ISSN: 2754-4761

Journal of Pulmonology Research & Reports

SCIENTIFIC Research and Community

Mini Review

Open Access

Is it Already Time to Recognize Diabetes as an Etiology of Interstitial Lung Disease? A Short Review of the Evidence

Upasna Agarwal[1], Amit Sharma[2]* and Poulomi Chatterjee[2]

[1]Senior Medical Specialist and Director, National Institute of Tuberculosis and Respiratory Diseases (NITRD), India

[2]Specialist, Department of Respiratory Medicine, National Institute of Tuberculosis and Respiratory Diseases (NITRD), Autonomous Institute under Ministry of Health and Family Welfare (MOHFW), Government of India

***Corresponding author**

Amit Sharma, Specialist, Department of Respiratory Medicine, National Institute of Tuberculosis and Respiratory Diseases (NITRD), Autonomous Institute under Ministry of Health and Family Welfare (MOHFW), Government of India.

Received: September 08, 2025; **Accepted:** September 12, 2025; **Published:** September 23, 2025

By now it is well known amongst the Medical Fraternity that Diabetes Mellitus (DM) is not a single disease but rather a heterogenous metabolic dysfunction demonstrating increased blood glucose levels (hyperglycemia) as its major manifestation. However, Diabetes is far more complex and insidious to be labelled as a mere increase in the blood glucose levels. The dysfunction of glucose control transcends the boundaries of blood vessels, neuro-muscular and various other organ systems, ultimately leading to any combination of renal, ocular, cardiac, skin, neurological and other organ damage, which makes it is a Legion of diseases, rather than a single pathology.

Diabetes has many etiologies and Insulin Dependent Diabetes Mellitus (IDDM) is seen in a much younger population and has a unique pathophysiology of its own. However, clinicians are now seeing a barrage of patients in their early middle age with Diabetes, what is commonly known as Diabetes Mellitus Type 2, mainly the result of sedentary lifestyle and poor dietary habits with Insulin Resistance as the basic pathophysiology. In fact, Delhi, the capital of India has been declared a hotspot for Diabetes prevalence [1]. For the purpose of this review, we will be talking about this group of Diabetic patients (Type 2) which also far more common.

The hyperglycemia caused by Diabetes targets the vascular system mainly, both at the macro and micro levels leading to a plethora of dysfunctions in the form of neuropathy (both autonomic and peripheral), myopathy, osteoporosis, cognitive impairment, vestibular disturbances and visual problems. Cardiovascular Disease (CVD), Infections especially of the Respiratory system and End stage renal disease (ESRD) are the major causes of mortality in Diabetes patients [2].

Even though much is known about involvement of major organ systems in DM, knowledge about involvement of the lungs is limited. This does not include the infections which are one of the major causes of mortality in these patients such as Tuberculosis, such as Tuberculosis, Pneumonia due to Klebsiella and other gram serious Gram-negative bacteria and invasive fungal infections. The aim of this short review is to focus on the non-infectious effects of Diabetes on the Lung parenchyma and Pulmonary Vasculature.

The lungs have an extensive Vascular system. The Pulmonary Circulation has very high capacity and can dilate up to 6 times its resting volume to accommodate blood volume changes. The mean Pulmonary artery pressure is only around 12-16 mm of Hg compared to mean systemic blood pressure which is around 70-120 mm of Hg. This reflects the enormous potential of the pulmonary vascular network to accommodate very high blood volumes. However, an increasing body of evidence is now emerging to shed light on the association of Diabetes with Pulmonary Hypertension (PH) and well as pulmonary microangiopathy leading to endothelial damage. Both DM and PH follow the common pathways of chronic inflammation involving mediators such as Tumor Necrosis factor (TNF) – α and certain cytokines particularly IL-8. The inflammatory pathways thus converge and lead to enhancement of the Pulmonary Vascular Resistance (PVR) and also exert a remodelling effect on the pulmonary vessels which may escalate to damage to the vascular endothelium, ultimately leading to PH [3]. Due to decreased oxygen transport across the pulmonary alveolo-capillary membrane, the resulting hypoxia further exacerbates PH due to vasoconstriction [4].

The alveolo-capillary network in the lung which is chiefly responsible for Gaseous exchange in the lungs, is a large micro-vascular unit and may be affected by microangiopathy [5]. The collagen in the interstitial lining of the alveoli also gets thickened due to non-enzymatic glycosylation. As oxygen is poorly soluble in the blood, oxygen absorption is adversely affected leading to hypoxia and the elastic recoil is also reduced, effectively decreasing Lung Volumes, both of which are hallmarks of ILD.

The large pulmonary vascular reserve however may preclude earlier manifestation of microvascular damage delaying symptoms such as dyspnea thus leading to clinical under-recognition of the condition. Studies have shown reduction in Lung Volumes, both forced expiratory volume in first second (FEV1) and forced vital

capacity (FVC) as well as diffusion capacity (DLCO) in patients with Diabetes. As we know in many Interstitial Lung Diseases such as sarcoidosis, the first change observed may be the reduced DLCO due to the thickening of the Interstitium either on rest or only on exercise Phrenic nerve dysfunction due to diabetic autonomic neuropathy may compromise diaphragm contractility further contributing to the lowered lung volumes [6-9]. Studies have shown features of ILD in patients of with long-standing Diabetes and poor glycemic control. However, the importance which this pathology deserves is yet to be fully explored and established [10].

Due to sharing of common structures of collagen and exchange of salts and fluids across tubular-endothelial membrane in a similar manner as the lungs, there is a great analogy of the Kidneys and the lungs and the adverse effects on both by diabetes. Indeed, studies have demonstrated reduced lung function parameters in diabetic in comparison to non-diabetic people. There is no reason to believe that Diabetic micro vascular complications will spare the lungs in preference to the Kidneys. A robust study on patients with type 2 Diabetes has shown diabetic nephropathy to be associated with poorer lung function even after excluding other risk factors. In fact, renal involvement in Diabetics should prompt the clinicians to look for Pulmonary Dysfunction in the form of compromised Lung Volumes and DLCO [11,12].

To conclude, the mounting body of evidence suggests a strong association between DM and ILD and Diabetes should now be considered one of the etiologies of ILD. By the means of this short article, it is our endeavor to stress that all patients of Diabetes should be actively screened for signs and symptoms of possible ILD such as dyspnea especially on exertion and cough, mostly dry. Non-invasive screening by pulse oximetry at rest and in cases of breathlessness on exertion (after a walk test or climbing stairs) can be conveniently used as an objective tool to diagnose hypoxia. If Clinical Screening is suggestive, a spirometry may be performed along with a Chest Radiograph. As non-enzymatic glycosylation and vasculopathy depend on poor glycemic control, such patients need to have rigorous glycemic control.

References

1. Madhu SV, Sandeep G, Mishra BK, Aslam M (2018) High prevalence of diabetes, prediabetes and obesity among residents of East Delhi - The Delhi urban diabetes survey. Diabetes MetabSyndr 12: 923-927.
2. Li S, Wang J, Zhang B, Li X, Liu Y (2019) Diabetes Mellitus and Cause-Specific Mortality: A Population-Based Study. Diabetes Metab J 43: 319-341.
3. Takahashi T, Yoshihisa A, Sugimoto K, Yokokawa T, Misaka T, et al (2018) Associations between diabetes mellitus and pulmonary hypertension in chronic respiratory disease patients. PLoS One 13: 0205008.
4. Shi H, Zhao Y, Li S, Wu H, Ma D, et al. (2023) TNF-α and IL-8 levels are positively correlated with hypobaric hypoxic pulmonary hypertension and pulmonary vascular remodeling in rats. Open Life Sci 18: 20220650.
5. Sandler M (1990) Is the lung a target organ in diabetes mellitus? Arch Intern Med 150: 1385-1388.
6. Klein OL, Meltzer D, Carnethon M, Krishnan JA (2011) Type II diabetes mellitus is associated with decreased measures of lung function in a clinical setting. Respir Med 105: 1095-1098.
7. Davis TME, Knuiman M, Kendall P, Vu H, Davis WA (2000) Reduced pulmonary function and its associations in type 2 diabetes, the Fremantle Diabetes Study. Diabetes Res Clin Pract 50: 153-159.
8. Klein OL, Kalhan R, Williams MV, Tipping M, Lee J, et al. (2012) Lung spirometry parameters and diffusion capacity are decreased in patients with Type 2 diabetes. Diabet Med 29: 212-219.
9. Pawar SG, Arun K, Santhanam J, Ganesanet SKN, Vidya TA, et al. (2022) Dynamic diffusion lung capacity of carbon monoxide (DLCO) as a predictor of pulmonary microangiopathy and its association with extra pulmonary microangiopathy in patients with type II diabetes mellitus. Diabetes & Metabolic Syndrome 16: 102360.
10. Klein OL, Krishnan JA, Jlick S, Smith LJ (2010) Systematic review of association between lung function and type 2 diabetes mellitus. Diabet Med 27: 977-987.
11. Shafiee G, Khamseh ME, Rezaei N, Aghili R, Malek M (2013) Alteration of pulmonary function in diabetic nephropathy. J Diabetes MetabDisord 12: 15.
12. Hamlin CR, Kohn RR, Luschin JH (1975) Apparent accelerated aging of human collagen in diabetes mellitus. Diabetes 24: 902-904.