



## A Study of Vitamin D in Different Stages of Lung Cancer

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### ABSTRACT

*The purpose of this study is to investigate the diagnostic value of Vitamin D in different stages of lung cancer. Lung cancer is the leading cause of cancer death in both men and women. Despite aggressive efforts, treatments are unsatisfactory and survival rates dismal. Clearly development of new approaches for studying and treating lung cancers are needed.*

*The majority of lung cancers are associated with smoking, and beyond the well-established causal connection with carcinogens in cigarette smoke, nicotine also appears to affect lung cancer growth. **Design/Methods:** Lung cancer patients were selected on the basis of stages of cancer. In this study, we demonstrated that serum vitamin D levels very helpful monitoring for different stages of lung cancer. **Results:** The levels of Vitamin D were found to be significantly decreased in different stages of lung cancer when compared with control **Conclusions:** Vitamin D as a steroid hormone. Its serum concentrations in healthy individuals positively correlate with lung cancer.*

**KEYWORDS :** Vitamin D, Lung cancer

### Introduction

Lung cancer is a major cause of morbidity and mortality worldwide both in men and women accounting for 29% of all other cancers. The incidence of lung cancer still remains very high. Tobacco smoke contains over 60 established carcinogens. Among the constituents of smoke the polycyclic aromatic hydrocarbons (PAHs) such as benzo(a)pyrene, play a major role in lung carcinogenesis<sup>1</sup>.

The WHO estimates that lung cancer is the most frequent cancers in the world today and the global incidence of lung cancer is increasing at the rate of 0.5% per year due to the fact that the smoking epidemic continuous to spread to developing countries. Lung cancer is strongly related to smoking. We know that 85-95% of lung cancer patients are smokers. In many developed countries the smoking prevalence is approximately the same among women and men<sup>2</sup>. Lung cancer is a common disease that is difficult to treat successfully. As such, any prospects for improved therapy are of great significance.

The 5-year survival rate is only 16% for patients diagnosed with advanced disease compared with 70% to 90% that can be achieved when lung cancer is diagnosed and treated at an earlier stage. 3-5 Early detection and treatment of lung cancer is a promising strategy to reduce lung cancer mortality. Technologies such as spiral computed tomography (CT) and auto fluorescence bronchoscopy can detect lung cancers down to the sub millimeter range.<sup>6</sup>

The discovery of Vitamin D (VD) falls back to 17<sup>th</sup> century with the origin of the disease rickets in children, in England<sup>3</sup>. In addition, during 19<sup>th</sup> century, the incidence of rickets increased in major cities due to industrial revolution, where the workers had indoor work activities most of the time and lacked exposure to sunlight<sup>4</sup>. Moreover, the cause of rickets was unknown until the beginning of 20<sup>th</sup> century.

On the basis of the experiments, the essential dietary importance of Vitamin D in preventing rickets and also the ability to cure rickets due to a new substance termed "Vitamin D" was well documented during the 20<sup>th</sup> century<sup>5</sup>. The new substance was named as VD because it was the fourth Vitamin to be discovered. At the same time, the VD activity could be induced by exposure to ultraviolet light and also found that the presence of ultraviolet

light activated an inactive substance to become a Vitamin-D-active material<sup>6</sup>. Hence, ultraviolet light could be used to irradiate foods, induce VD activity, and fortify foods to eliminate rickets. This discovery also made available a source of vitamin D for isolation and identification.

### Materials and Methods

#### Chemicals:

Vitamin D kits were purchased from Immune Diagnostic kits, USA. All the other chemicals used were of analytical grade.

#### IIb. Experimental Design

Out of 68 patients were divided into six groups. Group I : Normal subjects, Group-II : Stage-0 Lung cancer, Group-III: Stage-I Lung cancer, Group-IV: Stage-II Lung cancer, Group-V: Stage III Lung cancer and Group-VI: Stage IV Lung cancer patients. Patients demographic data, including sex, age, and risk factors for cancer events including high-risk age (49-64), smoking history, histopathological record, were recorded.

The study was conducted during the period of Feb 2015 to March 2016 in department of Biochemistry, Meenakshi Medical College and Research Institute, Kanchipuram, Tamil Nadu, India.

#### III. Statistical Analysis

Data were analyzed using the SPSS software package, version 17.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed using range, mean, SD, and median, whereas qualitative data were expressed as frequency and percentage. P value was assumed to be statistically significant at 0.05.

#### IV. ETHICAL CONCERN

Ethical clearance was obtained from the Ethical committee meeting conducted at Meenakshi Medical College and Research Institute, Kanchipuram, Tamil Nadu, India.

#### V. Results

##### Study Participants

The demographics, histological cell type, and stage of lung cancer of the 34 patients including 6,16,2,3 and 7 of cancer patients were Stage 0, stage I, Stage II, stage III and stage IV type of lung cancer respectively. The percentage of lung cancer stage-0, stage-I, Stage-II, Stage-III and Stage -IV levels in the groups are 18%, 47%, 5.9%, 8.8% and 20.5% respectively.

Particulars	Control	Stage-0 Lung cancer	Stage-I Lung cancer	Stage-II Lung cancer	Stage-III Lung cancer	Stage-IV Lung cancer	P value
Number of participants	34	6	16	2	3	7	
Percentage of participants	50%	8.8%	23.5%	2.9%	4.4%	10.29%	
25(OH)D	37.02±4.40	30.75±3.10	25.21±2.83	19.82±1.92	11.64±1.50	08.06±0.90	0.000* <sup>a,b</sup>

- A-Comparison between control subjects and Stages of lung cancer
- B-Comparison between stage 0 lung cancer and other stage lung cancer groups
- P < 0.001 is considered significant

The observed results in Table 1 clearly reveals that 8.8% (n=6) of the participants were found to have Vitamin D level between 28-32ng/ml (Stage 0) and 23.5% (n=26) of the participants were found to have Vitamin D level <26 ng/ml (Stage-I) and 2.9% (n=2) of the participants have Vitamin D level <20ng/ml (Stage-II) and 4.4% (n=3) of the study participants have Vitamin D levels between 10-12ng/ml and 10.29% (n=7) of the study participants have Vitamin D levels below 9.0ng/ml and also 50% (n=34) of the study participants have Vitamin D levels between 30-40ng/ml. The observed mean Vitamin D status of Normal subject, Stage-0, Stage -I, Stage-II, Stage-III and Stage-IV students were 37.02±4.40, 30.75±3.10, 25.21±2.83, 19.82±1.92, 11.64±1.50 and 08.06±0.90 respectively.

In this present study shows that concentration of vitamin D levels were significantly (p<0.001) increased in Normal subjects when compared with different stages of lung cancer. Vitamin D levels in Stage-0 group-II lung cancer patients were compared with Stage-I, Stage-II, Stage-III and Stage -IV groups were significantly (p<0.001) increased. The concentration of Vitamin D levels in Stage -IV (Group-VI) lung cancer patients have highly significantly decreased when compared with group-I control normal subjects.

#### Discussion:

A number of factors, including regional UV-B levels, vitamin D intake, skin pigmentation, sunlight exposure behaviors, and adiposity may influence *in vivo* vitamin D levels<sup>7</sup>. Seasonal variation in 25(OH)D concentrations have been observed for residents in Boston, with inadequate vitamin D intake and winter season being independent predictors of hypovitaminosis D<sup>8</sup>. We investigated the effects of season and vitamin D intake on lung cancer survival, and found that both higher UV-B exposure (patients who had surgery in summer) and higher vitamin D intake (diet and supplement) improved lung cancer survival.

The suggestion by our data that vitamin D may protect against lung cancer progression is supported by *in vitro* and animal studies. 1,25(OH)2D inhibits metastatic growth of lung cancer cells, and mice fed manipulated diets display an apparent inverse relationship between the physiological levels of serum 1,25(OH)2D and tumorigenesis<sup>9</sup>. In a metastatic Lewis lung carcinoma tumor model, vitamin D3 treatment increases intratumoral T-cell immune reactivity and limits metastasis and loco regional tumor recurrence. 1,25(OH)2D also inhibits proliferation and induces differentiation of lung cancer cell lines<sup>10</sup>, and increased expression of the 1-alpha-hydroxylase gene has been found in alveolar macrophages of patients with lung cancer.

In humans, 1,25(OH)2D may exert its anticarcinogenic effects through stimulating the secretion of protein glues such as E-cadherin and catenin that make cells more adherent to each other, making cells in the tumor mass more adherent to each other, reducing the likelihood of mobilization of large numbers of malignant cells into the lymphatic or blood circulation. Higher 1,25(OH)2D levels may up regulate the secretion of protein glues, make cancer cells adherent more tightly and the tumor less friable, and decrease the probability of cancer cells dislodge from the tumor tissue during surgery, which may be the reason that higher vitamin D levels at the time of surgery are associated with improved lung cancer survival. Therefore, although 1,25(OH)2D may have anti- invasion and anti- metastasis effects at various stages before and during carcinogenesis, the 1,25(OH)2D levels at the time of surgery may be particularly important. Reduced expression of E-cadherin and catenins has been associated with tumor cell dedifferentiation, local invasion, regional metastasis, and reduced survival in lung cancer<sup>11</sup>.

#### Conclusion:

In the present study results should be confirmed in a prospective study to assess the serum vitamin D levels at time of surgery. If the results are confirmed, our results, combined with findings in other studies, suggest that dietary vitamin D supplementation may be advisable for early stages of lung cancer patients, particularly during the winter season and in groups that tend to be deficient in vitamin D.

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