



Diabetes and Deteriorating Lung Function Based on Spirometry: A Narrative Review

Dona Das*, R.V. Sridhar and Midun Chandar

Department of General Medicine, Shri Sathya Sai Medical College and Research Institute,
Ammappettai, Kancheepuram, Nellikuppam, Tamil Nadu, India

*Corresponding e-mail: donaa35@gmail.com

ABSTRACT

Background: Many pulmonary dysfunctions are noted in both type 1 and 2 diabetes. This dysfunction can be mechanical in terms of muscle tone or strength, functional in terms of diffusion capacity or gaseous exchange and chemical with regards to mediators. Many hypothesis or mechanisms were proposed and changed along the course of time to support the issue. The studies have shown an increased evidence of lung dysfunction changes in diabetes, both at a time or during the course of time. So the lung complications should also be considered among micro vascular complications to actively search for a better prognosis. **Aim:** To study the association of diabetes and lung function based on spirometry. **Materials and methods:** We identified all studies in English Language that evaluated the association of diabetes mellitus and lung function using keywords like "diabetes, lung volume, lung function, diabetes micro angiopathy, spirometry" across various published research articles using Google Scholar Data Base. **Conclusion:** From our narrative review, a conclusion was made that both varieties of diabetes, type 2 and type1 have reduced lung functions as reviewed by spirometry not only due to adverse events like pneumonia but also due to the extensive period of consequence of diabetes which may be because of micro angiopathy or diminished elastic recoil capability of lungs.

Keywords: Diabetes, Lung function test, Angiopathy, Spirometry

INTRODUCTION

Diabetes is one of the most leading causes of morbidity and mortality across the world. The risk factors included can be both behavioral and metabolic. The risk factors consist of: Smoking, excessive consumption of alcohol, sedentary life style and unhealthy eating patterns. Diabetes, a disease due to deficient insulin secretion or insulin resistance leads to complications involving more than one target organ and hence named as a multi organ affecter disease. Diabetes can have both acute and chronic complication. Chronic complications are divided into micro vascular and macro vascular. Retinopathy, neuropathy, nephropathy, and cardiovascular dysfunction are frequent diabetic complications, and make way noteworthy to morbidity and death. These problems are by and large due to vascular damage, which has a fundamental responsibility in the pathophysiology of the disease [1-3].

So the symptoms or signs will appear once the subject's immune competence decreases or any other infection arises. However, failure of micro vascular reserve in the lung may become important clinically, with an augmented danger of hypoxia and lead to worsening of the existing disease or defect [4].

METHODOLOGY

The articles under taken for review were searched based on the MESH terminologies that are pulmonary function test, diabetes, angiopathy among others. The data search was largely done in pub med, Google scholar. Among the 44 studies analyzed, few were excluded from the study using exclusion criteria like patients with previous cardiovascular or respiratory diseases, and the others (eighteen) were divided and studied under pathological changes in lung tissue due to diabetes, and changes in pulmonary function tests due to diabetes.

Hypothesis Regarding Lung Damage

A theory to begin with can be the damage of lung parenchyma is due to accumulation of collagen. Gluconeogenesis of proteins along with non-enzymatic glycolysis in the lungs and chest wall makes the collagen less prone to proteolysis and directs to its upsurge in lung tissue. This process is exclusively facilitated by hyper glycemia, and therefore it is more discrete in patients with metabolic control that is poorly maintained. The dysfunction of elastic recoil capacity in the lung may be the core reason for a drastic reduction and decrease in small airways during exhalation [5,6].

The restrictive pattern of the lung can be due to the diminished muscle strength as observed in diabetes which is majorly caused by resistance to insulin [7]. Also, several other hypotheses aroused which is the susceptibility of diabetic subjects to many external factors, which mainly consist of tobacco particles, allergens, dust particles [8,9].

Leptin, a proposed mediator, plays an active role in the maturation of the lung and favours its development. Numerous studies have proved that a reduction in the leptin levels in obese individuals or in patients with insulin resistance and also can observe a significant alteration in lung diseases, thus concluding its role in diabetes and dysfunction of lungs [10-12]. Also, subjects with reduced metabolic control had amplified amount of inflammation markers (TNF-alpha, fibrinogen, and C-reactive protein), suggestive of a probable association of inflammation in damaged lung function [13-16].

Evidence from post mortem identified a significant change in lung parenchyma and its wall majorly in people with diabetes as compared to healthy controls. Also, there was suggestive data that hyper glycemia amplified the concentration of collagen and elastin in the lung. The altered properties of collagen involved in the metabolism of glucose lead to change in epithelial and alveolar capillary basal laminas [17-20].

Studies Related to Lung Dysfunction

Schuyler, et al., who carried out a study of lung function in 11 patients with type 1 diabetes and age-matched healthy subjects. The study subjects being undeviating non-smokers without any allergies or prior lung disease, their finding that decreased lung elastic recoil in these youths with diabetes was shown to replicate effect of diabetes on elastic proteins found in lung. This was the first study to spread information that lung can be an affected organ in diabetes. Loss of the elastic properties of lung parenchyma can make the person susceptible and prone to chronic and inflammatory diseases [21]. This reduction and consequence of this decreased elasticity was further affirmed by another study [22]. This study also confirmed decreased CO transport capability with reduced pulmonary capillary blood volume in 40 patients with insulin dependent diabetes in contrast to with healthy control subjects.

The result obtained from the studies directed researchers to concentrate more towards the field of pulmonary micro vasculature rather than the lung tissue as such. The histopathological evidence of thickening alveolar membrane also added with the damage in the alveolar membrane. So, thereafter studies started to concentrate in these two aspects of diffusion capacity; alveolar capillary thickness and pulmonary blood flow. Another study showed a reduction in the permeable property of the alveolar-capillary basement membrane in patients with diabetes [23]. Ljubic, et al., demonstrated that the reduced alveolar-capillary permeable property could be largely due to changes in collagen and elastin [24].

Pulmonary capillary blood quantity shows the quantity of blood in touch with the ventilated alveoli. It was established in a study that in diabetics, the lung is unsuccessful to receive on pulmonary capillaries which is in response to advanced load, as like in exercise or a postural change [25]. The study showed a decreased pulmonary blood flow and increased thickness in alveolar membrane which reduces conductance is a foretelling sign of reduction in diffusion capacity. The reduced diffusion capacity is a pointer towards micro vascular complication of lung.

There is a study which affirmed the decreased diffusion capacity, where different postural changes studied among diabetic patients. DLCO did not augment with modify from, in contrast to healthy subject. This showed the reduced capacity of lung to regenerate or extensive damage of pulmonary vasculature [26]. Studies done in 1980s led to conclusion that diabetes reduce spirometric measures. Later this got disregarded resulting from studies that came up with an evidence of nil significant difference in spirometric measures in diabetic patients and healthy subjects [27-29].

Niranjan, et al. showed that there is a significant decrease in total lung capacity (TLC) in type 1 diabetic patients when compared to healthy people. The decrease was markedly significant in the group of patients who showed a reduced

glycemic control [30]. Study has accounted a mild decrease in lung volumes of type 2 diabetic patients, and about 10% lesser than the predicted values resultant from a usual population [31]. Lung function was also calculated in a group of 495 patients with type 2 diabetes, who were devoid of any prior history of pulmonary disease, where 125 of the patients frequent these dimensions after a report on of approximately 7 years. FVC, FEV1, and vital capacity (VC) standards calculated at baseline were at the lesser confines of the usual expected values, but 29 of the 125 patients (23% of the patients who received part in the follow-up) had baseline FEV1 <70% of the expected rate and/or a VC <80% of the expected rate, with no proof of related lung disease [32].

Also, some studies have shown that the tone of bronchial muscles got damaged largely due to autonomic neuropathy which results in damage of the respiratory system mainly through injury of the bronchial neuro adrenergic nerves, thus altering the ventilatory reaction to central and peripheral stimulus [33-35].

It has been revealed that diabetes is related with episodic breathing, respiratory disorder on the basis of irregular central respiratory control. Another study established that the reaction to hyper capnia is reduced in diabetic patients with para sympathetic dys autonomia, while hyper capnic drive was faintly amplified in patients with sympathetic and parasympathetic injury [36,37].

There are studies that have demonstrated that micro vascular complications lead to a decreased respiratory muscle strength which in turn reduces the lung volumes. Also, a direct co-relation between muscle strength and glycemic control was shown using HbA1C in the study [38-40].

The time related studies have highlighted a significant decrease of pulmonary function test and diffusion capacity of lungs among the diabetic population. Majority of the studies have also shown an association of poor lung function with reduced glycemic control. The mechanism that was proposed is that hyperglycemia leads to insulin resistance, which mediates the damaged receptor uptake muscles and channels, where this alteration leads to thickness in alveolar membrane and pulmonary flow (Table 1) [41-44].

Table 1 Showing the lung function and its probable causes related to diabetes

Lung Function	Probable Causes
Lung volume	Thickening of alveolar capillary membrane
Diffusion capacity	Decreased pulmonary vasculature
Exchange of gases	Decreased pulmonary vasculature and thickening of alveolar capillary membrane
Ventilatory response to reduced oxygen and carbon-di-oxide	Autonomic neuropathy
Respiratory muscle strength	Decreased receptor sensitivity

CONCLUSION

Diabetes mellitus is now a preferred topic of the current decade. The current strategy in the management of the disease is preventing the occurrence, early diagnosis and preventing the complications if the disease appeared. The prevention and diagnosis can be seen as a fight in the outside of the pathophysiology, but protecting a person from going into complications needs much relevant evidence and research. Since the affection of diabetes towards lung didn't produce many external and investigative features, active search should be enhanced in such cases. As the patient undergoes extensive micro vascular complication diagnosis, lung should be involved majorly.

DECLARATIONS

Conflicts of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

- [1] Murea, Mariana, Lijun Ma, and Barry I. Freedman. "Genetic and environmental factors associated with type 2 diabetes and diabetic vascular complications." *The Review of Diabetic Studies: RDS*, Vol. 9, No. 1, 2012, pp. 6-22.
- [2] Bowden, Donald W., et al. "Review of the Diabetes Heart Study (DHS) family of studies: A comprehensively examined sample for genetic and epidemiological studies of type 2 diabetes and its complications." *The Review of Diabetic Studies: RDS*, Vol. 7, No. 3, 2010, p. 188.
- [3] International Diabetes Federation. <https://www.idf.org/>
- [4] Goldman, Michael David. "Lung dysfunction in diabetes." *Diabetes Care*, Vol. 26, No. 6, 2003, pp. 1915-18.
- [5] Ofulue, A. Felix, and William M. Thurlbeck. "Experimental diabetes and the lung: II. *In vivo* connective tissue metabolism." *American Review of Respiratory Disease*, Vol. 138, No. 2, 1988, pp. 284-89.
- [6] Cavan D. A., et al. "Lung function and diabetes." *Respiratory Medicine*, Vol. 85, No. 3, 1991, pp. 257-58.
- [7] Lazarus, Ross, David Sparrow, and Scott T. Weiss. "Handgrip strength and insulin levels: Cross-sectional and prospective associations in the normative aging study." *Metabolism*, Vol. 46, No. 11, 1997, pp. 1266-69.
- [8] Zanobetti, Antonella, and Joel Schwartz. "Are diabetics more susceptible to the health effects of airborne particles?" *American Journal of Respiratory and Critical Care Medicine*, Vol. 164, No. 5, 2001, pp. 831-33.
- [9] Walter, Robert E., et al. "Association between glycemic state and lung function: the Framingham Heart Study." *American Journal of Respiratory and Critical Care Medicine*, Vol. 167, No. 6, 2003, pp. 911-16.
- [10] O'Donnell, C. P., et al. "Leptin, obesity, and respiratory function." *Respiration Physiology*, Vol. 119, No. 2, 2000, pp. 163-70.
- [11] Hsia, Connie CW, and Philip Raskin. "Lung function changes related to diabetes mellitus." *Diabetes Technology and Therapeutics*, Vol. 9, No. 1, 2007, p. 73.
- [12] Sin, D. D., and S. F. P. Man. "Impaired lung function and serum leptin in men and women with normal body weight: A population based study." *Thorax*, Vol. 58, No. 8, 2003, pp. 695-98.
- [13] Litonjua, Augusto A., et al. "Lung function in type 2 diabetes: The normative aging study." *Respiratory Medicine*, Vol. 99, No. 12, 2005, pp. 1583-90.
- [14] Engström, Gunnar, and Lars Janzon. "Risk of developing diabetes is inversely related to lung function: A population-based cohort study." *Diabetic Medicine*, Vol. 19, No. 2, 2002, pp. 167-70.
- [15] Dennis, Rodolfo J., et al. "Inadequate glucose control in type 2 diabetes is associated with impaired lung function and systemic inflammation: A cross-sectional study." *BMC Pulmonary Medicine*, Vol. 10, No. 1, 2010, p. 38.
- [16] Ford, Earl S., and David M. Mannino. "Prospective association between lung function and the incidence of diabetes: Findings from the National Health and Nutrition Examination Survey Epidemiologic follow-up study." *Diabetes Care*, Vol. 27, No. 12, 2004, pp. 2966-70.
- [17] Ofuwe, A. Felix, Kozui Kida, and William M. Thurlbeck. "Experimental diabetes and the lung." *American Review of Respiratory Disease*, Vol. 137, No. 1, 1988, pp. 162-66.
- [18] Kida, Kozui, et al. "Changes in lung morphologic features and elasticity caused by streptozotocin-induced diabetes mellitus in growing rats." *American Review of Respiratory Disease*, Vol. 128, No. 1, 1983, pp. 125-31.
- [19] Farina, J., et al. "Nodular fibrosis of the lung in diabetes mellitus." *Virchows Archive*, Vol. 427, No. 1, 1995, pp. 61-63.
- [20] Vracko, Rudolf, David Thorning, and Thomas W. Huang. "Basal lamina of alveolar epithelium and capillaries: Quantitative changes with aging and in diabetes mellitus." *American Review of Respiratory Disease*, Vol. 120, No. 5, 1979, pp. 973-83.

- [21] Schuyler, Mark R., et al. "Abnormal lung elasticity in juvenile diabetes mellitus." *American Review of Respiratory Disease*, Vol. 113, No. 1, 1976, pp. 37-41.
- [22] Sandler, Malcolm, Anthony E. Bunn, and Roger I. Stewart. "Cross-section study of pulmonary function in patients with insulin-dependent diabetes mellitus." *American Review of Respiratory Disease*, Vol. 135, No. 1, 1987, pp. 223-29.
- [23] Ozsahin, Kemal, et al. "Evaluation of pulmonary alveolo-capillary permeability in Type 2 diabetes mellitus." *Journal of Diabetes and its Complications*, Vol. 20, No. 4, 2006, pp. 205-09.
- [24] Ljubic, Spomenka, et al. "Reduction of diffusion capacity for carbon monoxide in diabetic patients." *Chest*, Vol. 114, No. 4, 1998, pp. 1033-35.
- [25] Wheatley, Courtney M., et al. "Glycemic control influences lung membrane diffusion and oxygen saturation in exercise-trained subjects with type 1 diabetes." *European Journal of Applied Physiology*, Vol. 111, No. 3, 2011, pp. 567-78.
- [26] Fuso, Leonello, et al. "Postural variations of pulmonary diffusing capacity in insulin-dependent diabetes mellitus." *Chest*, Vol. 110, No. 4, 1996, pp. 1009-13.
- [27] Mori, Hiroshi, et al. "Abnormalities of pulmonary function in patients with non-insulin-dependent diabetes mellitus." *Internal Medicine*, Vol. 31, No. 2, 1992, pp. 189-93.
- [28] Asanuma, Yoshihide, et al. "Characteristics of pulmonary function in patients with diabetes mellitus." *Diabetes Research and Clinical Practice*, Vol. 1, No. 2, 1985, pp. 95-101.
- [29] Benbassat, Carlos A., et al. "Pulmonary function in patients with diabetes mellitus." *The American Journal of the Medical Sciences*, Vol. 322, No. 3, 2001, pp. 127-32.
- [30] Niranjana, Vis, et al. "Glycemic control and cardiopulmonary function in patients with insulin-dependent diabetes mellitus." *The American Journal of Medicine*, Vol. 103, No. 6, 1997, pp. 504-13.
- [31] Davis, Timothy ME, et al. "Reduced pulmonary function and its associations in type 2 diabetes: The Fremantle Diabetes Study." *Diabetes Research and Clinical Practice*, Vol. 50, No. 2, 2000, pp. 153-59.
- [32] Davis, Wendy A., et al. "Glycemic exposure is associated with reduced pulmonary function in type 2 diabetes: The Fremantle Diabetes Study." *Diabetes Care*, Vol. 27, No. 3, 2004, pp. 752-57.
- [33] Bottini, P., et al. "Impairment of the respiratory system in diabetic autonomic neuropathy." *Diabetes, Nutrition and Metabolism*, Vol. 13, No. 3, 2000, pp. 165-72.
- [34] Giordano, Alessandro, et al. "Potential use of iodine-123 metaiodobenzylguanidine radioaerosol as a marker of pulmonary neuroadrenergic function." *European Journal of Nuclear Medicine*, Vol. 24, No. 1, 1997, pp. 52-58.
- [35] Incalzi, Raffaele Antonelli, et al. "Neuroadrenergic denervation of the lung in type I diabetes mellitus complicated by autonomic neuropathy." *Chest*, Vol. 121, No. 2, 2002, pp. 443-51.
- [36] Tantucci, Claudio, et al. "Influence of autonomic neuropathy of different severities on the hypercapnic drive to breathing in diabetic patients." *Chest*, Vol. 112, No. 1, 1997, pp. 145-53.
- [37] Montserrat, J. M., et al. "Ventilatory control in diabetes mellitus." *European Journal of Respiratory Diseases*, Vol. 67, No. 2, 1985, pp. 112-17.
- [38] Fuso, Leonello, et al. "Reduced respiratory muscle strength and endurance in type 2 diabetes mellitus." *Diabetes/ Metabolism Research and Reviews*, Vol. 28, No. 4, 2012, pp. 370-75.
- [39] Heimer, D., et al. "Respiratory muscle performance in patients with type 1 diabetes." *Diabetic Medicine*, Vol. 7, No. 5, 1990, pp. 434-37.
- [40] Wanke, Theodor, et al. "Inspiratory muscle performance and pulmonary function changes in insulin-dependent diabetes mellitus." *The American Review of Respiratory Disease*, Vol. 143, No. 1, 1991, pp. 97-100.

- [41] Kaminsky, David A. "Spirometry and diabetes: Implications of reduced lung function." *Diabetes Care*, Vol. 27, No. 3, 2004, pp. 837-38.
- [42] Antonelli Incalzi, Raffaele, et al. "Decline of neuroadrenergic bronchial innervation and respiratory function in type 1 diabetes mellitus: A longitudinal study." *Diabetes/Metabolism Research and Reviews*, Vol. 23, No. 4, 2007, pp. 311-16.
- [43] Lange, Peter, et al. "Copenhagen City Heart Study: Longitudinal analysis of ventilatory capacity in diabetic and nondiabetic adults." *European Respiratory Journal*, Vol. 20, No. 6, 2002, pp. 1406-12.
- [44] Lange, P., et al. "Diabetes mellitus and ventilatory capacity: A five year follow-up study." *European Respiratory Journal*, Vol. 3, No. 3, 1990, pp. 288-92.