al*⁴ who obtained a normal range

of 24-37 mg/dl using a similar method and the study by the Beckman group using Beckman ICS rate nephelometer with a normal range of 17-42 mg/dl.¹ Fig. 1 shows the rocket immunoelectrophoresis of serum prealbumin profiles of some of the normal subjects. Although measurement of serum prealbumin using rocket immunoelectrophoresis method is laborious and limited by batch size of 10-15 samples, it is a less expensive method (RM 1.55 per test) compared to the automated method using Beckmann ICS Analyser (RM 9.28 per test).

The mean concentrations of serum prealbumin, albumin, ALT and bilirubin in patients with acute viral hepatitis (type B) and in chronic liver diseases are summarised in Table 1.

In acute viral hepatitis, the mean serum prealbumin was 15.3 ± 7.4 which is lower than the normal range (19.96-39.2 mg/dl). The mean serum albumin levels was 41.2 ± 4.0g/l, show-

TABLE 2: Biochemical parameters in patients with acute viral hepatitis: comparison of results of week 1 and week 3 samples

Biochemical values	Week 1 (Mean ± SD)	Week 3 (Mean ± SD)
Prealbumin (mg/dl)	14.7 ± 5.8	27.0 ± 9.1*
Albumin (g/l)	40.0 ± 5.2	41.7 ± 4.3
ALT (U/l)	921.9 ± 489.0	180.2 ± 116.0**
Bilirubin (umol/l)	125.2 ± 89.1	45.2 ± 44.2

*p < 0.05, **p < 0.01 as compared to week 1

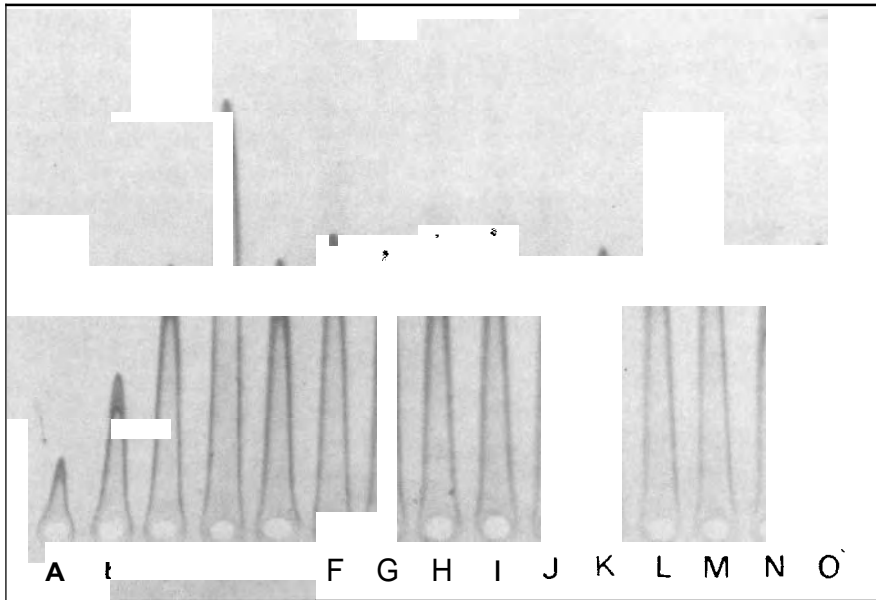


FIG. 1: Serum prealbumin profile of normal subjects as determined by rocket immunoelectrophoresis. A, B, C and D represent standard sera prealbumin concentrations of 4 mg/dl, 12 mg/dl, 20 mg/dl and 50mg/dl respectively. E-O represent prealbumin concentrations in normal subjects.

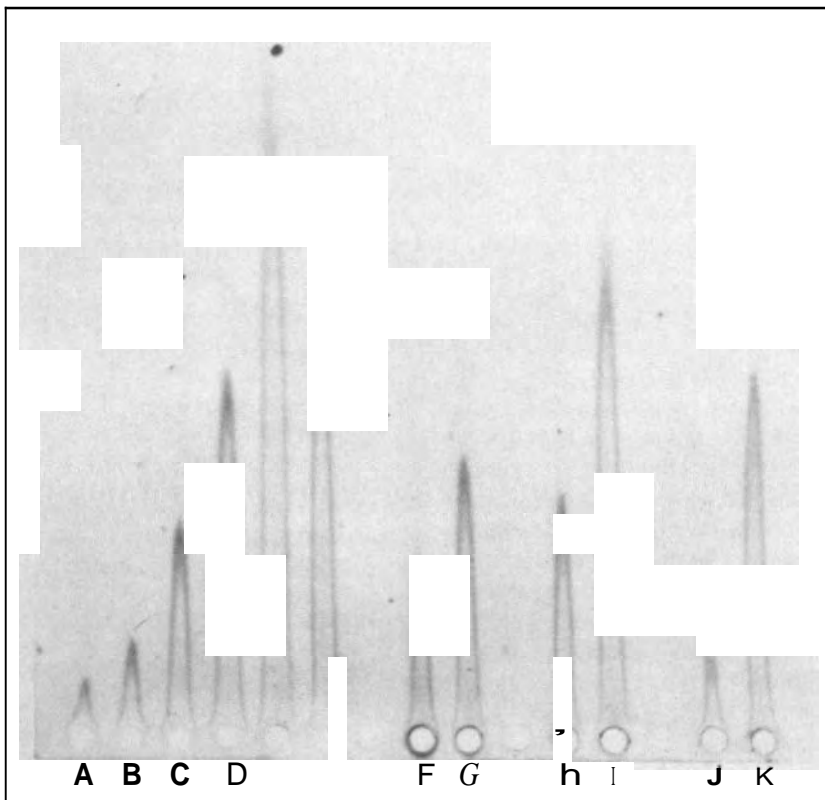


FIG. 2: Serum prealbumin profile of 3 patients with acute viral hepatitis. A, B, C and D represent standard sera. F-G, H-I, and J-K represent week 1 and week 3 samples of 3 hepatitis patients respectively.

ing that albumin levels were only slightly affected in acute hepatitis, that is a drop of 12.7% from the normal values. Serum ALT levels were 10-100x the normal range while bilirubin levels were 1-10x the normal range.

In chronic liver diseases (CAH, cirrhosis, hepatoma), the mean serum prealbumin ($10.27 \pm 5.9\text{mg/dl}$) was lower than that of patients suffering from acute viral hepatitis ($15.3 \pm 7.4\text{mg/dl}$). Albumin levels are decreased in chronic liver diseases, the lowest being in liver cirrhosis (mean = $28.1 \pm 8.0\text{l/l}$). Serum ALT levels in these patients were 2-10x normal levels. Serum bilirubin levels were almost the same in both acute and chronic cases.

In 11 patients with acute viral hepatitis, a second sample was obtained two weeks after the patient's first visit at the outpatient clinic for repeat analysis of serum prealbumin, albumin, ALT and bilirubin (Table 2 and Fig. 2).

Serum prealbumin levels were lower than the normal range in week 1 but returned to normal values by the third week. However, serum albumin levels hardly changed during the bout of viral hepatitis. Serum ALT levels were raised in week 1. By the third week serum ALT levels were significantly lowered but did not return to normal values. In week 1, bilirubin levels were high in 8 out of 11 patients while 3 out of 11 patients had serum bilirubin values within normal range ($< 20\ \mu\text{mol/l}$). By the third week, serum bilirubin levels in most of these patients had fallen to almost 70% of the initial week 1 value, but had not returned to normal levels.

DISCUSSION

By using a specific, sensitive immunological method, it is possible to show that serum prealbumin levels were significantly low in patients with acute viral hepatitis and in chronic liver diseases (Table 1). However, serum albumin levels in patients with acute viral hepatitis were only slightly affected and in some cases stayed within the normal range. This pattern is a reflection of the half-life of the two proteins, being 1-2 days in the case of prealbumin and 20 days in the case of albumin. Thus changes in

prealbumin levels reflect liver's synthetic function more sensitively than albumin.

The fall in serum prealbumin levels in chronic liver diseases as seen from Table 1 reflects the severity of liver injury more sensitively than albumin. Decreased levels of serum prealbumin have been shown in hepatobiliary diseases.^{1,2}

The present study shows that serum prealbumin levels were significantly low in patients with acute viral hepatitis. Two weeks after the presentation, serum prealbumin began to rise returning to almost normal levels. This elevation is accompanied by the falling levels of bilirubin and ALT. This is in line with the results of the study by Sawant *et al.*⁴ Pattern of serum prealbumin, ALT and bilirubin levels returning to normal values could have been seen more clearly if subsequent samples were included (fourth and fifth weeks after clinical presentation). Because of difficulties in getting patients to come for followups, availability of subsequent samples was not possible.

In acute hepatitis, low serum prealbumin levels tend to correlate inversely with raised serum ALT levels ($r = 0.40$) than albumin did ($r = 0.18$). This may suggest that for acute viral hepatitis, serum prealbumin level is a more sensitive indicator of early liver dysfunction than serum albumin.

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