# SERUM LEVELS AND $\alpha_1$-ANTITRYPSIN PHENOTYPES IN ACTIVE PULMONARY TUBERCULOSIS

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*$\alpha_1$-at phenotypes and serum levels were studied in 100 Greek patients of pulmonary TBC by starch-gel electrophoresis and radial immunodiffusion. The mean value of* $\alpha_1$-at ($315 \pm 77$) *was significantly lower* ($p < 0.005$) *than in the control group. An attempt is made to explain this finding based on the* $\alpha_1$-at *phenotypes distribution in the TBC patients.*

## INTRODUCTION

The various alpha$_1$-antitrypsin ($\alpha_1$-at) phenotypes constituting the Pi system (Fagerhol and Laurell 1967) are inherited as autosomal codominant characters through at least 23 alleles (Weisser et al. 1975). Some of them ($Pi^P$, $Pi^S$, $Pi^W$, $Pi^Z$) are thought to be responsible for low $\alpha_1$-at levels in the serum. Subjects of ZZ phenotype who have very low serum levels of $\alpha_1$-at are thought to be especially vulnerable to several diseases, i.e., chronic obstructive pneumonopathy (Eriksson 1964, 1965), juvenile hepatic cirrhosis (Sharp et al. 1969, Brunt 1974), and perhaps adult hepatic cirrhosis (Berg and Eriksson 1972, Sherlock 1974).

Whether the heterozygous $Pi^Z$ gene predisposes to these diseases, is as yet a matter of much controversy (Campra et al. 1973, Kanner et al. 1973, Morse et al. 1975, Duncan and Griffin 1975, Theodoropoulos et al. 1976). Several quantitative studies concerning $\alpha_1$-at have been carried out among patients suffering from pulmonary TBC, with contradictory results.

In the present work, $\alpha_1$-at serum levels and Pi phenotypes, as well as $\alpha_1$-at serum levels,

Table. $\alpha_1$-at *phenotypes and gene frequencies in TBC patients and in healthy Greeks*

*Phenotypes*

| | MM | MS | FM | MZ | MV | FS | ZZ | FF | SS |
|---|---|---|---|---|---|---|---|---|---|
| Controls (N = 504) | 468 | 26 | 3 | 1 | 2 | 1 | 1 | 1 | 1 |
| Patients (N = 100) | 85 | 12 | 0 | 0 | 0 | 1 | 1 | 1 | 0 |

*Gene frequencies*

| | $Pi^M$ | $Pi^S$ | $Pi^F$ | $Pi^Z$ | $Pi^V$ |
|---|---|---|---|---|---|
| Controls (N = 504) | 0.960 | 0.029 | 0.006 | 0.003 | 0.002 |
| Patients (N = 100) | 0.910 | 0.065 | 0.015 | 0.010 | 0 |

have been studied in Greek patients suffering from active pulmonary TBC, in order to investigate the relationship, if any, of the Pi system with pulmonary TBC.

## MATERIAL AND METHODS

Venous blood specimens were drawn from 100 hospitalized patients of both sexes originating from various areas all over Greece, suffering from active pulmonary TBC. The specimens were allowed to clot at 37°C and the sera were separated and stored at −20°C until used. Sera from 20 apparently healthy medical students of both sexes served as controls for the $\alpha_1$-at serum level, while 504 healthy Greeks, previously examined by the same method (Fertakis et al. 1974), served as a control population of the Pi system phenotypes and gene frequencies. $\alpha_1$-at phenotypes were studied by the vertical starch-gel electrophoresis with a discontinuous system of buffers (Kueppers and Bearn 1966). The $\alpha_1$-at phenotypes were recorded according to widely accepted criteria (Fagerhol 1967, 1968). Antigen-antibody crossed electrophoresis (Kueppers and Bearn 1966, Fagerhol and Laurell 1967) was carried out when a serum gave MM zones and reduced staining intensity of zones in the Z region. $\alpha_1$-at serum levels were estimated by the radial immunodiffusion method (Mancini et al. 1965) on suitable agarose plates, containing $\alpha_1$-at antibody. (Partigen-Behringwerke, Marburg). Statistical analysis was performed by conventional procedures.

## RESULTS

The mean $\alpha_1$-at level was found to be $315 \pm 77$ mg% and $370 \pm 65$ mg% among patients and controls, respectively. The mean value is significantly lower in patients than controls ($t = 3.444$, $p < 0.005$).

A total of five Pi phenotypes were found among the patients (MM, MS, FS, ZZ, FF). The ZZ phenotype was observed only once.

## DISCUSSION

Since the original reports of Eriksson (1964, 1965) concerning the association of $\alpha_1$-at deficiency with a very distinctive type of chronic obstructive pulmonary disease, several studies have been carried out to investigate the relationship, if any, between other pneumonopathies, i.e., pulmonary TBC, and $\alpha_1$-at.

Hunter et al. (1968) have studied the serum trypsin inhibitory capacity in 22 patients with pulmonary TBC. Their mean value was in close agreement with that found in healthy controls as well as in chronic obstructive pneumonopathy patients. On the contrary, Clarke et al. (1970), after having studied 16 TBC patients, concluded that their $\alpha_1$-at serum level was significantly higher than in controls.

Similar results were reported from the study of 42 patients with active pulmonary TBC (Geisler et al. 1972).

Our results are quite different from those of the other studies. The mean $\alpha_1$-at level among our patients was significantly lower than in the healthy controls. It should be noted that we found 14 phenotypically MS, FS, and ZZ patients, in whom the $\alpha_1$-at serum levels were expected to be low. Indeed, their mean $\alpha_1$-at value was of only 227 mg%. This finding could explain the observed low $\alpha_1$-at serum levels in our patients.

Concerning the phenotypic distribution of Pi system in our material, the following observations should be made. The ZZ phenotype, responsible for $\alpha_1$-at deficiency, was found in only one patient. Nevertheless, 13 patients had the $Pi^s$ gene. This gene has also been incriminated for low levels of $\alpha_1$-at.

Kellermann and Walter (1970) had studied the $\alpha_1$-at polymorphism in 400 Greeks who "were not from a particular geographic area" of the country. Their results differ significantly from our own ones in the control group. Although this discrepancy may possibly arise from differences in the sample populations, their MS phenotype and $Pi^s$ gene frequencies (0.005 and 0.0025) differ considerably from our own ones (0.12 and 0.065).

On the contrary the $Pi^z$ gene frequency has not been found to be high in our pulmonary TBC patients.

We have no plausible explanation for these

findings at present. However, the sample for pulmonary TBC is too small to be representative and unbiased estimates of gene frequencies cannot be obtained from this sample. Therefore, we cannot substantiate our results with any statistical analysis. Nevertheless one could postulate that other genes of the Pi system, giving low levels of $\alpha_1$-at, might participate in the pathogenesis of various diseases including pulmonary TBC.

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