ALPHA$_1$ ANTITRYPSIN LEVELS IN CHRONIC OBSTRUCTIVE LUNG DISEASE AND PULMONARY TUBERCULOSIS IN SINGAPORE

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SYNOPSIS

The levels of serum α_1—antitrypsin (AAT) were determined in a selected group of 47 Chinese patients with pulmonary emphysema and in 133 patients with pulmonary tuberculosis. The results were compared with a healthy control group. Raised concentrations of AAT were found in patients with active pulmonary tuberculosis, whereas none of the emphysematous patients had "deficient" AAT levels. AAT deficiency appears to be rare among the Chinese.

INTRODUCTION

In 1963, Laurell and Eriksson first described an association between α_1—antitrypsin (AAT) deficiency and chronic obstructive pulmonary disease. The rare homozygotes with less than 15 per cent of the normal amount of protein were found to have a high incidence of pulmonary emphysema. In the past ten years since the first report of this association, more than 100 cases have been described in the literature. As the level of AAT in the blood is genetically determined, it is likely that the prevalence of AAT deficiency will vary in different ethnic groups.

This report describes the findings of a study on the levels of AAT in the local adult Chinese population and in a selected group of Chinese patients with chronic obstructive lung disease attending the Tan Tock Seng Hospital, Singapore. In addition AAT estimations were also made on patients with active and inactive pulmonary tuberculosis.

MATERIALS AND METHODS

Serum AAT levels were measured in the following:

(i) A control group consisting of 78 healthy Chinese blood donors.

(ii) 47 patients who fulfilled the diagnostic criteria of emphysema.

(iii) 60 patients with bacteriologically proven active pulmonary tuberculosis and

(iv) a group consisting of 73 patients with inactive pulmonary tuberculosis.

The radiological and physiological criteria for pulmonary emphysema were similar to those adopted by Jones and Thomas (1971).

AAT levels were measured by a quantitative immunoelectrophoresis technique (Laurell, 1966). This technique is specific for AAT and gives better quantitation than that using single radial immunodiffusion as described by Mancini *et al* (1965).

Patients with levels less than 100 mg.% were considered deficient in AAT whilst those having levels of 100—200 mg.% and more than 200 mg.% were regarded as intermediate and non-deficient respectively.

RESULTS

The results of the controls and the group with emphysema are presented in Table I. There were no patients with AAT levels less than 100 mg.%. 14 emphysematous patients had levels ranging from 125 mg.% to 200 mg.%, and thus came into the intermediate category.

Table II shows the clinical data and the radiological distribution of emphysema in the 47 patients.

Comparison of the AAT levels in the patients with active and inactive pulmonary tuberculosis shows significant differences (Table III). The majority of the active cases had either moderately advanced or far advanced disease.

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TABLE I

α_1 ANTITRYPSIN LEVELS IN EMPHYSEMATOUS PATIENTS AND IN CONTROLS

Group	No.	Mean Age	α_1 antitrypsin (mg%)		
			Range	Mean	S.D.
Non deficient	33	62.2	205—390	267.0	49.6
Intermediate	14	59.8	125—200	173.1	22.6
Controls	78	24.8	128—317	192.2	35.7

TABLE II

CLINICAL DATA AND RADIOLOGICAL DISTRIBUTION OF EMPHYSEMA IN THE 47 PATIENTS

Group	No.	Sex	Smoker	Chronic Bronchitis	Emphysema		
					Mainly U.Z.	Mainly L.Z.	Both
Non deficient	33	32 M 1 F	31	22	11	2	20
Intermediate	14	12 M 2 F	11	10	3	5	6

TABLE III

α_1 ANTITRYPSIN LEVELS IN PULMONARY TUBERCULOSIS AND CONTROLS

Group	No.	α_1 antitrypsin (mg%) Mean and S.D.	Significance at 5% level
Active disease < 3 weeks chemotherapy	27	351·2 (103·6)	Yes
3—12 weeks chemotherapy	33	262·6 (83·9)	
Active disease 3—12 weeks chemotherapy	33	262·6 (83·9)	Yes
Inactive disease	73	203·2 (40·8)	
Inactive disease	73	203·2 (40·8)	No
Controls	78	192·2 (35·7)	

The group with antituberculous chemotherapy of less than 3 weeks' duration exhibited significantly higher levels of AAT than those who had received a longer period of chemotherapy. A decline to normal levels is noted in the group with inactive disease.

DISCUSSION

The main component of the α_1 globulin fraction on serum electrophoresis is AAT, which is responsible for about 90 per cent of the total serum trypsin inhibitory capacity. A variety of conditions and stimuli are known to affect the level of AAT. AAT concentrations are frequently elevated in malignancy (Clark *et al*, 1948), surgical stress and corticosteroids (Faarvang and Lauritsen, 1963) during therapy with oestrogenic substances (Schumacher and Pearl, 1968), and in acute infections (Jacobsson, 1955). The high concentrations seen in patients with active pulmonary tuberculosis in this study are in agreement with previous observations. It is interesting to note that with the achievement of the inactive status, AAT levels fall to within the normal limits.

It is known that the "intermediate deficiency" category consists of a number of phenotypes and that no precise correlation exists between the heterozygous state and intermediate levels of trypsin inhibitory capacity or the AAT concentration. Controversy exists as to whether the intermediate deficiency state increases the risk of developing chronic obstructive lung disease, although Mittman, Lieberman and Rumsfeld (1974) conclude from their recent study that "intermediate as well as severe AAT deficiency appears to predispose to the development of chronic obstructive pulmonary disease." They found the relationship to be most apparent in patients who were young, smoked little, did not work or live under conditions associated with bronchitis and who otherwise appeared not to be particularly prone to develop these diseases.

Relatively few studies have been reported on the prevalence of AAT deficiency in different ethnic groups. Webb *et al* (1973) in a study of serum AAT variants in 500 subjects attending a multiphasic screening clinic found only 3 (6 per cent) of the 53 Negro subjects were not MM or "normal" types, compared to 12 per cent of the white subjects. It has been suggested (Mittman, 1971) that AAT deficiency occurs most commonly in persons of northern, western, and central European origin, and that low serum trypsin inhibitory capacity values are rare in non-whites, Jews and Italians. Our data would tend to confirm this observation. No case with "deficient" AAT was found in the 47 emphysematous patients studied although previous reports using similar criteria for emphysema have shown an incidence ranging from 11 to 18·4 per cent in European patients (Pedersen *et al*, 1969; Jones and Thomas, 1971; and Hutchinson *et al*, 1971).

ACKNOWLEDGEMENTS

We wish to thank the Permanent Secretary (Health)/Director of Medical Services, Singapore, for a medical research grant and Mr. C.W. Sam, Ministry of Health, for statistical assistance.

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