Original Article

Serum IGF-1 Levels as Clinical Marker in Assessing the Risk of Lung Cancer

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**A B S T R A C T**

Keywords:
- ELISA
- Insulin like growth factor-1 (IGF-1)
- Lung cancer

**Aims:** Insulin-like growth factor-1 (IGF-1) play a pivotal role in cellular proliferation, differentiation and apoptosis in a variety of cancer cells, including lung cancer. The aim of the present study was to examine the possible causal role of serum IGF-1 in development and progression of lung cancer. **Method:** In this study an enzyme-linked immunosorbent assay (ELISA) was used to quantify serum IGF-1 level in lung cancer patients. The study comprised 150 patients with histological confirmed lung cancer and 150 age & sex matched control subjects. Data were analysed to assess the association between serum IGF-1 concentration and lung cancer risk. The independent sample t-test was used to compare the means of different variables in the two group. **Results:** Serum IGF-1 concentration was found significantly elevated in lung cancer group compared to those in control group (p<0.00). A statistically significant positive association was found between IGF-1 levels and risk of lung cancer. **Conclusion:** Our results show that increased level of IGF-1 in serum may play an important role in the development and disease progression of lung cancer, suggesting that IGF-1 may be associated and potentially contribute in the etiology of lung carcinoma.

**Introduction**

Lung cancer has become more prevalent than any other cancer in worldwide. It has been remained the leading cause of cancer mortality in both sexes. It is commonest in men in India accounting for 11.3% of all new cancers and the most common cause of cancer death (13.7%) [1].

Tumor cells exhibit characteristic features of abnormal cellular differentiation, transformation, proliferation, and apoptosis which are maintained and regulated by interaction of cancer cells with peptide growth factors. Among the growth factors, Insulin-like growth factor-1 is prominent factor to be involved in regulation of cell growth and transformation. IGF-1 has an important role in childhood growth but in old age more than 40 years it can contribute to tumor growth also [2]. This is an important mitogenic and antiapoptotic peptide [3] which plays a pivotal role in proliferation of normal and malignant cells through both endocrine and autocrine or paracrine behavior [4]. These deregulations of IGF system has been reported in several carcinomas, including lung carcinoma [5-10]. In vitro studies revealed that lung cancer cell lines express an increased functional IGF-1 [11]. This escalates the concern over possible role of IGF-1 in the etiology of lung carcinogenesis.

As a result of the presence of IGF-1 in LUNG cells, numerous studies have been performed to illustrate the role of IGF-1 in growth and development of lung cancer in past years and correlated a high circulating level of IGF-1 in lung carcinoma. However there are other studies showing the decreased level of IGF-1 in lung cancer. The role of IGF-1, investigated in lung cancer, is uncertain and the clinical significance of serum IGF-1 concentrations in lung cancer patients remains to be elucidated. Due to conflicting results reported in recent epidemiological and clinical studies, the present study is aimed to explore serum IGF-1 concentrations in newly diagnosed patients.

**Materials and Methods**

**Patients:** A total number of 150 patients with histological or cytological confirmed of lung cancer treated in the Institute of Oncology (SMS Hospital, Jaipur) were included in the study. The patients recruited, were newly diagnosed and without a history of chemo/radiotherapy. Patients having hypertension, diabetes, endocrinial disease, tuberculosis, PCOS, cardiovascular, cerebrovascular, hepatic and renal diseases, on physical examination were excluded from this study. The lung cancer patients were staged according to the 7th edition of the International Staging of Lung Cancer, 2009 [12].
The clinical history, physical examination, series of biochemistry tests and complete blood cell counts were used as the pretreatment evaluation. Age and sex matched 150 control subjects who voluntarily participated were included in the study. The study was approved by the Ethics Committee. Written informed consent was obtained from all the patients.

**Measurement of serum IGF-1 level:** Samples were collected from patients and healthy controls by venipuncture under sterile condition and allowed to clot at room temperature on first admission prior to the treatment. The serum was separated from the clotted specimen by centrifugation at 1300-1800 rpm for 10 minutes and stored at -80 °C in aliquots for analysis of IGF-1. IGF-1 was measured by ELISA methods using the kit DRG IGF-1 600 on Mindray ELISA analyzer.

**Statistical analysis:** The presentation of the results is in the form of mean ± standard deviation. SPSS for windows (version 15, Chicago, IL, USA) was used for the analysis of data collected. The independent sample t-test was used to compare the means of different variables in the two groups. For all statistical assessment a value of p<0.05 was accepted to be significant.

**Results:**

Table 1 presents the serum IGF-1 concentration in lung cancer patients v/s control group. The mean value of serum IGF-1 in patients v/s control groups was (83.27±44.35 v/s 41.81±20.92) ng/ml. Serum IGF-1 concentration was found significantly elevated in lung cancer group compared to those in control group (p<0.00).

Table 2 describes serum IGF-1 concentration of stage 1, 2 and 3, 4 lung cancer patients. The mean value of serum IGF-1 in patients v/s 3, 4 stage was (41.10±13.15 v/s 101.43±40.36) ng/ml. In the 3, 4 stage (advanced stage disease) lung cancer group, the mean serum IGF-1 level was significantly higher compared in patients with stage 1, 2 disease, indicating that with the progression of disease serum IGF-1 level also increase.

**Table 1: Serum IGF-1 level in Lung Cancer Patients v/s Control Subjects**

<table>
<thead>
<tr>
<th>Character</th>
<th>Patient</th>
<th>Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>150</td>
<td>150</td>
<td></td>
</tr>
<tr>
<td>IGF-1(ng/ml)</td>
<td>83.27±44.35</td>
<td>41.81±20.92</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**Table 2. Serum IGF-1 level in Lung Cancer Patients 1&2 stage v/s 3&4 stage**

<table>
<thead>
<tr>
<th>Character</th>
<th>stage 1&amp;2</th>
<th>stage 3&amp;4</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>45</td>
<td>105</td>
<td></td>
</tr>
<tr>
<td>IGF-1 (ng/ml)</td>
<td>41.10±13.15</td>
<td>101.43±40.36</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**Discussion:**

In this case–control study, we found that higher plasma levels of IGF-1 is associated with an increased risk of lung cancer and the difference between patients and control group was statistically significant and as disease progression occurs from early to late stage, serum IGF-1 also significantly increase, suggesting that IGF-1 may be involved in mechanism underlying cancer causation and metastasis.

Our study results are in agreement with study performed by Yu H et al. [5] that expression of control group (P<0.001 and P=0.01, respectively). In another study, Zhang M et al. [6] also measured the serum levels of IGF-1 in 80 lung cancer patients and found that the serum IGF-1 levels in the lung cancer patients were significantly elevated compared to the controls (P<0.00) and advanced stage (III-IV) lung cancer group tended to exhibit increased serum IGF-1 concentrations compared to those with early stage (I-II) group. These results indicated that serum concentrations of IGF-1 may be useful tumor markers for assessing lung cancer risk.

IGF-1 is a multifunctional peptide, involved in mechanisms underlying tumorigenesis, mitosis, metastasis, angiogenesis and antiapoptosis [13], these mitogenic and antiapoptotic effects has a profound impact on tumor growth. IGF-1 increases DNA synthesis and up-regulates the expression of cyclin D1 and accelerates the cell cycle from G1 to S phase [14]. Any alteration in cyclin D1 expression causes tumor formation. Besides cell proliferation stimulation, IGF-1 also interrupts programmed cell death [15,16]. IGF-1 induces angiogenesis in tumors and this tumor induced neovascularization underlies cancer metastasis. Hypoxia is also another triggering factor for tumor induced angiogenesis [17,18]. IGF-1 increases the expression of hypoxia-inducible factor 1α and regulates the transcription of vascular endothelial growth factor (VEGF) [19], a major tumor-derived angiogenic factor.

Besides acting as an endocrine hormone, IGF-1 controls cellular growth in autocrine or paracrine manner also [4]. Autocrine production of IGF by the tumor cells and high levels of IGF 1 have been reported in the lung tumor tissue [20,21].

In conclusion, our results suggest that expression of IGF-1 in serum may play an important role in the development of lung cancer. Increased level of IGF-1 may also involve in disease progression of lung cancer, suggesting that IGF-1 may be associated and potentially contribute in the etiology of lung carcinoma. However, we evaluated only a single time sample but included all stages, so this study contributes a significant deal. By assessing predictive and prognostic values of the two serum assays and larger-scale studies in larger patient populations may be more helpful to determine the exact role of serum IGF-1 levels in lung cancer.

**Reference**

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