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RESEARCH ARTICLE

AN INSIGHT ON DIABETES AND DETERIORATING LUNG FUNCTION BASED ON PULMONARY FUNCTION TEST- A NARRATIVE REVIEW

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ABSTRACT

Introduction: The World Health Organization estimates that more than 180 million people worldwide have diabetes, and by 2030 it is expected that this number will have doubled.[1] There is an alarming increase in the incidence and prevalence of diabetes mellitus (DM) in Asian Indians. **Epidemiology of Diabetes in India:** The prevalence of diabetes is rapidly rising all over the globe at an alarming rate[13]. Over the past 30 years, the status of diabetes has changed from being considered as a mild disorder of the elderly to one of the major causes of morbidity and mortality affecting the youth and middle aged people. **Pulmonary function test** (**PFT**) is a complete evaluation of the respiratory system including patient history, physical examinations, and tests of pulmonary function. with insulin-dependent diabetes compared with age-matched control subjects, all lifelong nonsmokers. Lung CO transfer capacity is significantly affected by the integrity of lung capillary endothelium and, therefore, the findings of Sandler *et al.* focused attention on pulmonary vascular changes. The concept of the lung as a target organ for diabetic microangiopathy received continuing attention. Reports of lung function tests in patients with diabetes over the next 15 years have focused largely on pulmonary microangiopathy with relatively few studies of pulmonary mechanical function **Diabetes and Lung Function Test :** Some studies showed that all the pulmonary parameters, that is, FVC, FEV_1, FEF_{25}, FEF_{50}, FEF_{75}, $FEF_{25–75}$, $FEF_{0.2–1.2}$, and PEFR were significantly reduced except FEV_1/FVC in patients of type 2 DM as compared with the healthy controls. **Conclusion :** It can be concluded from our narrative review that the Type II or Type I diabetes is definitely having decreased lung functions assessed by spirometry not only because of diabetic complications like pneumonia or other but also due to long term effect of diabetes may be because of micro-angiopathy or decreased elastic recoil capacity of lungs.

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INTRODUCTION

The World Health Organization estimates that more than 180 million people worldwide have diabetes, and by 2030 it is expected that this number will have doubled. [1] There is an alarming increase in the incidence and prevalence of diabetes mellitus (DM) in Asian Indians. [2] Diabetes is a micro-macrovascular disorder with debilitating effects on many organs. Pulmonary complications of DM have been poorly characterized with conflicting results. The alveolar capillary network in the lung is a large micro-vascular unit and may be affected by microangiopathy [3]. However, because of its large reserve, substantial loss of the microvascular bed can be tolerated without developing dyspnoea. As a result, pulmonary diabetic micro-angiopathy may be under-recognized clinically. In DM pulmonary functions have been studied frequently in countries other than India, [4] while in our country there are few studies concerning these abnormalities and their relationship with glycosylated hemoglobin (HbA1c) and duration of the disease. Reduced elastic recoil, reduced lung volume, diminished respiratory muscle performance, chronic low grade inflammation, [5,6] decrease in pulmonary diffusion capacity for carbon monoxide, [7] autonomic neuropathy involving respiratory muscles [8] are some of the important changes occurring in DM. Type 2 Diabetes mellitus is characterised by persistent hyperglycaemia and abnormal metabolisms of carbohydrates, proteins and lipids. These metabolic disorders result from impaired insulin secretion, an altered tissue sensitivity to insulin or coexistence of both these mechanisms. Type 2 Diabetes mellitus is associated with long term damage, dysfunction and failure of various organs and its complications are mostly caused by macro vascular and micro vascular damages [9,10,11]. Though great attention was centred on the diabetic complications which had a cardiovascular nature, nephropathy, diabetic retinopathy, and neuropathy, the pulmonary complications of type 2 diabetes mellitus have been poorly characterised. Of late, the concept of the lung as a target organ for diabetic microangiopathy is receiving continuing attention. The aim of the present study was to assess the effects of chronic hyperglycaemia on lung functions, which focused on mechanical aspects of lung dysfunction maximal forced

spirometric Pulmonary Function Tests like FVC, FEV1, PEFR, FEV1/FVC%, to be specific. Spirometry (which means 'measuring the breath') is the most common of the pulmonary function tests (PFTs) which measures mechanical lung function, specifically the amount (volume) and/or speed (flow) of air that can be inhaled and exhaled.[12] So we have reviewed the various literature to study correlation of diabetes and lung function based on Pulmonary Function Test across various published research articles.

Epidemiology of Diabetes in India: The prevalence of diabetes is rapidly rising all over the globe at an alarming rate[13]. Over the past 30 years, the status of diabetes has changed from being considered as a mild disorder of the elderly to one of the major causes of morbidity and mortality affecting the youth and middle aged people. It is important to note that the rise in prevalence is seen in all six inhabited continents of the globe [14]. Although there is an increase in the prevalence of type 1 diabetes also, the major driver of the epidemic is the more common form of diabetes, namely type 2 diabetes, which accounts for more than 90 per cent of all diabetes cases. Nowhere is the diabetes epidemic more pronounced than in India as the World Health Organization (WHO) reports show that 32 million people had diabetes in the year 2002. The International Diabetes Federation (IDF) estimates the total number of diabetic subjects to be around 40.9 million in India and this is further set to rise to 69.9 million by the year 2025[15] The first national study on the prevalence of type 2 diabetes in India was done between 1972 and 1975 by the Indian Council Medical Research (ICMR, New Delhi) [16]. Screening was done in about 35,000 individuals above 14 years of age, using 50 g glucose load. Capillary blood glucose level >170 mg/dl was used to diagnose diabetes. The prevalence was 2.1 per cent in urban population and 1.5 per cent in the rural population while in those above 40 yr of age, the prevalence was 5 per cent in urban and 2.8 per cent in rural areas. Subsequent studies showed a rising trend in the prevalence of diabetes across different parts of India. In 1988, a study done in a small township in south India reported a prevalence of 5 per cent [17] . The prevalence of impaired glucose tolerance in the same study was 2 per cent. A national rural diabetes survey was done between 1989 and 1991 in different parts of the country in selected rural populations [6]. This study which used the 1985 WHO criteria to diagnose diabetes, reported a crude prevalence of 2.8 per cent [18].

Pulmonary function test (PFT) is a complete evaluation of the respiratory system including patient history, physical examinations, and tests of pulmonary function. The primary purpose of pulmonary function testing is to identify the severity of pulmonary impairment.[19,20] Pulmonary function testing has diagnostic and therapeutic roles and helps clinicians answer some general questions about patients with lung disease.[3]

Diabetes and Lung Dysfunction: More than a quarter-century ago, Schuyler *et al.* ([21]) investigated lung function in 11 young (21–28 years old) patients with type 1 diabetes and age matched normal control subjects. This classic study was the first to report measurements of nearly all the available tests of lung function, including lung elasticity, capacity to transfer carbon monoxide (CO, a surrogate for oxygen transfer capacity), absolute thoracic gas volumes, airflow resistance, and maximal forced spirometric pulmonary function tests (PFTs). As their subjects were lifelong nonsmokers without allergies or lung disease, their finding that lung elastic recoil was decreased in these young patients with diabetes was interpreted to reflect effects of diabetes on lung elastic proteins. This was the first suggestion in the literature that the lung may be a target organ of diabetes. Because the elastic structure of the lung supports the intrathoracic airways and helps to maintain their patency, the authors suggested that patients with diabetes were at risk for developing chronic airflow obstruction. While small changes in lung elastic recoil do not have direct clinical implications, subsequent development of chronic airflow obstruction could incur significant disability due to mechanical dysfunction of the lungs and airways. Schernthaner *et al.* ([22]) could not confirm the findings of Schuyler *et al.* in patients with type 1 diabetes. However Sandler *et al.* ([23]) did find decreased lung elasticity. In addition, they found decreased CO transfer capacity with decreased pulmonary capillary blood volume in 40 patients (15–60 years of age) with insulin-dependent diabetes compared with age-matched control subjects, all lifelong nonsmokers. Lung CO transfer capacity is significantly affected by the integrity of lung capillary endothelium and, therefore, the findings of Sandler *et al.* focused attention on pulmonary vascular changes. The concept of the lung as a target organ for diabetic microangiopathy received continuing attention. Reports of lung function tests in patients with diabetes over the next 15 years have focused largely on pulmonary microangiopathy with relatively few studies of pulmonary mechanical function. Lung function tests relating specifically to pulmonary microangiopathy include CO transfer capacity and pulmonary capillary blood volume.

In patients with type 1 diabetes, decreased lung transfer capacity for CO has been documented in association with evidence of other diabetic microangiopathy ([24–26]). Decreased CO transfer capacity has also been correlated with the prevalence and/or severity of retinopathy and renal microangiopathy in patients with type 2 diabetes ([27–31]), supporting the concept of the lung as a target organ for diabetic microangiopathy. Sandler ([32]) concluded that the lung should be considered a target organ in diabetes, but noted that the documented physiological abnormalties were modest in degree, and clinical implications of those findings were not clearly defined in terms of respiratory disease at that time. Subsequent studies demonstrated further evidence of pulmonary microangiopathy, including thickening in alveolar capillary and pulmonary arteriolar walls in human postmortem studies of patients with diabetes ([33]) and decreased lung capillary blood volume in patients with type 1 diabetes ([34]). In contrast to the substantial evidence supporting the concept of the lung as a target organ for diabetic microangiopathy, reports of lung mechanical abnormalities in diabetes have been less convincing. Tests relating to lung mechanical function include lung elasticity (particularly dynamic breathing changes in lung elasticity), airflow resistance, and maximal forced spirometric PFTs. Most reports of lung mechanical function have utilized spirometric PFTs, which are commonly interpreted as indicative of airflow obstruction. In practice, however, PFTs are influenced by a wide variety of factors: they are physically demanding, maximally forced, coordinated efforts that are subject to deterioration with any debilitating disease, aging, loss of muscle strength from any cause, and obesity. An early study ([27]) showed decreased spirometric PFTs in patients with diabetes and this was confirmed by Schnack *et al.* ([26]), who also documented a clear relationship between spirometric PFTs and long-term metabolic control . However, spirometric PFTs

in other studies failed to show significant differences between patients with diabetes and normal control subjects, differences from normal population-predicted values, or a relationship with diabetes control or duration of disease (8, 14–16). Recent large epidemiologic studies ([37–40]) have used associations between simple spirometric PFTs and either complications or duration of diabetes to determine statistical significance after controlling for height, sex, age, BMI, and cigarette smoking. Davis *et al.* ([37])

Diabetes and Lung Function Test : Some studies showed that all the pulmonary parameters, that is, FVC, FEV_1, FEF_{25}, FEF_{50}, FEF_{75}, $FEF_{25–75}$, $FEF_{0.2–1.2}$, and PEFR were significantly reduced except FEV_1/FVC in patients of type 2 DM as compared with the healthy controls. [41–45] Some of the prospective and cross sectional studies have shown low vital capacity or restrictive pattern in type 2 DM. [46,47] Meta-analysis by van den Borst, *et al.* showed that DM is associated with statistically significant, impaired pulmonary function in a restrictive pattern. Moreover, these results were irrespective of body mass index (BMI), smoking, diabetes duration, and HbA1c levels.[48] Uchida, *et al.* found that there was decreased pulmonary diffusing capacity in patients with diabetes with perfusion defect on ventilation perfusion scintigrams.[49] It was not possible for us to analyze the pulmonary diffusing capacity because of practical difficulties. Davis, *et al.* conducted a study in Western Australia in large number of patients of type 2 DM. They found that VC, FVC, FEV_1, and PEFR decreased at an average of between 1.1% and 3.1% of predicted values/year in type 2 DM patients.[41] Ehrlich, *et al.* showed that patients with type 2 DM were at increased risk of several pulmonary condition like - asthma, Chronic Obstructive Pulmonary Disease (COPD), fibrosis, and pneumonia.[40] Few studies have mentioned that no significant differences were observed in patients of type 2 DM.[41–43] Probably the small sample size is the reason behind these findings.

Pathophysiology of reduced lung function is still an interesting research issue. Normal lung mechanics and gas exchange are influenced by the integrity of the pulmonary connective tissue and microvaculature. Acceleration of aging process in connective tissue cross links and presence of nonenzymatic glycosylation and modification of alveolar surfactant action causes reduction in PFTs.[43] There have been reports of histopathological changes in the diabetic patients. In the study by Weynand *et al.* it was found that alveolar epithelium, endothelium capillary, and basal laminaes were thickened in lungs on electron microscopy, when compared with the controls. In addition, the thickening of basal laminae was of the same magnitude in lung and kidney. Diabetic microangiopathy might be existing in the pulmonary vascular bed. Moreover, reduced pulmonary capillary blood volume was found, favoring the evidence of microangiopathy. This could lead to redistribution of the pulmonary circulation, resulting in well ventilated areas to become underperfused. The thorax and lungs are rich in collagen and elastin. Stiffening of thorax and lung parenchyma can occur because of nonenzymatic glycosytion of these structural compounds. This may lead to restrictive pattern.[43] In our studies, since the FVC/FEV_1 ratio is statistically not significantly different in DM patients as compared with normal controls, other PFT values are lower in DM patients; this strongly suggests restrictive pattern in DM patients. Studies have even shown diabetic polyneuropathy, which affects respiratory neuromuscular function and thus reducing pulmonary volumes.[44] The clinical implications of this is that ; pulmonary dysfunction should be regarded as a specific derangement induced by DM. Further studies may clarify whether this should be included as a long-term complication of diabetes. The role of strict glycemic control on pulmonary function in diabetic patients is another interesting aspect and needs further studies. The impairment in PFTs can lower the threshold for clinical manifestations of acute or chronic lung disease. Patients with DM admitted with pneumonia have increased risk of complications and mortality [45,46-58].

Conclusion

It can be concluded from our narrative review that the Type II or Type I diabetes is definitely having decreased lung functions assessed by spirometry not only because of diabetic complications like pneumonia or other but also due to long term effect of diabetes may be because of micro-angiopathy or decreased elastic recoil capacity of lungs.

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