Clinical utility of serum TNF alpha and alpha-1 anti-trypsin in predicting the stage and progression of lung cancer

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Abstract
Lung cancer is the commonest cause of cancer death in developed countries and throughout the world. Cigarette smoking is the main risk factor for lung cancer; it was responsible for 80–90% of lung cancer death and ex-smokers today comprise 50% of all new lung cancer cases. In addition, occupational exposures increase the incidence of lung cancer. Determination of tumor biomarkers in serum proposed as an alternative and noninvasive way of establishing diagnosis for lung cancer. The study population consisted of 120 patients with lung cancer. They were 90 males and 30 females. Their age ranged from 30-72 years. Besides 40 matched healthy individuals served as control. Serum TNF-α, Alpha–1-antitrypsin (AAT), total lipids, triglycerides and alkaline phosphatase were determined in all subjects using Enzyme Immunoassay. The aim of this study was to evaluate the clinical importance of some biochemical parameters in diagnosis and prediction of lung cancer stage among Egyptian patients. The results showed that the TNF-α level increased in the patients compared to control, although the difference was not statistically significant. Serum ALP levels significantly increased in metastatic patients compared to control group. AAT levels showed statistically significant elevation in patients compared to controls. Total lipids and the triglycerides showed non-significant decrease in the patients compared to controls. TNF–α and alkaline phosphatase were superior to alpha-1 antitrypsin in the diagnosis of lung cancer patients. In conclusion, TNF–α could be of value in predicting the clinical stage of lung cancer and this value could strengthened by simultaneous estimation of alkaline phosphatase. The significant elevation in AAT levels could attribute to the fact that it is an acute phase reactant. Total lipids could be of clinical importance to estimate the nutritional status of such patients.

Keywords: lung cancer, TNF–α, Alpha-1-antitrypsin, alkaline phosphatase, Total lipids, Triglycerides.

INTRODUCTION
Lung cancer is one of the most important diseases in respiratory medicine. Worldwide, it is the commonest cancer in men, virtually the commonest in women, and has a greater total incidence than that of colorectal, cervical, and breast cancer combined. The death rate for lung cancer exceeds the combined total for breast, prostate and colon cancer in developed countries (Atlanta, 1999).

The etiology of the great majority of lung cancers known for nearly 50 years (Diederich et al., 2002) but it failed to make serious inroads into the powerbase of the tobacco industry. Smoking is one of the avoidable causes of mortality, considered a major risk factor for cardiovascular diseases, chronic obstructive pulmonary diseases, and bronchopulmonary cancer (Didilescu et al., 2009). It was shown that smoking is a well-known predisposing factor to cancer lung (Vanni et al., 2009). Lung cancer is a disease for which there is no established screening, which presents late in its course, and has a median survival of 6–12 months from the time of diagnosis with an overall 5 years survival of 5–10%, and yet the major cause of this disease clearly understood. Communities and countries addressing a smoking ban would probably achieve far more in the long term than which currently are with the available treatments (Shopland, 1995).

Although surgery offers the best chance of cure in lung cancer, particularly in the case of non–small cell lung cancer, only a small proportion of patients are ever suitable for curative resection and the majority must...
Clinical utility of serum TNF alpha and alpha-1 anti-trypsin rely on nonsurgical and adjuvant therapies (Heyneman et al., 2001).

Lung carcinogenesis is a chronic process involving multiple genetic, cellular, and tissue alterations. These results from mutagenic damage to growth regulating genes and their products that ultimately leads to the development of invasive or metastatic cancer. Staging and classification of lung cancers are important for appropriate patient management and for estimating prognosis. In 1997, the International Union against Cancer/American Joint Committee on Cancer (UICC/AJCC) published the fifth edition of the TNM classification system for lung cancer (Mountain, 1997).

Reflecting different clinical behavior and sensitivity to chemo- and radiotherapy, lung cancers can be grouped in two major histological types, i.e. non-small cell and small cell lung cancer (NSCLC and SCLC respectively). NSCLC accounts for 75-85% of lung cancer patients and consists of several subtypes, predominantly squamous cell carcinomas, adenocarcinomas and large cell carcinomas, which treated in the same manner. Small cell lung cancer accounts for 15-25% of lung cancer patients, often has neuroendocrine components, and primarily treated with chemotherapy and/or radiotherapy. Many lung cancers constitute histologically mixed tumor types consisting of non-small cell and small cell components (Stupp et al., 2004).

Human tumor necrosis factor-alpha is a 233 a residue, nonglycosylated polypeptide that exists as either a transmembrane or a soluble protein. When expressed as a 26 kDa membrane bound protein. Tumor necrosis factor (TNF) is a pro-inflammatory cytokine that regulate the growth and differentiation of a variety of immune cells (Zheng et al., 2009). Increased levels of TNF-α found in both infectious pleural effusion and malignant pleural effusion; it plays an important role in a variety of cellular processes that include cell survival, proliferation, differentiation, and apoptosis (Aggarwal, 2003). The ability of TNF to induce apoptosis in cancer cells makes it a potential therapeutic agent. However, most cancer cells that were resistant to TNF induce death (Wajant et al., 2005). Although the mechanism has not been well elucidated; it is believed that the survival signals induced by TNF may blunt the apoptotic pathway, which results in the resistance of cells to TNF-induced apoptosis (Wajant et al., 2003). Therefore, interventions that inhibit TNF-α induced survival signals may sensitize cancer cells to TNF-α induced apoptosis.

Tumor necrosis factor (TNF)-α production reported in patients with several types of pulmonary dysfunction including chronic obstructive lung disease (De Godoy et al., 1996 and Di Francia et al., 1994), hypoxic lung injury (Horinouchi et al., 1996, Jensen et al., 1992), bronchopulmonary dysplasia (Bagchi et al., 1994), and asthma (Broide et al., 1992). Some of these processes have also been associated with pulmonary neuro-endocrine cell hyperplasia (Gosney et al., 1989). There are several clues as to the mechanism of the anti-tumor activity of (TNF) directly by killing of tumor cells, and indirectly through blocking of tumor blood vessels, promoting host inflammatory response (Kull and Cuatrecasas, 1981).

Alpha1-protease inhibitor is an acute phase glycoprotein with antiprotease activity, previously referred to as Alpha-1-antitrypsin (AAT). The gene responsible for AAT synthesis is located on chromosome 14, and production occurs principally in hepatocytes, although other cells, such as mononuclear phagocytes and epithelial cells of the lung and intestine, can contribute (Serra et al., 2008). Alpha1-antitrypsin is increased during pregnancy, smoking, rheumatic disorders, acute myocardial infarction, acute hepatitis, acute inflammation and severe infection (Chappell et al., 2008). Alpha-1-antitrypsin deficiency (Alpha-1-ATD) predisposes to the development of emphysema and other features of chronic obstructive pulmonary disease (COPD), particularly in smokers (Risk et al., 2005).

The aim of this study was to find out the possible role to TNF-α in the diagnosis and prediction of the clinical stage of lung cancer. Alpha 1-antitrypsin, total lipids, ALP and triglycerides estimated aiming to find if such combination could add to the possible significance in the diagnosis of lung cancer patients.

SUBJECTS AND METHODS

The studied population consisted of 120 patients with lung cancer from the Surgical Clinic of National Cancer Institute Hospital, Faculty of Medicine, Cairo University, Egypt.

All patients subjected to standard evaluation included medical history, clinical examination, blood chemistry, chest x-ray, CT scan whenever needed, bronchoscope and histopathological typing. Tumors staged according to the TNM classification (Sobin and Wittekind, 1997) and graded using criteria recommended by the World Health Organization (WHO, 1982). Any patients with history of liver disease or suffering from any hepatic problem, renal disorder, recent history of cardiovascular disease and diabetes were excluded from the study.

Samples collection

After obtaining informed written consent from the individuals, sharing in this study, 10 -ml fasting blood samples collected in dry clean plastic tubes. The blood
were allowed to clot and sera were separated by centrifugation for 10 min at 3000 r.p.m, divided into several aliquots and stored at –80 °C until assayed.

**Laboratory investigation**

All participants subjected to the following investigations:
1. Complete blood picture.
2. Liver function tests including:
   - Detection of bilirubin level by using commercially available kit from Bio-Merieux Company, France (Berry et al., 1983).
   - Detection of AST, ALT and alkaline phosphatase (ALP) levels by using the method recommended by the committee on enzymes of the Scandinavian Society for Clinical Chemistry and Clinical physiology, (1974). The test performed using commercially available kit from Boehringer-Mannheim Company, Germany.
3. Renal function tests including:
   - Detection of urea level by using commercially available kit from Randox, Laboratories Ltd., USA (Husdan and Rapoport, 1968)
   - Detection of creatinine level by using Jaffe reaction (Fawcett and Scotto, 1960).
4. Tumor necrosis factor alpha (TNF-α) was determined quantitatively by immunoenzymometric assay manufactured by ANOGEN Catalogue Number: EL10019 (Chieregatti et al., 1990). This TNF-α enzyme linked immunosorbent assay (ELISA) applies a technique called a quantitative sandwich immunoassay.
5. Alpha-1-antitrypsin (AAT) was determined quantitatively by immune enzymometric assay manufactured by Immundiagnostik K 6750MTP (Faust et al., 2002). The assay utilizes the sandwich technique with two selected polyclonal antibodies that bind to human alpha-1-antitrypsin.
6. Total lipids was determined using a colorimetric test Phosphovainilline manufactured by Reactivos Spinreact, S.A. (Stein and Myers, 1994).
7. Triglycerides were determined quantitatively using enzymatic colorimetric test manufactured by Stamio (Stein and Myers, 1994).

**Statistical analysis**

The data processed and analyzed using the program (SPSS) statistical package for social sciences version II under windows XP. Descriptive statistics performed for categorical data using percents for quantitative data using the mean and standard deviation. Inter group comparisons conducted using Pearson chi-square for categorical data. Quantitative variables were tested for normality and pooled T test was used for inter group comparisons involving such variables. The significance level preset at the 0.05 level.

**RESULTS**

The studied groups of lung cancer patients were 90 males and 30 females. Their age ranged from 30-72 years with a mean of 54.6±10 years. Beside 40 healthy, sexes and age matching healthy individuals served as control. They were 25 males and 15 females, their age ranged from 25-67 years with a mean of 49.7±10.1 years.

All patients have normal levels of renal function tests (urea & creatinine) and liver function tests (bilirubin, AST and ALT) except the patients with liver metastasis who show a high level of liver enzymes.

The Clinicopathological findings of lung cancer patients before treatment were 44 cases of adenocarcinoma, 28 small cell carcinoma, 26 squamous cell carcinoma and 22 large cell carcinoma. Regarding the grades of tumor, twenty patients out of 120 were of grade I or II, and 100 of grade III. 28 patients out of 120 cases had metastasis (16 bone metastasis, 8 liver and 4 both liver and bone metastasis). 40 patients out of 120 had pleural effusion and 54 out of 120 cases were positive for lymph nodes. 72 patients had a history of smoking. The clinical and biochemical data of the studied subjects showed in Tables 1, 2 and 3 [Supplementary data] and Fig. 1, 2 and 3.

**Figure 1:** Comparison of different biochemical parameters in controls and in different histopathological types of lung cancer.

**The values of biochemical parameters among studied groups**

In control, the levels of TNF-α showed a mean of 5.6±5 pg/ml, AAT 152.3±14.6 mg/dl, total lipids 553.6±82.12 mg/dl, triglycerides 101±31.3 mg/dl and ALP 67.65±10.4 (IUL-1). In patients TNF-α showed an elevation compared to control, although the difference was not statistically significant. Alpha-1-antitrypsin showed statistically significant elevation (P=0.04) in patients compared to controls. Total lipids showed non-significant decrease in patients compared to controls. Triglycerides in patients showed no difference
Clinical utility of serum TNF alpha and alpha-1 anti-trypsin compared to controls. Alkaline phosphatase showed a statistically significant elevation in the patients.

**Figure 2:** Comparison of TNF pg/ml in controls and in different histopathological types of lung cancer.

**Relation of the different studied parameters to smoking**

A significant elevation of AAT in smokers 229±90.6 mg/dl compared to non smokers 173.5±70.85 mg/dl (P=0.01). There was also a significant decrease in triglycerides levels in smokers 94.1±32.9 mg/dl compared to non smokers 123.2±56.5 mg/dl (P=0.01). TNF-α increased in non-smokers 17.1±33.9 pg/ml compared to smokers 12.2±21.5 pg/ml, but the difference was not statistically significant. Total lipids values were lower in smoker 418.5±105.8 mg/dl than in non-smoker 440.9±180.5 mg/dl.

**Figure 3:** Mean levels of alkaline phosphatase among different studied groups.

**Relation of the different studied parameters to lymph nodes positivity**

Higher values of AAT and triglycerides observed in cases with positive lymph nodes 205.1±86.6 and 113.2±48.9 mg/dl respectively compared to their corresponding values in cases with negative lymph nodes 189.9±82.6 and 102.7±49.8 mg/dl respectively. The differences were statistically not significant. Whereas TNF-α and total lipids values were lower 12.8±21.8 pg/ml and 420.9±158.8 mg/dl respectively in cases with positive lymph nodes compared to those with negative lymph nodes 14.7±31.8 pg/ml and 449.9±130.7 mg/dl respectively. The difference was only significant for total lipids (P=0.01). A significant elevation (P=0.001) in ALP were observed in cases with positive lymph nodes 314.33±179.37 (IUL−1) compared to their corresponding values in cases with negative lymph nodes 137.83±97.60 (IUL−1).

**Relation of the different studied parameters to pleural effusion**

TNF-α and AAT showed lower values 17.6±26.8 pg/ml and 179±65.8 mg/dl respectively in cases with pleural effusion compared to those without pleural effusion 20.1±30.2 pg/ml and 202±91.4 mg/dl respectively. The differences were statistically not significant. While total lipids and triglycerides showed higher values 459.4±169.8 and 116.8±43.5 mg/dl respectively in cases with pleural effusion compared to those without pleural effusion 418.5±132.6 and 102.4±49.6 mg/dl respectively. The difference for total lipids only were statistically significant (P=0.007). A significant elevation (P=0.001) in ALP were observed in cases with positive pleural effusion 357.62±160.29 (IUL−1) compared to their corresponding values in cases with negative pleural effusion 108.75±48.19 (IUL−1).

**Relation of the different studied parameters to metastasis**

TNF-α and triglycerides values showed an elevation in cases with metastasis 18.7±27.8 pg/ml and 122.1±62 mg/dl respectively compared to those without metastasis 11.7±25 pg/ml and 102±38 mg/dl respectively. AAT and total lipids showed no difference between their values in both cases with metastasis 188.9±96.7 and 425.8±178 mg/dl respectively and without metastasis 204±80 and 441±41 mg/dl respectively. A significant elevation (P=0.001) in ALP were observed in cases with metastasis 299.71±188.12 (IUL−1) compared to their corresponding values in cases without metastasis 181.44±148.52 (IUL−1).

**Relation of the different studied parameters to the site of metastasis**

TNF-α and AAT showed an elevation in cases with bone metastasis 27.3±29.6 pg/ml and 209.9±128.6
mg/dl respectively compared to cases with liver metastasis 20.5±35.2 pg/ml and 151.2±74.4 mg/dl respectively. On the other hand, total lipids and triglycerides showed an elevation in cases with liver metastasis 440.2±182.9 and 121.2±74.6 mg/dl respectively compared to cases with bone metastasis 346.3±144.6 and 111.6±62.8 mg/dl respectively. A significant elevation (P=0.001) in ALP were observed in cases with bone metastasis 280.14±114.98 (IUL) and in cases with liver metastasis 330.27±140.45 (IUL).

Relation of the different studied parameters to the histological type

TNF-α level elevated in cases with large cell carcinoma and squamous cell carcinoma with a mean of 23.8±42 and 16.8±25 pg/ml respectively, compared to controls 5.6±5 pg/ml, small cell carcinoma 14.3±17.2 pg/ml and to adenocarcinoma 13.8±15.7 pg/ml. While no statistically significant difference detected between these groups and each other except for large cell carcinoma. AAT was elevated in all histological type, in large cell carcinoma 220.6±93 mg/dl, squamous cell carcinoma 210±98 mg/dl, adenocarcinoma 196.5±79 mg/dl, small cell carcinoma 172±51 mg/dl compared to controls 152.3±14.6 mg/dl, but no statistically significant difference could be detected between these groups and each other except for large cell carcinoma. Total lipids showed a decrease in all histopathological types compared to controls 553.6±82.1 mg/dl. Squamous cell carcinoma showed the lowest value 345±171 mg/dl P=0.003, large cell carcinoma 378.6±82.6 mg/dl, adenocarcinoma 479.1±149 mg/dl and small cell carcinoma 502±170 mg/dl. Triglycerides showed an elevation in adenocarcinoma type 129.9±49.5 mg/dl compared to squamous cell carcinoma and large cell carcinoma 91.9±39.9 and 88.9±38.6 mg/dl respectively. The difference between those groups was statistically significant (P=0.05). Triglycerides showed a non-significant increase in grade I and II compared to grade III, 132.2±50.1 and 101.7±40.2 mg/dl respectively. Triglycerides showed a non-significant increase in grade I and II compared to grade III, 132.2±50.1 and 101.7±40.2 mg/dl respectively.

Relation between the different studied parameters

There was only a negative relation between AAT and T.G. (P=0.005). Regarding the age, only TNF-α values showed increased with aging although it was not statistically significant (P=0.06). Regarding ALP there was no significant difference between control and cases without metastasis, negative pleural effusion nor negative lymph nodes.

DISCUSSION

The lung can be involved in a variety of neoplasm. Bronchogenic carcinoma accounts for over 90 percent of all lung tumors. It is one of the most common cancers in the world (Jemal et al., 2003). Progress towards an early diagnosis of bronchogenic carcinoma is a welcome development and all will contribute to a more favorable outcome of the disease.

Recent advances have outlined the role of cytokines and their receptors in the transformation and proliferation of tumor cells particularly those of hemopoietic system. Several cytokines have shown to promote the growth of malignant cells in vitro and therefore believed to contribute to the aggressiveness of the disease (Aaronson, 1991). However, few data are available regarding cytokine production in vivo in patients with malignant tumors (Takeuchi et al., 1996).

Tumor necrosis factor-alpha (TNF-α) is a cytokine with pleiotropic activities, which initially identified in animal studies, as a factor responsible for fever, anorexia and cachexia (Satoru et al., 2004). TNF-α is a multifunctional cytokine involved in the pathogenesis of various inflammatory and malignant diseases (Fleto et al., 2009). TNF-α also exhibits a cytotoxic activity against certain tumor cells and has multiple immunologic and local as well as systemic inflammatory activities (Takashi et al., 1994). It induces antitumor defenses to suppress in vivo human tumor cell growth, which could provide a rationale for transferring a human TNF-c DNA directly to malignant cells for the therapy of human lung cancer (Han et al., 1994).

In this study TNF-α evaluated in cancer lung patients trying to find out possible role in diagnosis and prediction of the clinical stage of the patients. AAT, ALP, total lipids and triglycerides also measured to study if such combination could have any prognostic significance in monitoring lung cancer patients.
Our results showed that the increase in TNF–α was proportional to deterioration of the grade where cases with grade III showed significant increased with a mean of 20.5 pg /ml compared to those with grade I and II with a mean of 10.5 pg /ml. In accordance to our results Gatti et al., in 1995 reported that TNF values higher than 14.4 pg /ml were associated with far advanced disease stage (IIIB and IV) and poor performance status. Also, our results are in agreement with that obtained by Dalaveris et al. (Dalaveris et al., 2009) reported that TNF-alpha, is elevated significantly in the serum of lung cancer patients than control group and its level is related to advanced disease. An elevation of TNF–α was found in our cases showing metastasis more than those without metastasis.

TNF-α appears to be a highly active cytokine that induces widespread alterations in the host. It is a central mediator of the host response to bacterial infection (Anderson et al., 1988). The variation among patients partially explains the variation in the severity of responses of such patients. Wide variations observed in serum levels of TNF–α as estimated by different workers. Trejo et al. (Trejo et al., 2001) estimated tumor necrosis factor-alpha in a group of untreated lung cancer patients and they reported marked elevation in TNF-α levels with a mean of 450 pg /ml. While Gatti et al., (Gatti et al., 1995) studying a group of newly diagnosed lung cancer patients, reported a much less elevation in TNF-α values with a mean of 16.3 pg/ml. On the other hand Ardizzoni et al. (Ardizzoni et al., 1994) reported that serum TNF-α level were undetectable in a study done on 11 NSCLC patients tested before treatment and became detectable in only 2 patients after IL-2 treatment.

Regarding ALP, the results showed a statistical significant value (P=0.01) in patients having metastasis compared to patients have no metastasis. Therefore, simultaneous estimation of TNF–α and alkaline phosphatase could be of great help in early detection of metastasis in lung patients.

The results of the present study showed that TNF–α level correlated to the age of the patients as it found to increase with ageing. On the contrary, Gatti et al., in 1995 did not find out any relationship between TNF–α levels and patients age.

Proteolytic enzymes are associated with normal and neoplastic tissue. The alpha–1–anti-trypsin in malignant cells may be a controlling factor against tumor proliferation. Several studies suggest that the inhibitory level is very important since increased its activity is associated with transformation and uncontrolled tumor proliferation (Senn et al., 2008).

AAT being an acute phase reactant showed a statistically significant elevation in lung cancer patients (P=0.04). In addition, 72.7 % of cases showed a value exceeding the mean control value while only 27.3 % of cases showed lower values. A significant elevation of AAT was observed among patients having positive history of smoking (P=0.01) these results were in accordance to that obtained by Wolf et al. (Wolf et al., 1982) reported that elevated AAT levels was related to smoking. Our data were in agreement with that obtained by Zelvyte et al. (Zelvyte et al., 2004) showed that plasma level of AAT was elevated in lung cancer patients by 1.43-fold, p<0.01 when compared to controls. In addition, they found that level of AAT was higher by 1.47-fold, p<0.001 in lung cancer cases with metastasis compared to localized tumor. In addition, they conclude that these inhibitor levels may provide measures of cancer progression in individual patients and possibly offer useful information for an understanding of the mechanisms of metastasis.

AAT contrary to TNF–α showed no difference between their values in both cases with metastasis and without metastasis. AAT reported by Ameshima et al. (Ameshima et al., 1992) to have an inhibitory effect on the production of TNF–α by alveolar macrophages in patients with lung cancer. Thus, the slight elevation of TNF–α level in our study compared to the significant elevation of AAT explained by the humoral inhibitory role of AAT against the production of TNF–α by alveolar macrophages. Another explanation could be the possible consumption of TNF–α by elevated levels of soluble TNF receptors (STNFRs) which could increase in lung cancer (Gatanaga et al. 1991). In addition, it found that serum concentrations of STNFRs in cancer patients correlate with the staging of the disease (Marie et al., 1997). In addition, Grosen et al. (Grosen et al. 1993) have demonstrated that ovarian cancer cell lines were releasing STNFRs, which could be a powerful marker of impending relapse.

Total lipids showed a significant decrease in newly diagnosed lung cancer patients compared to controls, (P=0.001), while triglycerides showed no deviation. The drop in total lipids in lung cancer patients could be explained by being a part of cancer cachexia seen in such patients, which is induced by hyper-metabolic effect of cytokines causing proteolysis and lipolysis in muscle and fat tissue (Tisdale, 1996).

Contrary to our results Gatti et al., in 1995 reported hypertriglyceridemia in patients with advanced disease (stage IIIb, IV, and poor performance status). Hyperlipidemia, primarily due to accumulation of very low-density lipoprotein (VLDL) is generally associated with the acute phase response. A variety of cytokines mediate hyperlipidemia by decreasing adipocyte lipoprotein lipase activity, an enzyme which is present in adipose tissue and is essential for the normal storage of fat (Beutler et al., 1985).
The relations between the levels of the four parameters estimated in this work and the presence of lymph nodes and pleural effusion studied. No relation could be found between TNF–α and AAT and the presence of lymph nodes or pleural effusion. While elevated triglycerides levels were observed in cases having positive lymph nodes more than those with negative lymph nodes. Also total lipids and triglycerides showed higher values in cases with pleural effusion compared to those without pleural effusion. The difference was not statistically significant; therefore, it needed a large-scale study for better evaluation of such relations.

Regarding the site of metastasis TNF–α and AAT showed higher values in bone metastasis compared to liver metastasis while triglycerides and total lipids showed the reverse. A significant negative relation found between AAT and triglycerides; this explained by the relationship between TNF–α and AAT on one hand and the relationship between TNF–α and triglycerides on the other hand. AAT has an inhibitory effect on TNF–α which in turn inhibits lipoprotein lipase resulting in increase in triglycerides levels. A significant decrease in triglycerides levels was observed among lung cancer patients having positive history of smoking (P=0.01), this could be explained by the negative correlation found between AAT and triglycerides and the positive correlation between AAT and smoking (Beutler et al., 1985).

CONCLUSION

From this study we can conclude that TNF–α has a clinical value in diagnosis of lung cancer patients and this value could be strengthened by simultaneous estimation of alkaline phosphatase.

AAT tumor marker expressed and released at the time of primary diagnosis are likely to be the most relevant markers for detection of clinical stage and the significant elevation in AAT levels could be attributed to the fact that it is an acute phase reactant.

It could be concluded that TNF–α has a very limited diagnostic value as it showed a slight elevation among newly diagnosed lung cancer patients. But a role in predicting the stage and monitoring lung cancer patients could be considered where TNF–α elevation was proportional to the deterioration of the disease grade and cases with metastasis showed higher TNF–α than those having no metastasis. Moreover, simultaneous estimation of TNF–α and alkaline phosphatase could be of great help in early detection of metastasis in lung cancer, and could be valuable factors in following high-risk lung cancer patients. In addition, estimation of triglycerides and total lipids could be of importance in evaluating the nutritional status in lung cancer patients especially those in advanced condition. Further longitudinal studies warranted for the evaluation of the prognostic role of these biomarkers in lung cancer.

References


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