# Study of Correlation between Diabetic Pulmonopathy with Serum Adiponectin Levels in Patients of Type 2 Diabetes Mellitus

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## Abstract

Diabetes mellitus a disease with various macro and micro vascular complications due to its various metabolic dysregulations, is well known to involve lungs in long run in both type 1 and 2 diabetes mellitus, causing tremendous burden on health care system. Common simple lung function tests alone are likely to underestimate the prevalence and degree of lung dysfunction in diabetes, but newer noninvasive tests of lung mechanical function provide a more sensitive assessment of peripheral airway function, hence by establishing a marker and risk factors for pulmonary involvement in diabetic individuals, cases with high risk for pulmonary involvement can be found before hand and proper medical therapy can be started for primary prophylaxis of same, Hence in this study we tried to find out any correlation between serum adiponectin levels and pulmonary dysfunction in patients of type 2 diabetes mellitus, which shows a significant role of adiponectin as early marker of the disease with p value of 0.04, the decrease in serum adiponectin level is also associated with more severe disease, hence adiponectin levels can be used as early markers of pulmonary dysfunction in diabetic patients


**Table 1: Severity of lung function impairment**

| Pulmonary dysfunction | Severity of any spirometric abnormality based on FVC |
|---|---|
| Degree of severity | FVC % predicted |
| Mild | 60-80 |
| Moderate | 40-59 |
| Severe | <40 |

## Introduction

Diabetes mellitus is associated with the ongoing malfunction of various organs and its complications are mainly a consequence of macro-vascular and micro-vascular damage. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system. Diabetes mellitus involves the lungs in the course of the complex phenomena it generates. Pulmonary complications of Diabetes Mellitus have been poorly characterized, although some authors had reported normal pulmonary function, others found abnormalities in lung volumes, pulmonary mechanics, and diffusing capacity. Early investigations of lung function in type 1 diabetes suggested that the lung is a target organ for diabetes, subsequent reports of lung transfer capacity for CO and postmortem histopathology studies support the notion that the lung is indeed a target organ for diabetic microangiopathy, in both type 1 and type 2 Diabetes Mellitus., additional evidence documented peripheral airway dysfunction in type 1 diabetes in the absence of cigarette consumption, allergies, or other common causes of airflow obstruction. Common simple lung function tests alone are likely to underestimate the prevalence and degree of lung dysfunction in diabetes, but newer noninvasive tests of lung mechanical function provide a more sensitive assessment of peripheral airway function. Hence in this study we tried to find out any correlation between serum adiponectin levels and pulmonary dysfunction in patients of type 2 diabetes mellitus.

## Material and Methods

Present study will be conducted from Nov. 2015 to October 2016 in S.P. Medical College and Associated Group of P.B.M. Hospitals, A total of 60 patients attending medical outdoor, Geriatric care and research center and those admitted in hospital was selected after applying the various inclusion and exclusion criteria. Healthy matched controls were selected as control after matching age and sex. They were non-smokers, diabetics, and had no history of any acute or chronic lung disease and they came for their routine checkups.

The detailed history and physical examination was carried out. All patients having any acute or chronic pulmonary disease, and smokers (defined as smoking of any number of cigarettes) were excluded. Informed consent was taken from all subjects.

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**Table 2: Distribution of cases serum adiponectin level in relation to pulmonopathy**

| Adiponectin level | Restrictive lung disease in diabetic patients | | Total |
|---|---|---|---|
| | Present | Absent | |
| | No. (%) | No. (%) | |
| Decreased | 14 (46.7) | 17 (56.7) | 31 |
| Normal | 16 (53.3) | 13 (43.3) | 29 |
| Total | 30 | 30 | 60 |

p = 0.04, chi square - 9.29

### Inclusion Criteria

All cases of Type 2 diabetes mellitus patients and non- diabetic controls aged between 30-70 years attending medical outdoor, Geriatric care and diabetes research center and those admitted in hospital.

### Exclusion Criteria

1. Patients with chronic lung disease caused due to factors other than Diabetic pulmonopathy
2. Acute myocardial infarction in last 6 months.
3. Patients on losartan therapy
4. Patients with history of alcohol abuse.
5. chronic smoker
6. Patients receiving anti-obesity drugs

7. Patients with history of bariatric surgery
8. Patient on modified diet plan for obesity
9. Malabsorption or chronic diarrhea
10. Patient not taking statin therapy
11. Hypothyroidism
12. Patients with evidence of peripheral vascular disease/arteritis
13. Collagen vascular disease

Pulmonary functions including forced vital capacity (FVC), forced expired volume in one second ($FEV_1$), $FEV_1$/FVC ratio, slow vital capacity (SVC), and peak expiratory flow rate (PEFR) were measured by spirometer according to the American Thoracic Society (ATS) criteria. Spirometry was performed before and 15 min after inhalation of 0.2 mg salbutamol inhaler at room temperature ranged from 19°C to 24°C, with a mean of 22±0.5. The subject breathed in from room air and then exhaled into the spirometer. The wedge opened as air was blown into the spirometer, and a marker moved accordingly along a sheet of paper for 6 seconds. The spirometer was computerized and printed the $FEV_1$ and FVC values after the forced expiration had been performed. There was no time lag between the onset of forced expiration and the onset of timing for $FEV_1$. No extrapolation was performed. Best of three satisfactory readings was taken for the analysis. Highest value for FVC and the highest value for $FEV_1$ were used in the ratio $FEV_1$/ FVC. The variables were reported in absolute volume as well as the percent predicted based on the regression equations. HRCT chest was done in doubtful cases or if required. Severity scores are most appropriately derived from studies that relate pulmonary function test values to independent indices of performance, such as ability to work and function in daily life, morbidity and prognosis. In general, the ability to work and function in daily life is related to pulmonary function, and pulmonary function is used to rate impairment in several published systems. Pulmonary function level is also associated with morbidity, and the patients with lower function have more respiratory complaints.

**Table 3: Distribution of cases according serum adiponectin level in relation to severity of pulmonopathy**

| Adiponectin level | Restrictive lung disease | | | Total |
|---|---|---|---|---|
| | Mild | Moderate | Severe | |
| | No (%) | No (%) | No (%) | |
| Decreased | 1 (100) | 13 (72.2) | 10 (90.9) | 24 |
| Normal | 0 | 5 (27.8) | 1 (9.1) | 6 |
| Total | 1 | 18 | 11 | 30 |

Chi Square - 9.38, p value - 0.04

A method of categorizing the severity of lung function impairment based on the FVC % predicted is given in Table 1. It is similar to several previous documents, including GOLD,[1] and the American Medical Association (AMA).[2]

## Observations

Table 2 shows Distribution of cases Serum Adiponectin level in Relation to Pulmonopathy, of the total of 60 patients 30 were cases and 30 were controls, among 30 patients with restrictive lung disease (RLD) 46.67% of patients had decreased serum adiponectin levels while among patients without lung involvement 56.67 % patients had decreased level of adiponectin and this correlation was found to be significant statistically with p value of 0.04.

Table 3 shows distribution of cases according Serum Adiponectin level in Relation to Pulmonopathy, out of total of 60 study subjects 30 were found to have pulmonopathy, on assessing the adiponectin level in patients with pulmonopathy and categorizing patients according to level of serum Adiponectin in Relation to severity of Pulmonopathy it was found that 90.91 percent of patients with severe pulmonopathy had decreased adiponectin levels while 72.22 percent of patients with moderate severity had decreased level of adiponectin, this correlation was found to be statistically significant.

## Discussion

Adiponectin is an adipocytokine that is derived from adipocytes. Adiponectin inhibits the expression of pro-inflammatory cytokines such as tumor necrosis factor (TNF)-alpha.[6] Low levels of adiponectin have been reported to be related to high levels of C-reactive protein, a biomarker of inflammation, in patients with obesity, type 2 diabetes, or coronary artery disease.[6] In addition, adiponectin alters the phenotype of macrophages from pro-inflammatory macrophages (M1) to anti-inflammatory macrophages (M2).[7] Therefore, there is accumulating evidence that suggests the role of adiponectin in anti-inflammatory, anti-atherosclerotic, and cardio-protective pathways.

To date, 3 institutes have reported on pulmonary phenotypes in adiponectin-deficient mice. Summer's and Nakanishi's groups demonstrated the development of emphysematous changes in adiponectin-deficient mice.[3,4] In null mice, alveolar macrophage activation and the secretion of matrix metalloproteinase-12, a macrophage-derived protease that promotes emphysema, were confirmed.[4] In addition, they observed emphysematous development in accordance with aging; further, the extra-pulmonary phenotypes were commonly observed in human COPD patients, such as weight loss, fat atrophy, and osteoporosis.[3] These results are in accordance with evidence that adiponectin has anti-inflammatory properties, and that the loss of adiponectin results in a reduced protective capacity against the development of emphysema. However, as many studies have shown, circulating adiponectin levels in patients with COPD were not reduced; in fact, they were increased.[8-10] Even if adiponectin is anti-inflammatory and pulmonary-protective, the elevation of adiponectin levels is not enough to suppress the impairment of pulmonary function in COPD patients. In contrast, Miller et al. demonstrated that adiponectin deficiency protected mice from tobacco-induced inflammation and increased emphysema.[5] Thus, their new evidence showing the pro-inflammatory effects of adiponectin challenges the established theory regarding the anti-inflammatory role of adiponectin. They demonstrated that adiponectin deficiency suppressed the production of pro-inflammatory cytokines such as TNF-alpha and keratinocyte-derived chemokines in the lungs, which resulted in the protection of the lungs from cigarette smoke in adiponectin-null mice. Their study on adiponectin-deficient mice agrees with clinical evidence that shows an elevation of adiponectin in COPD patients.

In the present study, we demonstrated an inverse correlation between plasma adiponectin levels and lung dysfunction in diabetic patients in a general population of North West Rajasthan. Out of total of 60 study

subjects 30 were cases of pulmonopathy, on assessing the adiponectin level in patients with pulmonopathy and categorizing patients according to level of serum Adiponectin in Relation to severity of Pulmonopathy it was found that 90.91 percent of patients with severe pulmonopathy had decreased adiponectin levels while 72.22 percent of patients with moderate severity had decreased level of adiponectin, this correlation was found to be statistically significant. Clear decrements in lung function have been reported in patients with diabetes over the past 2 decades, and many reports have suggested plausible pathophysiological mechanisms. However, at the present time, there are no reports of functional limitations of activities of daily living ascribable to pulmonary disease in patients with diabetes. Accordingly, this review is directed toward a description of the nature of reported lung dysfunction in diabetes, with an emphasis on the emerging potential clinical implications of such dysfunction.

## Conclusion

There is inverse correlation between serum adiponectin level and lung dysfunction among diabetic patients, this inverse correlation also hold true with respect to severity of diabetic pulmonopathy i.e. low level of serum adiponectin level not only predisposes patient for lung dysfunction but also associated with more severe disease. Hence Serum adiponectin level can be used as a early marker to predict the pulmonary dysfunction in diabetic patients, as it also correlates with the severity of disease, it can be used as a marker for appropriate initial therapy in diabetic patients with low serum adiponectin level so to prevent the pulmonary morbidities especially in obese individuals.

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