Original Research Article

Assessment of lung function and diffusion capacity among cases with and without microvascular complications of diabetes mellitus - A cross sectional study

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Abstract

Background: Diabetes mellitus is a major public health problem in India. Microvascular complications add burden of the disease in terms of increasing mortality and morbidity. The well known fact is that microvascular complications usually affect eyes, nerves and kidneys and hence the aim of this study is to find out the lung function and diffusion capacity among cases with and without microvascular complications of type 2 Diabetes Mellitus. **Methods:** A cross-sectional study was conducted among type 2 diabetes mellitus cases presented to outpatient department of general medicine in Thiruvarur Medical College, Thiruvarur, from September 2017 to December 2017. A total of forty patients with type 2 diabetes mellitus were included after assessing the inclusion and exclusion criteria. Data was collected by the principal investigator using a proforma. Data entry was done using Microsoft excel and the statistical analysis like independent sample t test, analysis of variance (ANOVA) and odds ratio were calculated using Statistical Package for Social Sciences (SPSS) software version 17. **Results:** This study found significant difference between duration of diabetes, fasting and post prandial blood sugar, HbA1c, serum cholesterol and triglycerides with the presence and absence of microvascular complications. FEV1 was found to be reduced among patients with microvascular complications (p=0.0049). Also with reduction in DLco, diabetic nephropathy and retinopathy were found to be statistically significant among cases with microvascular complications. **Conclusion:** FEV1 and DLco can be recommended for routine screening in all type 2 diabetic individuals for early identification and for assessing the progression of lung dysfunction.
Key Word: Diabetes mellitus, lung function, microvascular complication, diffusion capacity

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INTRODUCTION

Among the various forms of diabetes mellitus, type 2 diabetes mellitus is the most common form which increases in prevalence day by day, is considered to be a major worldwide cause of morbidity and mortality.[1] According to International Diabetes Federation (IDF) 425 million people have diabetes in the world and 82 million people in the SEA Region and by 2045 this will rise to 151 million. In India, there were over 72.946.400 cases of diabetes.[2] The vascular complications of diabetes mellitus are separated into macrovascular and microvascular complications. Former include myocardial infarction, peripheral vascular disease, and cerebrovascular accidents and later include diabetic nephropathy, neuropathy, and retinopathy.[3] Development of these complications may be related to biochemical alterations in connective tissue constituents, particularly collagen and elastin, as well as microangiopathy due to a non-enzymatic glycosylation of

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proteins induced by chronic hyperglycemia.[4] The lung, which have extensive vascular network is one another target of diabetes, yet asymptomatic. But the effects of diabetes on lung have many morphological and physiological alterations leading to functional impairment, increased morbidity and mortality. The pulmonary functions like ventilation and diffusion can be assessed non invasively. Several clinical studies[4-8] have suggested a possible association between pulmonary function abnormalities and diabetic renal microangiopathy and retinopathy. Changes in pulmonary diffusing capacity for carbon monoxide (DLco) as a manifestation of pulmonary microangiopathy have also been reported.[9] A study conducted by Marvisi *et al*[5]on pulmonary functions in patients among T2DM, suggested possible associations between pulmonary function abnormalities and diabetic renal microangiopathy, retinopathy and diabetic control. Isotoni *et al*[9] showed independent changes in pulmonary diffusing capacity for carbon monoxide (DLco) as a manifestation of pulmonary microangiopathy. Theoretically, several pathological changes may affect the lungs in patients with T2DM. Collagen and elastin changes, which may occur due to small vessel involvement, can lead to significant structural changes. Ljubic *et al*[4] showed that diabetes could lead to the development of pulmonary complications due to collagen and elastin changes, as well as microangiopathy. Increased non-enzymatic glycation of proteins and peptides of the extracellular matrix at chronic high circulating glucose levels may also have an important role in the pathological changes of the lungs in Type2DM patients[10]. These studies suggested a relationship between pulmonary complications and other chronic complications in diabetes. In order to assess the in-depth of association between the micro and macrovascular complications of diabetes mellitus on lung, this study was conducted.

OBJECTIVES

The aim of this study is to find out the lung function and diffusion capacity among cases with and without microvascular complications of type 2 Diabetes Mellitus.

METHODS

A cross-sectional study was conducted among type 2 diabetes mellitus cases presented to outpatient department of general medicine in Thiruvarur Medical College, Thiruvarur. The study was conducted from September 2017 to December 2017. The patients, who were diagnosed to have type 2 diabetes mellitus based on ADA criteria[11], between 20-60 years of age were included in the study. Patients with coronary artery disease, abnormal ECG findings, past history of stroke, transient ischemic attack, tuberculosis, peripheral vascular diseases, chronic obstructive lung disease and smokers were excluded from the study. A total of forty patients with type 2 diabetes mellitus were finally included in this study. After obtaining the written informed consent from the patients, detailed history was collected by the principal investigator using a proforma. Height, weight, waist and hip circumference were measured. Body Mass Index (BMI) and Waist hip ratio (WHR) were calculated. Following which venous blood samples were collected from the patients. Fasting blood samples were collected after overnight fasting and assessed for fasting and post prandial blood sugars, HbA1c, fasting lipids profile (FLP), and hemoglobin. All the participants were assessed for the presence of microvascular complications of diabetes. Assessment of pulmonary function test was done using spirometer as per ATS guidelines[12] and all the reports were documented in the proforma. Data entry was done using Microsoft excel and the statistical analysis like independent sample t test, analysis of variance (ANOVA) and odds ratio were calculated using Statistical Package for Social Sciences (SPSS) software version 17.

RESULTS

In our study 65% of the participants were found to be in the age group of 41-50 years followed by 20% below 40 years of age and 15% between 51-60 years. Females were found to be 75% in this study. Based on Body Mass Index 22.5% of the study participants were found to have obesity. Waist hip ratio was normal among 72.5% of the participants and 27.5% were obese based on WHR. Among 40 participants the duration of diabetes mellitus was found to be more than 5 years in 30% of the patients. Poor control of HbA1c was recorded among 32.5% of the study population. 40% of the study population had microvascular complications and remaining 60 % are free.

Table 1: Clinical profile of the study participants

Variable	Frequency (N=40)	Percentage (%)
Age group		
<40 years	8	20
41-50 years	26	65
51-60 years	6	15
Sex		
Male	10	25
Female	30	75
BMI		
Normal	31	77.5
Obese (> 25)	9	22.5
Waist Hip Ratio (WHR)		
Normal	29	72.5
Obese (>0.9-females and >1.0 -males)	11	27.5
Duration of diabetes mellitus		
≤ 5 years	28	70
> 5 years	12	30
HbA1c		
Good control	27	67.5
Poor control	13	32.5
Microvascular complications		
Present	16	40
Absent	24	60

The study shows among 40 diabetic participants, 16 participants had microvascular complications. The mean age of patient with micro vascular complications was 50.00 ±6.26 and BMI was found to be 23.3±2.27 and p value was not significant when comparing the participants with and without microvascular complications. Mean Waist hip ratio among participants with micro vascular complication was statistically significant (p value = 0.0021) when compared to participants without microvascular complications. Blood sugar values, HbA1C, Cholestrol, TGL, DLco was found to be highly statistically significant (in patients with micro vascular complications)with p value of 0.0001. FEV1 among diabetic participants with micro vascular complication was 84.37±8.36, with statistical significance.

Table 2: Mean and Standard Deviation compared with the presence of microvascular complications

Variables	Micro vascular complications		P value
	Present (N=16) (Mean±SD)	Absent (N=24) (Mean±SD)	
Age (years)	50.00±6.26	47.88±5.88	0.2831
BMI	23.3±2.27	22.10±2.16	0.0998
Waist-Hip Ratio	0.93±0.05	0.87±0.06	0.0021*
Hb (%)	11.83±0.61	12.28±0.91	0.0914
FBS (mg/dl)	160.93±59.73	108.58±23.98	0.0001*
PPBS (mg/dl)	253.75±81.08	159.75±54.71	0.0001*
HbA1c	8.44±0.70	7.19±0.40	0.0001*
Duration of DM (years)	7.35±2.75	2.84±1.6	0.0001*
Total Cholesterol (mg/dl)	219.62±40.69	199.45±18.43	0.0001*
TGL (mg/dl)	162.0±40.45	118.54±39.16	0.0001*
FEV1 (%)	84.37±8.36	92.37±8.26	0.0049*
DLco (%)	71.21±8.17	88.04±6.16	0.0001*

*Significant [Independent sample t test]

Based on the diffusion capacity of carbon monoxide and the severity of diabetic retinopathy 7 participants were found to be normal, 2, 5 and 2 participants had mild, moderate and severe diabetic retinopathy changes respectively, and it was found to be statistically significant. (p value <0.0001). Five participants with diabetic nephropathy were found to have decreased DLco and it was found to be highly statistically significant, whereas diabetic neuropathy with decreased DLco was observed in 3 patients with no statistical significance.

Table 3: Comparison of DLco (%) with various microvascular complications

Variable	Frequency	Mean±SD	P value
DLco (%) and diabetic retinopathy			
Normal	7	78.0±3.69	
Mild	2	75.45±4.87	
Moderate	5	67.40±3.97	0.000*#
Severe	2	60.25±1.76	
Total	16	71.21±8.17	
DLco(%) and diabetic neuropathy			
Present	3	65.33±6.50	0.175
Absent	13	72.56±8.11	
DLco(%) and diabetic nephropathy			
Present	5	66.13±6.21	0.0001*
Absent	11	78.39±6.34	

*Significant #[ANOVA]

Male diabetics were at 3 times greater risk of micro vascular complications compared to females, but there was no statistical significance found in our study. Patients with less than 6 years of diabetes are at lesser risk of micro vascular complications, and it was highly statistically significant. Normal the HbA1c among diabetes lesser the risk of developing micro vascular complications and it was statistically significant. In this study participants with normal FVC and DLco were at lesser risk to develop microvascular disease with p value of 0.006 and 0.0001 respectively.

Table 4: Association of various factors with microvascular complications

Variables	Microvascular complications		Odds ratio	95% CI	P value
	Present	Absent			
Sex					
Male	6(15)	4(10)	3.0	0.69-13.1	0.1444
Female	10(25)	20(50)			
Duration of diabetes mellitus					
≤ 5 years	5(12.5)	23(57.5)	0.0198	0.002-0.19	0.0007*
> 5 years	11(27.5)	1(2.5)			
BMI					
Normal	10(25)	21(52.5)	0.2381	0.05-1.15	0.0745
Obese	6(15)	3(7.5)			
Waist-HipRatio					
Normal	9(22.5)	20(50)	0.26	0.06-1.1	0.068
Obese	7(17.5)	4(10)			
HbA1c					
Good control	4(10)	23(57.5)	0.01	0.00-0.14	0.0003*
Poor control	12(30)	1(2.5)			
FVC (%)					
Normal	7(17.5)	21(52.5)	0.11	0.023-0.53	0.006*
Obese	9(22.5)	3(7.5)			
DLco (%)					
Normal	2(5)	20(50)	0.029	0.00-0.18	0.0001*
Abnormal	14(35)	4(10)			

*Significant

DISCUSSION

On analyzing the data, we could find several significant observations apart from lung parameters, on comparing the patients with and without microvascular complication of type 2 diabetes mellitus. Mean age of the study group with micro vascular complications is 50 years, which in control group without micro vascular complications is 47.9 years. This was statistically not significant. Similar reports were reported in previous studies conducted by Guvener *et al*[7]and Sinha S *et al*[6].Females form the major portion of study participants, since many males were rejected due to smoking habit. There was no significant association of microvascular complications among either group. There was significant difference between duration of diabetes and microvascular complications and similar observations were found by Guvener *et al*[7]and Mori H *et al*[13], whereas other studies which was conducted by Ljubic S *et al*[4] and Agarwal AS *et al*[14]did not show significant relation with duration of the disease. Micro

vascular complications of nerves, kidney and eyes are very well documented to increase with duration of diabetes. Similar involvement in lungs progressively decreases diffusion capacity, as showed in this study. BMI was not significantly different with micro vascular complications whereas Waist Hip Ratio was significantly found to be higher among those with microvascular complications. Studies from New Delhi and Nagpur, India showed significant difference of BMI with microvascular complications.[6,14] In this study there was no significant difference was reported among two groups in mean haemoglobin value. Fasting and post prandial blood sugar levels have significant difference with microvascular complications, with typical high values of fasting and postprandial sugar levels among the cases with microvascular complications. Other Indian studies conducted by Sinha S *et al*[6] and Agarwal AS *et al*[14] reported significant association of above parameters with microvascular complications. HbA1c level was also found to be significantly different with the presence of complications indicating that poor glycemic control damages the alveolar capillaries and basement membrane. Sinha S *et al*[6] showed similar results, whereas Agarwal AS *et al* [14] didn't show such difference. Serum total cholesterol and triglycerides are elevated in uncontrolled diabetes mellitus and they are well known for its adverse effects on vascular endothelium. Dyslipidemia therefore leads to all microvascular complications, which also could affect the endothelium of pulmonary vessels. This study showed significant increase in total cholesterol level and triglycerides among the cases with microvascular complications and the same was found to be statistically significant. Another important observation in our study was significant reduction of FEV1% among those with microvascular complications when compared to cases without microvascular complications. A study conducted on type 1 diabetes patients showed reduction in FEV1 and FVC[15]. A large prospective study, among type 2 diabetes in Australia showed that FVC, FEV1, VC and PEF decrease with duration, magnitude of which was more than normal control group[16].But there are other studies that do not show significant reduction in lung volumes.[6,14,17] *DLco and Microvascular complications* In this study there was significant reduction of DLco among those with microvascular complication, confirming that the capillary network in pulmonary circulation also gets affected simultaneously with those in other organs. There was statistically significant reduction in DLco among patients with diabetic nephropathy and similar difference was observed by studies conducted by Ljubic S *et al*[4]Guvener N *et al*[7]Agarwal AS *et al*[14]and Lau AC *et al*[8].Protienuria, which is being considered as a marker of cardiovascular mortality can also be a predictor of pulmonary morbidity. Among the patients with microvascular complications, the DLco was compared among those with normal retina, mild, moderate and severe diabetic retinopathy. The DLco value decreased from those with normal retina to those with severe diabetic retinopathy. The severity of retinopathy correlates with severity of reduction in DLco. Significant variation between DLco and retinopathy was observed in the study conducted by Agarwal *et al*[14]. Weak, but non-significant correlation was reported by Marvisi *et al*[5]. There was no significant difference of diabetic neuropathy and DLco among patients with microvascular complications. But diabetic neuropathy was postulated as a cause for decreased pulmonary functions, like FEV1 and FVC. This was explained to be caused by neuropathy of nerves supplying respiratory muscles and diabetic myopathy.[16]

CONCLUSION

Asymptomatic involvement of lung goes unrecognized both by patients and clinicians. Assessment of parameters like FEV1 and DLco can be recommended for routine screening in all type 2 diabetic individuals for early identification and for assessing the progression of lung dysfunction. Diffusion study, a non-invasive and harmless study can be done in selected patients to assess the degree of morbidity.

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