SERUM CONCENTRATIONS OF COMPLEMENT COMPONENTS 3 AND 4 IN LIVER DISEASE

Pages with reference to book, From 33 To 35

Tariq Z. Lodi (PMRC Research centre, Jinnah Postgraduate Medical centre, Karachi.)
Talat J. Hassan, Sarwar J. Zuberi (PMRC Research Centre, Jinnah Postgraduate Medical Centre, Karachi.)

Abstract

Serum C3 and C4 levels have been measured in healthy subjects and patients with hepatitis, cirrhosis of the liver and liver cancer. A significant elevation of serum C4 was found in liver cancer and reduction in cirrhosis. There was a direct correlation between bilirubin levels and C3 in hepatitis and serum albumin and C3 in cirrhosis. Serum C4 appears to be a more sensitive indicator of liver disease than C3 (JPMA 31:33, 1981).

Introduction

Complement, a group of serum proteins are disturbed in a variety of disease states especially those involving antigen-antibody reactions (Asherson, 1960; Townes, 1967), acute inflammatory diseases where they act as acute phase reactants (Townes, 1967) and in various hepatocellular disorders. Liver is the main site for the production of various components of complement especially C3 and C4 (Alper et al., 1969; Thorbecke et al., 1965). This study presents the results of C3 and C4 levels in healthy subjects and patients with hepatic disorders.

Material and Method

Present study included 20 heaithy subjects (M:F 4:1) and 58 patients with liver disease (M:F3.8:1). Diagnosis of liver disease was made on clinical and oiochemical findings and confirmed by histological examination of liver tissue obtained by needle biopsy. Sera of the patients and controls were stored at-20°C for 5-7 days before analysis. Estimation of C3 and C4 components of the complement was done by radial-immunodiffusion technique (Shanbrom et al., 1967). Serum protein levels were determined by the method of Kingsley (1942), albumin and globulin by (Doumas et al., 1971) and serum bilirubin by that of Meites and Hogg (1959).

Results

Levels of serum C3 and C4 in healthy controls and patients with liver disease are shown in table I.

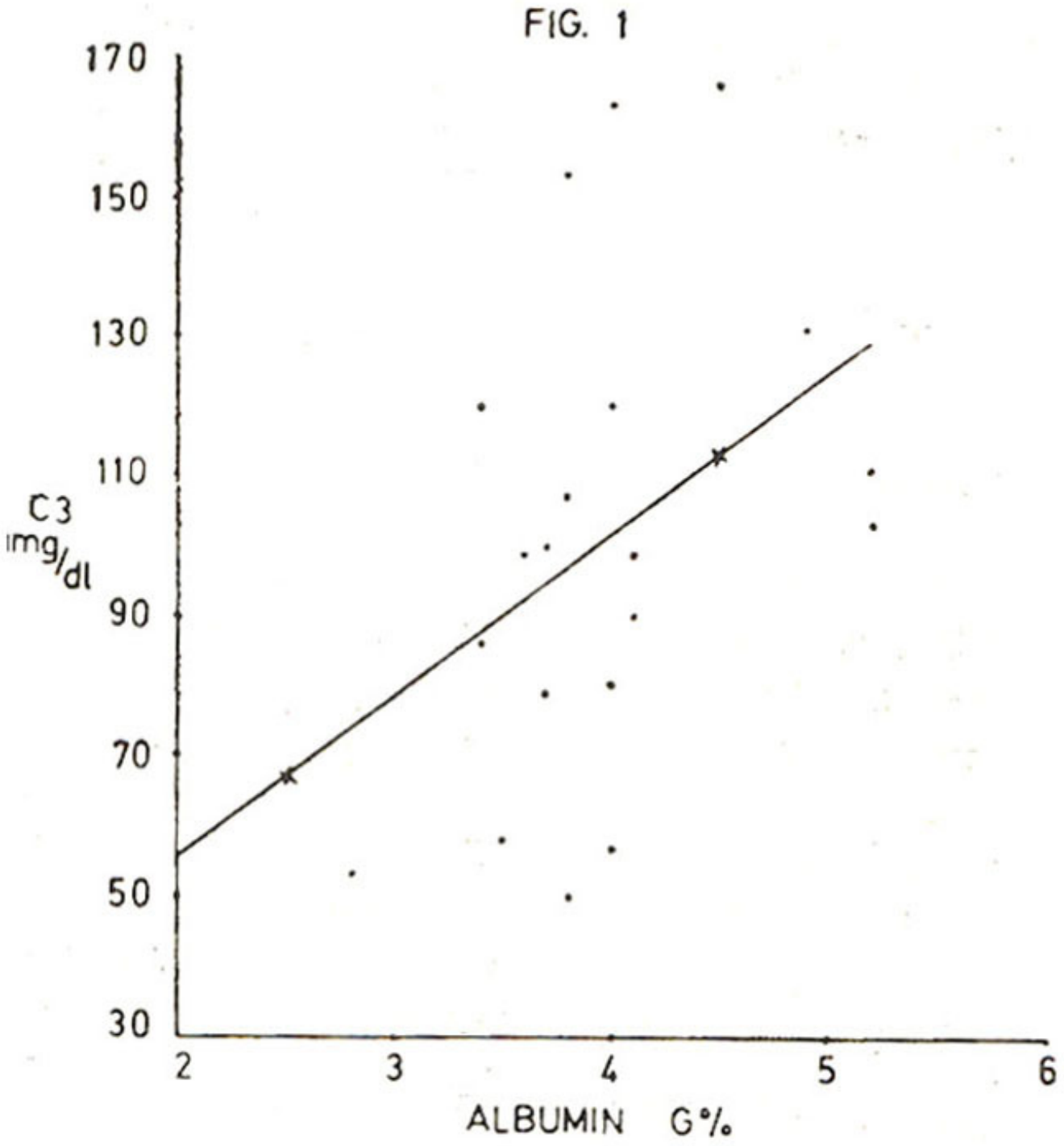
Table I: Serum C3 and C4 in Liver Disease

Groups studied	*No. studied*	*Complement C3 mg/dl Mean ± S.D.*		*Complement C4 mg/dl Mean ± S.D.*	
Healthy controls	20	141.85	58.8	35.40	14.52
Acute viral hepatitis	20	174.85	87.9	34.12	15.96
Cirrhosis	20	121.35	62.3	21.60	14.01
Primary liver cancer	18	167.0	63.3	45.45	14.49

Range of C3 in healthy controls was 102-187 mg/dl and of C4 12.4-53.8 mg/dl. An increase in serum C3 level was observed in patients with acute viral hepatitis and liver cancer and a decrease in cirrhosis of the liver but these differences were not significant.

Levels of C4 were significantly lower in cirrhosis ($P<0.05$) and higher in liver cancer ($P<0.05$). The difference in C4 levels between controls and patients with acute viral hepatitis was not significant.

A positive correlation was obtained between the levels of serum albumin and C3 in patients with hepatic cirrhosis (Fig. I).



A direct relationship was observed between bilirubin and Serum C3 levels in hepatitis and no relation between serum glutamic oxaloacetic transaminase and serum complement levels.

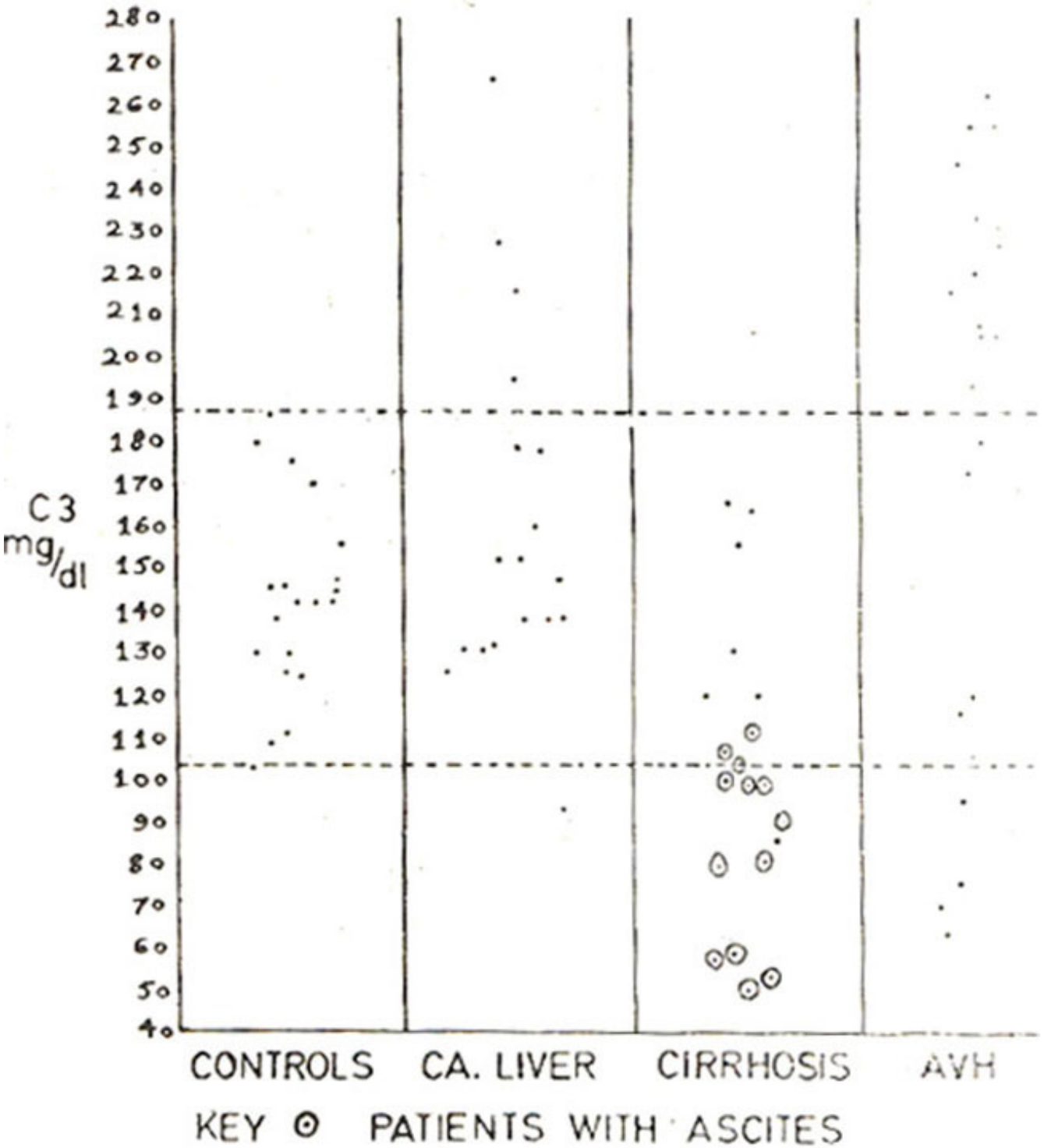
Discussion

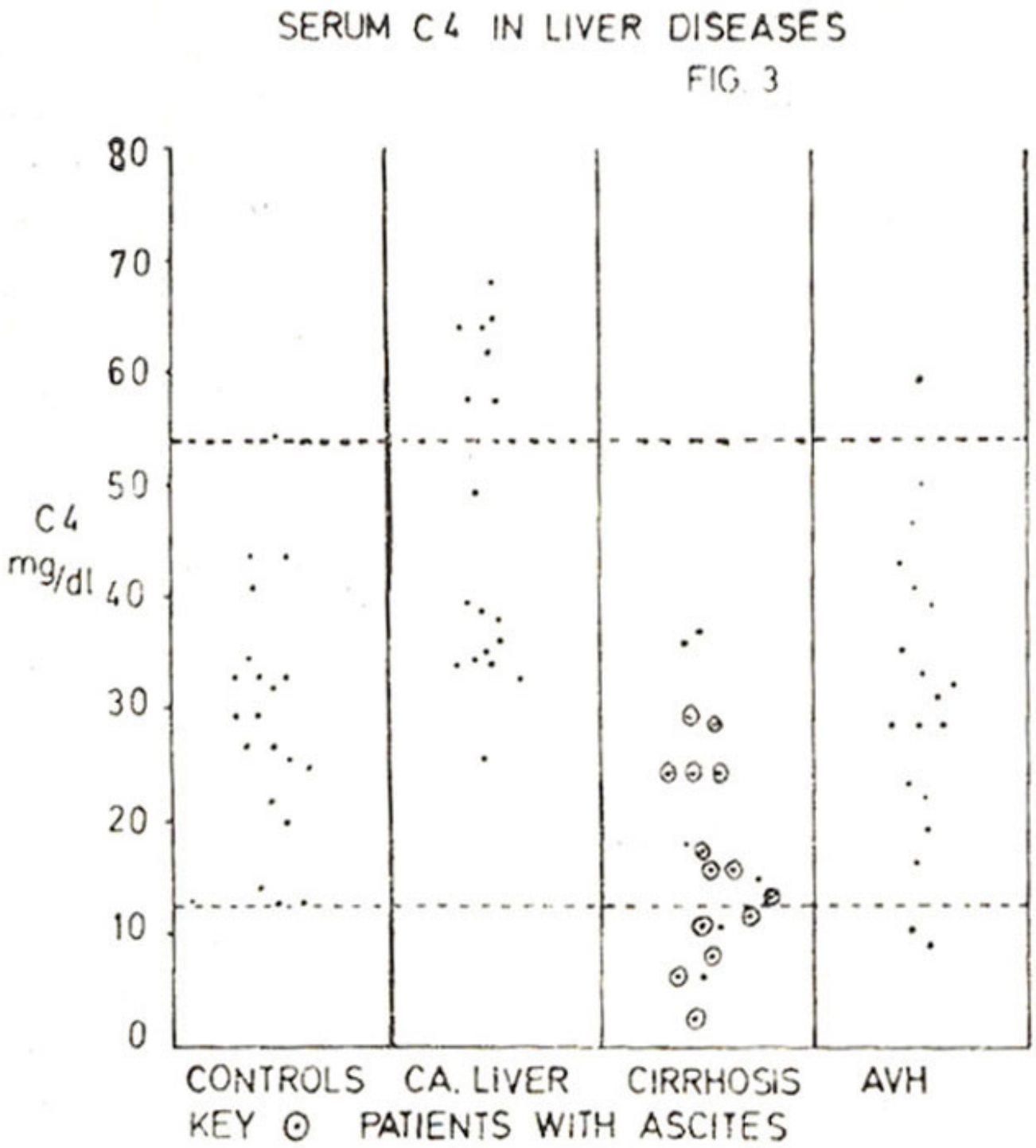
Serum complement levels vary with the age of the sera and the temperature at which they are stored. In the present series C3 levels in healthy subjects ranged from 102-187 mg/dl (mean 141.8 mg/dl). In Perrin's (1975) series where specimens were kept at 37°C mean level in fresh sera was 102 mg/dl (Range 60-160 mg/dl) and in 7 days old sera 134 mg/dl (Range 92-190 mg/dl). The range reported by

Fox et al (1971) in sera stored at 4°C was 85-370 mg/dl.
Fifty five percent patients with viral hepatitis and 33.3% with liver cancer had elevated C3 and 50% with liver cancer elevated C4 levels. Elevation of C3 was insignificant in both diseases but C4 values were significantly raised in liver cancer patients.
Reduction in the level of C3 was observed in 40% and C4 in 15% of patients with cirrhosis. All cirrhotics with hypocomplementaemia with the exception of one for C3 (Fig. 2) and two for C4 (Fig. 3) had ascites.

SERUM C 3 IN LIVER DISEASES

FIG. 2





Reduced complement levels obtained in cirrhosis were significant for C4 and insignificant for serum C3.

Complement levels in hepatitis depend on the extent of liver involvement. Serum C3 was consistently reduced in 18 patients with acute viral hepatitis and massive necrosis while in patients with less severe disease values were not as low and returned to normal as the patients recovered (Fox et al., 1971). None of the patients in this study had fulminant hepatitis and they were seen at various stages of the disease which may account for variations in serum C3 and C4.

Simultaneous elevation of scrum C3 and bilirubin was seen in hepatitis but there was no association between serum complement and serum transaminase levels.

A positive correlation between C3 and serum albumin in cirrhosis (Fig. I) suggests a definite relationship between serum complement and the synthetic function of the liver (Finlayson et al., 1972; Alper et al., 1969; Colten, 1972).
Low serum complement in cirrhosis with ascites (Fig. 2 and 3) may be due to increased plasma volume (Leiberman and Reynolds, 1967; Potter et al., 1973).
Hypercompiementaemia in liver cancer may be due to increased complement synthesis by rapidly multiplying cancer cells (Pagaltsos et al., 1971; Fox et al., 1971) and the levels may vary according to the size of the tumour.
Serum C4 appears to be a more sensitive indicator of complement abnormalities than C3 in acute and chronic liver disease.

References

1. Alper, C.A., Johnson, A.M., Britch, A.G. and Moore, F.D. (1969) Human C3: Evidence for the liver is the primary site of synthesis. Science, 163:286.
2. Asherson, G.L. (1960) Serum complement levels in systemic lupus erythematosis and other disease. Aust. Ann. Med., 9:57.
3. Colten, H.R. (1972) Ontogeny of the human complement system. In vitro biosynthesis of individual complement components by fetal tissues. J. Clin. Invest., 51:725.
4. Doumas, B.T., Watson, W.A. and Briggs, H.G. (1971) Albumin standards and the measurements of serum albumin with bromocresol green. Clin. Chim. Acta., 31:87.
5. Finlayson, N.D.C., Krohn, K., Fauconnet, M.H. and Anderson, K.E. (1972) Significance of serum complement levels in chronic liver disease. Gastroenterology, 63:653.
6. Fox, R.A., Dudley, F.J. and Sherlock, S. (1971) The serum concentration of the third component of complement B, C/B, A in liver disease. Gut, 12:574.
7. Kingsley, G.R. (1942) The direct biuret method for the determination of serum proteins as applied to photo electric and visual colorimetery. J. Lab. Clin. Med., 27:840.
8. Leiberman, F.L. and Reynolds, T.B. (1967) Plasma volume in cirrhosis of the liver. Its relation to portal hypertension, ascitis and renal failure. J. Clin. Invest., 46:1297.
9. Meites, S. and Hogg, C.K. (1959) Studies on the use of van den berg reagent for determination of serum bilirubin. Clin. Chem., 5:470.
10. Pagaltsos, A.P., Smith, M.G.M., Eddleston, A.L.W.F. and Williams, R. Serum total hemolytic complement in liver disease. Immunology of the liver. Edited by Martin Smith and Roger Williams. London, Heinemann, 1971, pp. 93-100.
11. Perrin, J. (1975) Letter: C 3 standards. Lancet, 1:1189.
12. Potter, B.J., Trueman, A.M. and Jones, E.A. (1973) Serum complement in chronic liver disease. Gut, 14:456.
13. Shanbrom, E., Khoo, M. and Lou, K. (1967) Simplified quantitation of C3 byradial immunodiffusion. Clin. Res., 15:114.
14. Townes, A.S. (1967) Complement levels in disease. Johns Hopk. Med. J., 120:337.
15. Thorbecke, G.J., Hockwald, G.M., Furth, R., Vaw et al. Problems in determining the sites of synthesis of comple ment component. Complement Edited by G.E. Wolstem holme. J. Knight.
16. Ciba Foundation Symposium Boston, Litle, Brown, 1965, pp. 59-119.