

# Alpha-1 antitrypsin ( $\alpha_1$ -AT) plasma levels in lung, prostate and breast cancer patients

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## Abstract

**BACKGROUND AND OBJECTIVES:** Alpha-1 antitrypsin ( $\alpha_1$ -AT) is one of the most important extra-cellular serine protease inhibitors. Elevation of  $\alpha_1$ -AT serum levels have been observed in the course of a large number of malignant diseases. In this study, using Radial Immunodiffusion Method, we studied the serum levels of  $\alpha_1$ -AT in lung, prostate and breast cancer patients.

**RESULTS:** Lung and prostate cancer patients have shown a significant elevation in  $\alpha_1$ -AT serum levels compared with those of healthy controls (*P*-value = 0,0001, 0,003 respectively). On the other hand, breast cancer patients did not show a significant change in these levels. Serum levels of  $\alpha_1$ -AT were  $261.7 \pm 107.26$ ,  $222.7 \pm 87.30$  and  $183.8 \pm 45.05$  mg/dl of lung, prostate and breast cancer patients, respectively, while those of healthy controls were  $163.9 \pm 23.2$  mg/dl in males and  $186.13 \pm 39.81$ mg/dl in females.

**CONCLUSION:** These data demonstrated that  $\alpha_1$ -AT plasma levels might be an alarming factor to be considered in the diagnosis as well as in the follow up of cancer cases.

## INTRODUCTION:

Human alpha 1-antitrypsin ( $\alpha_1$ -AT) is one of the major components of the plasma proteins. It inhibits serine proteases and acts as an acute phase glycoprotein [1].  $\alpha_1$ -AT is the principle inhibitor of leukocyte elastase, trypsin, chymotrypsin, cathepsin G, plasmin, thrombin, tissue kallikrein, factor Xa, plasminogen and proteinase III [2,3,4].  $\alpha_1$ -AT

concentrations are known to rise in the blood during the course of malignant diseases such as: hepatocellular carcinoma (HCC) [5,6], multiple myeloma and lymphoma [7,8], pancreatic carcinoma [9], prostatic carcinoma [10,11], primary carcinoma of the lung [12,13,14,15], primary liver cancer (PLC)[16], bowel cancer [17], cervical carcinoma [18,19], gastric cancer [20], laryngeal carcinoma [21], breast cancer at the time of recurrence [22],

and colorectal carcinoma [23]. This increase in  $\alpha_1$ -AT levels was also observed in chronic diseases such as, liver cirrhosis and hepatitis [6,24], duodenal ulcer disease [25], active retinal vasculitis [26], and crohns disease [27]. In addition a comparative analysis of tumors and normal tissues of origin showed a good correlation between reduced local  $\alpha_1$ -AT expression and more aggressive tumor growth [28]. In this study we tested the  $\alpha_1$ -AT serum levels in Jordanian lung, prostate and breast cancer patients and compared with those of healthy controls.

## MATERIALS AND METHODS:

Blood samples were obtained from eighty-three patients with three different types of cancer, thirty-three breast cancer, twenty-five male lung cancer, and twenty-five prostate cancer at Radiotherapy and Chemotherapy Treatment Department in Al-bashir Hospital. Blood samples of sixty-seven non-smokers healthy adult controls (forty-three females and twenty-four males) were obtained from blood donors at National Blood Bank in Al-bashir Hospital and Princess Basma Teaching Hospital. Venous blood was drawn into plain tubes. All serum samples were evaluated for  $\alpha_1$ -AT concentration within 2hrs after blood samples collection using Radial Immunodiffusion Technique (RID), following the company instructions. Duplicate measurements were carried out for each sample and the average result was used. The accuracy of the procedure was determined with control sera containing predetermined concentration of  $\alpha_1$ -AT.

Statistical analysis was performed using t-test and ANOVA test. Differences between mean levels were considered significant if obtained *P-value* was less than 0.05.

## RESULTS:

The mean plasma levels of  $\alpha_1$ -AT in patients with prostate and lung cancer compared with those of healthy male controls have shown significant differences. As shown in Table-1, the mean plasma  $\alpha_1$ -AT levels in prostate and lung cancer patients were  $222.7 \pm 87.3$ mg/dl and  $264.7 \pm 108.4$ mg/dl respectively, while in male controls the mean level was  $163.9 \pm 23.2$ mg/dl, *P-value* = 0.003 and 0.0001, correspondingly. Breast cancer patients have shown mean serum level of  $183.8 \pm 45.05$ mg/dl, this value was very close to that in healthy female controls  $186.13 \pm 39.8$ mg/dl (*P-value* = 0.815), as shown in Table-2. Among the three types of cancer, lung cancer patients have shown the highest  $\alpha_1$ -AT serum levels followed by prostate cancer.

## DISCUSSION:

Proteolytic enzymes play an important role in cancer pathology, but the role of the body's natural inhibitors of these enzymes in this process is not very well stud-

ied.  $\alpha_1$ -AT is the major serine protease inhibitor in plasma. Researchers have been trying to find a correlation between  $\alpha_1$ -AT and the process of neoplasia that may help in the diagnosis and the follow up of the cancer patient. Various studies were performed on the behavior of  $\alpha_1$ -AT in different types of cancer such as; lung, breast, liver, prostate, pancreas, cervix, and colorectal cancer. Most of these studies were reported the elevation of  $\alpha_1$ -AT plasma levels in cancer patients. [5,6,9,10,11,12,13,15,16,17,18,19,22,23]. In this work we studied a group of eighty-four patients with three different types of cancer, lung, prostate and breast. Each patient had the  $\alpha_1$ -AT serum level measured by radial immunodiffusion. As results indicated, nineteen out of twenty-five lung cancer patients 76%, have shown a significantly higher mean levels of serum  $\alpha_1$ -AT than that in male controls. Our data were similar to what was reported in earlier studies [29,12,13,14,15]. Daddi *et al.*, demonstrated that in more than 90% of lung cancer patients the serum level of  $\alpha_1$ -AT was significantly higher than that of controls [13]. The lower percentage of lung cancer patients with elevated  $\alpha_1$ -AT levels in our study compared with those found by Daddie *et al.*, might due to the fact that patients in this study were randomly selected, independent on being treated or untreated. Patients with prostate cancer, as well, have shown a significant rise in the concentration of  $\alpha_1$ -AT. Thirteen out of twenty-five (52%) had a higher  $\alpha_1$ -AT concentration compared with controls. This finding is in accordance with that observed by Zietek *et. al.*, 1996 and Milford *et. al.*, 1977. They found that  $\alpha_1$ -AT serum levels and activity were increased with the development of prostate cancer [10,11]. Kuvibidila and Rayford also demonstrated a significant elevation in serum  $\alpha_1$ -AT in prostate cancer patients and their direct correlation with prostate-specific antigen serum levels [30]. In the results section the high standard deviation numbers of  $\alpha_1$ -AT serum levels in lung and prostate cancer patients due to wide range concentrations of this protein in these patients. This wide range serum levels among different cancer patients might be explained by the differences in the stage and the grade of the disease as well as the type and duration of treatment they were receiving. This explanation is supported by Daddi *et. al.*, demonstrated that the level of  $\alpha_1$ -AT in lung cancer patients vary during the course of the disease [13]. Also, Milford *et. al.*, have shown that there were differences in  $\alpha_1$ -AT serum level between prostate cancer patients with different stages of the disease [11].

Breast cancer patients who were studied in this work did not show an elevation in their  $\alpha_1$ -AT serum concentration. These findings concerning breast cancer were different from what was reported in previous studies. Increased  $\alpha_1$ -AT blood level was shown to be associated with breast tumors [22,31,32]. Thompson *et. al.*, and Demidove *et. al.*, have observed a rise in the serum levels of breast cancer patients as compared with healthy individuals and this elevation was associated with

**Table-1:**  $\alpha_1$ -AT levels in lung and prostate cancer patients

Group	No. of individuals	$\alpha_1$ -AT mean values mg/dl	SD
Lung cancer	25	264.7*	± 108.4
Prostate cancer	25	222.7**	± 87.3
Control (males)	24	163.9	± 23.2

\*P-value = 0.0001; \*\*P-value = 0.003

tumor advancement [31,32]. On the contrary, Doustjalali S.R *et al.*, showed that the expression of  $\alpha_1$ -AT in breast cancer patients was apparently lower than that of the controls [33].

In conclusion, our data demonstrated that elevated  $\alpha_1$ -AT plasma levels might be an alarming factor to be considered in the diagnosis as well as in the follow up of lung and prostate cancer but it is a poor marker for breast cancer.

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**Table-2:**  $\alpha_1$ -AT levels in breast cancer patients and female controls.

Group	No. of individuals	$\alpha_1$ -AT mean values mg/dl	SD
Breast cancer	33	183.8	± 45.05
Control (females)	43	186.13	± 39.81

P-value = 0.815

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