## COMPARATIVE STUDY OF PULMONARY FUNCTION TESTS WITH MICROVASCULAR COMPLICATIONS, RETINOPATHY AND NEPHROPATHY IN TYPE 2 DIABETES MELLITUS AND CORRELATION WITH DURATION OF DIABETES

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## ABSTRACT

Background: The major morbidity in type 2 diabetes mellitus is due to microangiopathic and macroangiopathic complications. Though lung has been widely acknowledged to be a target organ in diabetes mellitus, its severity of involvement and correlation with other microvascular complications has not been studied. Aim: To study pulmonary function tests in type 2 diabetes mellitus and evaluate association of PFTs with microvascular complications, retinopathy and nephropathy and further assess the relationship of retinopathy, nephropathy and lungs with duration of diabetes. Methods: A cross sectional study was carried out in 100 male type 2 diabetic patients attending diabetic clinic in tertiary hospital. 100 non- diabetic subjects were selected as control from general population. PFTs tests were performed. Results were interpreted by one way ANOVA test. Association of PFT parameters FVC, FEV<sub>1</sub>, FEV<sub>1%</sub> in type 2 diabetic patients with nephropathy and retinopathy was analysed by Pearson's correlation coefficient. The patient population was subdivided according to the duration of diabetes into 2 groups; less than 10 years of illness and more than 10 years. Relationship of retinopathy, nephropathy and pulmonary function tests with duration of diabetes was assessed by one- way ANOVA test. Results: There was a significant decrease in PFT parameters as compared to non-diabetic controls. The PFTs in type 2 diabetic subjects with nephropathy showed decline in FVC, FEV<sub>1</sub>, FEV<sub>1%</sub>, however association of these parameters with Glomerular filtration rate (GFR) and microalbuminuria was not significant. Also, a similar decline of PFT parameters was observed with increasing grade of retinopathy, though not significant. There was a significant positive correlation of retinopathy with microalbuminuria and GFR (nephropathy) in type 2 diabetic subjects. Also, there was significant association of microalbuminuria, GFR and retinopathy with increase in duration of diabetes. On the contrary the decline in FVC, FEV1, FEV1% with duration of diabetes was not statistically significant. Conclusion: Type 2 diabetic patients with poor glycaemic control and longer duration of diabetes history had significant correlation with microvascular complications, nephropathy and retinopathy as compared to pulmonary complications (PFT parameters). It is highly suggestive that diabetic patients with retinopathy must be screened for nephropathy.

**Keywords**: Type 2 diabetes mellitus; Microvascular complications; Pulmonary function tests (PFTs); Nephropathy; Retinopathy; Glomerular filtration rate (GFR).

## **INTRODUCTION**

Diabetes mellitus is common metabolic disease worldwide and type 2 diabetes mellitus (T2DM) is the commonest form of diabetes. The chronic hyperglycaemia in diabetes mellitus is usually associated with longterm damage and spectrum of complications involving various systems mainly eyes, nerves, kidneys, and heart. [1] In initial stages, the illness remains silent and asymptomatic which delays the diagnosis and thereby increases the risk of complications. The actual onset of diabetic hyperglycaemia and clinical diagnosis has asymptomatic phase lasting for approximately 4-7



years, resulting in 30-50% of population remaining undiagnosed. [2] Thus, there exists quite some population with hyperglycaemia who are untreated in T2DM. This unchecked hyperglycaemia which prevails during the asymptomatic phase may account for high prevalence of microvascular complications even in newly detected T2DM. In fact, the significant morbidity and mortality in T2DM can be attributed to the microvascular and macrovascular complications.[3] Microvascular complications include retinopathy, nephropathy, and neuropathy which has been well established in literature. [3,4] Many research studies conducted worldwide, have been conclusive of lung being target organ in diabetes mellitus [5, 6] thus adding a further to the list of microvascular complications. The extensive pulmonary microvascular circulation and abundant connective tissue in lungs raises the possibility of it being involved in microvascular complications. Various microvascular changes in diabetes mellitus show close association with one another, as diabetic nephropathy and reti-

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nopathy exits in majority of patients, and one might entertain another cause for nephropathy only in the absence of retinopathy [7]. Thus, intensity of involvement of kidneys and retina seem to correlate with each other. Whether similar association between deranged pulmonary functions and other microvascular complications exists needs to be studied further. Though there are many studies which confirm the microvascular affection of lungs and several comparative studies of PFTs in diabetic population with microvascular complications, but there are hardly any studies on association of lung function tests with individual microvascular complications, retinopathy and nephropathy. The present study was carried out to study the pulmonary function tests in T2DM and assess its association with microvascular complications, particularly nephropathy and retinopathy.

In view of increased prevalence of microvascular complications in the eyes and kidneys, diabetic patients are advised regular screening of retina and periodic urine examination. Whether similar association between deranged pulmonary functions and other microvascular complications exists needs to be studied further. [8] Unlike this, screening for lung functions is not regular phenomenon in Indian diabetic population. Whether evaluation of lungs by PFT's needs to be incorporated for regular screening, as is done for retina and kidney in T2DM would depend on chronicity and intensity of lung involvement. The intensity of involvement of the lungs vis-a-vis retina and kidneys needs to be studied and evaluated. This aspect has not been looked in detail by previous research studies. Hence further assessment of association of these microvascular complications (nephropathy, retinopathy, PFT parameters) with duration of diabetes was analysed in the present study.

## **MATERIALS & METHODS**

**Study design**: An observational, analytical, cross sectional study.

**Ethics approval**: The study was approved by the institutional ethical review committee and participants were recruited for study after obtaining written consent.

**Study location**: The present study was conducted in a tertiary hospital, Mumbai.

**Sample size**: Total 200 participants were included in the study.

**Study populations**: A total of 100 type 2 diabetic patients attending diabetic clinic in tertiary hospital were selected for the study. 100 non-diabetic subjects belonging to the same socio-economic status were selected from the general population for comparison. A detailed medical, personal and family history was obtained followed by general examination.

Inclusion criteria: Males of age 35- 55 years, Non-

smokers, Type 2 diabetics with HbA1C≥7.

**Exclusion criteria**: Obese, Hypertensives, Overt cardiac, pulmonary or renal disease due to non diabetic causes.

## Methodology:

The following anthropometric parameters were studied: age in years, height in cm, with the help of height measurement stadiometer, weight in kg.

BMI: BMI was measured by the formula BMI = Weight (in Kg) / Height (in m2).

**Glycosylated haemoglobin**: HbA1c levels of all subjects in the study were determined by ion exchange resin method by diagnostic glycohaemoglobin kits of Asritha Diatech as per guidelines provided. [9] HbA1c was used as an index of diabetic control over last 3 months. Values over 7.5% were considered as poor glycemic control.

**Blood glucose estimation**: Fasting and postprandial blood glucose was estimated by glucose oxidase method. [10] The oral glucose tolerance test (OGTT) was done for control group to exclude diabetes. Only those control subjects with a normal fasting blood glucose of <110 mg/dL and 2 hours post oral glucose of <140 mg/dL were selected for study. Fasting blood glucose of 2126 mg/dL was used to define diabetes.

Serum urea was estimated by Berthelot's method [11] while creatinine was estimated by alkaline Jaffe's Picrate method. [12] These biochemical parameters were determined by using fully automated clinical chemistry analyser. The GFR per 1.73 m<sup>2</sup> BSA was calculated with serum creatinine, urea nitrogen, and albumin levels using an equation developed from the Modification of Diet in Renal Disease (MDRD) study as follows: GFR = 170 × [serum creatinine]  $-0.999 \times [age] -0.176 \times [0.762]$  if female] × [1.180 if non-Hispanic black] ×[blood urea nitrogen] $-0.170 \times [serum albumin] -0.318.[13]$ 

The presence of diabetic glomerulopathy was determined by estimating 24-hour protein excretion rate by semi-automated analyser. An albumin excretion rate between 30-300 mg per day was considered as indicative of microalbuminuria. [14,15] The presence of retinopathy was determined by using direct ophthalmoscopy, carried out by an experienced ophthalmologist in all the patients. The disease was graded according to the diabetic retinopathy disease severity scale as recommended by the American Academy of Ophthalmology. Non-proliferative retinopathy was diagnosed as grade 1,2,3 by the presence of cotton wool spots, micro aneurysms and boat shaped hemorrhages respectively on direct ophthalmoscopic examination. [16] Proliferative retinopathy was diagnosed by the presence of neovascularization in the retina (grade 4).

Spirometry was performed in a quiet room in sitting position by trained personnel and adequate spirograms as per the American Thoracic Society (ATS) guidelines was obtained. [17] The PFT helps to detect abnormali-

ties in lung function even when there are no signs and symptoms. The following PFT parameters were measured: forced vital capacity (FVC), forced expiratory volume in one second (FEV<sub>1</sub>), percentage of forced expiratory volume in one second (FEV<sub>1%</sub>). These measurements are crucial for interpretation of spirometry results. If FVC and FEV<sub>1</sub> are within 80% of the reference value, results are considered normal. The normal value for FEV<sub>1</sub>/FVC ratio is 70%. Best out of the three readings were selected. Mean ± SD were calculated.

Statistical analysis: Statistical analysis was carried out using SSPS software version 21. One-way analysis of variance (ANOVA) was used to compare mean values in control group and type 2 diabetic patients. Pearson's correlation coefficient was used to quantify the extent of relationship between each of PFT parameters FVC, FEV<sub>1</sub>, FEV<sub>1%</sub> with microalbuminuria, GFR and retinopathy. To study association of microvascular complications, nephropathy, retinopathy and pulmonary parameters with duration of diabetes, type 2 DM patients were divided into 2 groups, 1) those with duration less than 10 years of diabetes and 2) those with duration more than 10 years. Pearson's correlation coefficient was used to study the extent of relationship between each of PFTs parameters, nephropathy and retinopathy with duration of diabetes. Group comparisons were adjusted for the level of severity of retinopathy with Chi square test for trend (Mantel-Haenszel method).

Mantel-Haenszel method produces a single, summary measure of association which provides weighted average of the risk ratio or odds ratio across the different strata of the confounding factor. The correlation of retinopathy with nephropathy was analysed by Spearman's Rank correlation coefficient, which is used to identify and test the strength of relationship between two sets of data. It is often used as a statistical method to aid with either proving or disproving a hypothesis. All statistical tests used for analysis were twotailed (SPSS software version 21). A p value of < 0.05 was considered statistically significant.

## RESULTS

**Table 1** indicates mean ± SD for anthropometric measurements in non-diabetic subjects (control group) andT2DM / NIDDM. There was no significant difference inthe age, height, weight and BMI.

**Table 2** indicates mean  $\pm$  SD of fasting and post meal blood sugar levels and glycosylated haemoglobin (HbA1c) levels, GFR, micro albuminuria in the control and T2DM. There was significant increase in fasting blood sugar (FBS) and post meal blood sugar (PBS) levels, HbA1c levels and significant decrease in GFR in T2DM as compared to control group. There was significant decrease in FVC, FEV<sub>1</sub> and FEV<sub>1%</sub> in T2DM as compared to control group.

Parameters	Groups	N	Mean ±SD	P value	Significance
Age (years)	Control	100	50.65 ± 4.983	0.102	NS
	NIDDM		51.1 ± 4.833		
Height (cms)	Controls	100	162.27 ± 6.19	0.117	NS
	NIDDM		161.3 ± 5.339		
Weight (kg)	Control	100	56.63 ± 5.571	0.38	NS
	NIDDM		56.88 ± 6.133		
BMI (kg/m2)	Control	100	21.68 ± 2.484	0.225	NS
	NIDDM		21.378 ± 3.15		

## Table 1. Comparison among study groups for anthropometric measurements

b-standard deviation, NiDDM- non- insulin dependent diabetes melintus, bivir body mass index

Table 2. Comparison among study groups for FBS, PBS, HbA1c, micro albuminuria, FVC, FEV $_1$ , FEV $_{1\%}$ 

Parameters	Groups	Mean ± SD	P value	Significance
FBS	Control	80.74±8.967	0.000	S
	NIDDM	102.56±19.552		
PBS	Control	127.353±9.054	0.000	S
	NIDDM	182.96±20.515		
HbA1c	Control	5.112±0.308	0.000	S
	NIDDM	6.887±0.963		
GFR	Control	125.46±12.665	0.000	S
(ml/min/1.73m <sup>2</sup> )	NIDDM	90.521 ± 16.29		
micro albuminuria	Control	$1.3 \pm 0.180$	0.000	S
	NIDDM	115.06 ± 62.60		
FVC	Control	2.761±0.285	0.05	S
	NIDDM	2.577±0.341		
FEV1	Control	2.384±0.259	0.000	S
	NIDDM	2.091± 0.283		
FEV <sub>1%</sub>	Control	84.741± 4.5	0.000	S
	NIDDM	81.477±4.314		

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Table 3. Mean ± SD of PFT parameters in different grades of retinopathy							
MEAN ±SD	1	2	3	4	Р	Significance	
FVC	2.655±0.346	2.544±0.212	2.509±0.336	2.45±0.212	0.327	NS	
FEV <sub>1</sub>	2.173±0.285	2.065±0.286	2.009±0.258	1.9±0.1414	0.098	NS	
FEV <sub>1%</sub>	82.368±4.358	81.5±4.70	80.590±3.445	78±1.414	0.284	NS	

# Table 3. Mean ± SD of PFT parameters in different grades of retinopathy

As the grade of retinopathy increases, there is a non- significant decrease in PFT values

## Table 4. Correlation of Pulmonary function tests: FVC, FEV<sub>1</sub>, FEV<sub>1</sub>% with micro albuminuria and GFR.

Correlation of Parameters	r <sub>2</sub> correlation coefficient	t for correlation	P value	Significance
FVC with GFR	- 0.003	0.033	0.973	NS
FVC with micro albuminuria	0.081	0.808	0.420	NS
FEV <sub>1</sub> with GFR	-0.054	0.536	0.592	NS
FEV <sub>1</sub> with micro albuminuria	-0.070	0.697	0.487	NS
FEV <sub>1%</sub> with GFR	-0.148	1.483	0.141	NS
$FEV_{1\%}$ with micro albuminuria	-0.406	4.399	0.05	S

## Table 5. Indicating anthropometric measurements in type 2 diabetics according to duration of illness

50.854 ± 4.544 51.5 ± 5.310 161.338 ± 5.360	58     0.926	NS NS
51.5 ± 5.310           161.338 ± 5.36	58 0.926	
161.338 ± 5.36		NS
		NS
$161.236 \pm 5.36$	54	
57.709 ± 6.361	1 0.074	NS
55.526 ± 5.559	Э	
21.966 ± 3.155	5 0.015	NS
20.420 ± 2.955	5	
	21.966 ± 3.155	21.966 ± 3.155 0.015

# Table 6. Comparison among type 2 diabetics for FBS, PBS, HbA1c and micro albuminuria according to duration of diabetes

Parameters	Duration of diabetes in years	Mean ± SD	P value	Significance
FBS	Less than 10	95.806 ±17.089	0.01	S
-	More than 10	113.578±18.445		
PBS	Less than 10	175.596±14.218	0.01	S
	More than 10	194.973±23.530		
HbA1c	Less than 10	6.459±0.674	0.000	S
	More than 10	7.584±0.962		
GFR	Less than 10	90.532±4.412	0.01	S
(ml/min/1.73m <sup>2</sup> )	More than 10	88.947±2.931		
micro albuminuria	Less than 10	72.919±51.666	0.000	S
	More than 10	137.289 ±4 0.121		
FVC	Less than 10	2.619±0.337	0.115	NS
	More than 10	2.507±0.341		
FEV <sub>1</sub>	Less than 10	2.132±0.278	0.065	NS
	More than 10	2.023±0.284		
FEV <sub>1%</sub>	Less than 10	81.903± 4.629	0.287	NS
	More than 10	81± 3.734		

## Table 7. Association between retinopathy grades and duration of diabetes

Retinopathy Grades	Duration >10 yrs	Duration <=10yrs	Total
1	2(5.2%)	36(13.68%)	38
2	18(47.3%)	20(7.6%)	38
3	16(72.7%)	6(1.32%)	22
4	2(100%)	0(0%)	2

Chi square for trend (extended to Mantel-Haenszel) =33.57, p value =0.000, S

	Parameters	Correlations	Retinopathy	GFR
	Retinopathy	Correlation Coefficient	1.000	0.662**
		Sig. (2-tailed)		
Spearman's rho		•		0.000
	GFR	Correlation Coefficient	0.662**	1.000
		Sig. (2-tailed)		
		•		0.000
	Parameters	Correlations	Retinopathy	Micro albuminuria
Spearman's rho	Retinopathy	Correlation Coefficient Sig. (2-tailed)	1.000	0.569**
	Micro albuminuria	Correlation Coefficient Sig. (2-tailed)	0.569**	1.000
				0.000

Table 8.	Correlation of	retinopath	v with GFR and	micro albuminuria
			,	

\*\*Correlation is significant at the 0.01 level (2-tailed).

P value= 0.000 significant correlation between retinopathy and GFR

This shows that higher grades of retinopathy are associated with higher values of GFR

Correlation between retinopathy and micro albuminuria = 0.569

P value= 0.000 significant correlation between retinopathy and micro albuminuria

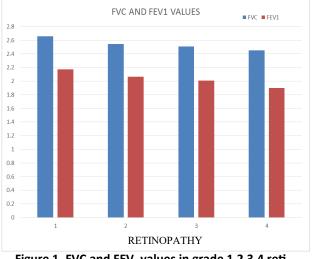


Figure 1. FVC and FEV<sub>1</sub> values in grade 1,2,3,4 retinopathy

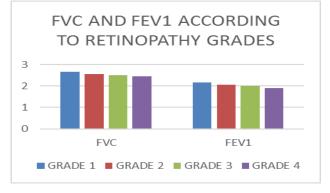


Figure 2. Comparative decline in FVC and  $\mbox{FEV}_1$  with increase in grades of retinopathy

Table 3 shows mean ± SD of the FVC, FEV1 and FEV1% in T2DM diabetic subjects with different grades of retinopathy. There was a decline in PFTs with increasing grades of retinopathy but none were statistically significant. Table 4 shows correlation of FVC, FEV1 and FE-V1% with (nephropathy) micro albuminuria and GFR. There was no correlation of PFT parameters with nephropathy. Table 5 Indicating anthropometric measurements in type 2 diabetics according to duration of illness. T2DM subjects were divided into 2 groups based on duration of diabetes: 1) those less than 10 years of diabetes and 2) those more than 10 years of diabetes. Both groups did not show any significant difference in anthropometric measurements as indicated in Table 5. Table 6 indicates that there was significant positive association of micro albuminuria and negative correlation of GFR with duration of illness respectively but none of the PFT parameters showed significant correlation with increase in duration of diabetes. Similarly, as indicated in Table 7, association between retinopathy grades and duration of diabetes was analysed by Chi square for trend (extended to Mantel-Haenszel) and showed that as, number of diabetic cases with duration more than 10 years increases, retinopathy grades also went on increasing. This directly indicates that more the duration of diabetes, severe will be the grade of retinopathy. Table 8 indicates a significant correlation of micro albuminuria and GFR each with diabetic retinopathy.

## DISCUSSION

There was a significant reduction in FVC,  $\mbox{FeV}_1$  and  $\mbox{Fe-V1\%}$  in type 2 diabetes mellitus as compared to the

control group in the present study. When each of these PFT parameters, FVC, FEV<sub>1</sub> and FEV<sub>1</sub>% were correlated with micro albuminuria and GFR in T2DM with nephropathy there was a positive correlation but it was not significant. The PFT parameters were further correlated with different grades of retinopathy, a similar decline was seen with increasing grades of retinopathy, but the decline was not significant as depicted in Figure 1 and 2. However, significant correlation was observed for microvascular complications, nephropathy and retinopathy in the study. Thus, in the present study, significant correlation was observed for microvascular complications nephropathy and retinopathy, but a similar correlation was not observed for any PFT parameters with either diabetic nephropathy and retinopathy. This is thereby suggestive of the fact that presence of retinopathy can be said to act as a red flag for the beginning of or co-existing nephropathy in T2DM. This significant association of nephropathy with increasing grades of retinopathy may serve to adopt preventive measures in diabetic patients with retinopathy from proceeding to overt nephropathy and worsening of retinopathy. The Diabetes Control and Complications Trial (DCCT) have confirmed a strong relationship between diabetic retinopathy and elevated albumin excretion.[18] Similar strong association between diabetic nephropathy and retinopathy was demonstrated by Arora et al.[19] F He et al 20 in his meta- analysis analysed the predictive value of diabetic retinopathy in differentiating diabetic nephropathy from non-diabetic renal diseases and suggested proliferative diabetic retinopathy to be a highly specific indicator for diabetic nephropathy. Shafiee et al [21] in his study on type 2 diabetic patients with nephropathy found that with progression of diabetic nephropathy to more advanced stages, there was significant impairment of pulmonary function. Also, in study conducted by Cilek P, the degree of proteinuria and frequency of retinopathy correlated with the severity of restrictive lung function in diabetic patients.[22]

I M Stratton [23] in his study on patients with T2DM had reported a strong association of complications with hyperglycaemia. Sinha et al studied pulmonary functions with macroangiopathic complications in T2DM Asian Indian patients and observed no differences for pulmonary functions, forced vital capacity, forced expired volume in one second, peak expiratory flow rate, maximal static inspiratory and expiratory pressures but significant impairment of pulmonary diffusion capacity for carbon monoxide.[24]

Various studies reported [25, 26, 27, 28] significant reduction in diffusion capacity with micro vascular complications like retinopathy, nephropathy and neuropathy and significant positive correlation with high sugar levels, long duration of diabetes. The possible pathophysiological mechanism of illness in diabetes mellitus suggested by most authors was thickening of alveolar epithelial and pulmonary capillary basal lamina in these group of patients. Overall, most studies have investigated PFTs in diabetic subjects and compared them with the same in those diabetics with microvascular complications. Also, there has been meticulous research on association of PFTs with duration of diabetes and glycaemic index. But no studies conducted so far have studied association of each PFT parameters with both microvascular complications retinopathy and nephropathy. Also, comparative association of each microvascular complication with duration of diabetic illness, has not been studied before. The frequency and severity of involvement of these complications has hardly been compared and evaluated before.

To study the association of microvascular complications with duration of diabetes, We have included this as a part of our study to assess the relationship of duration of diabetes with intensity of following microvascular complications PFTs (lung), nephropathy, retinopathy. T2DM subjects in the study were divided into 2 groups, those more than 10 years of duration and less than 10 years. There was significant increase in micro albuminuria and decrease in GFR and also a similar increase in grade/ severity of retinopathy respectively with increase in duration of diabetes. However, when PFT parameters were analysed, decrease in values of PFT parameters FVC, FEV1 and FEV1% with increase in duration of diabetes was not significant. Thus, unlike PFT parameters, micro albuminuria, GFR and retinopathy showed a significant association found to be with duration of diabetes in our study as depicted in Figure 2. The significant association of micro albuminuria and decreased GFR (nephropathy) with increasing grades of retinopathy and also the association of the two with increasing duration of diabetes points out to its severity of involvement unlike PFT which showed a non- significant decline with increased duration of diabetes illness. This may also allude to the fact that intensive treatment of hyperglycaemia in diabetic subjects with retinopathy at earlier stages might hinder its further progression to advanced stages of retinopathy and serve as a check to early detection and prevention of nephropathy in T2DM as well.

Also T2DM comprises individuals bearing insulin resistance (IR) which is usually relative rather than absolute insulin deficiency. Chronic hyperglycaemia is associated with long-term damage and failure of various organ systems mainly affecting eyes, nerves, kidneys, and heart.[4] The onset T2DM is often silent and insidious and chronic hyperglycaemia is usually found to be existing in most type 2 DM patients even before the diagnosis. Also at the onset most of the T2DM are usually treated with lifestyle modification, dietary advice and then followed by oral anti hyperglycemic drugs. This stepwise approach may result in further, accumu-

lation of glycaemic burden. [3] Nephropathy, retinopathy and neuropathy are the most common microvascular complications in diabetes.[4] Longer the duration of diabetes, longer would be the persistence of hyperglycaemia. The long standing hyperglycaemic state in diabetes mellitus results in glucose, forming covalent adducts with plasma proteins through non-enzymatic process known as glycation. [29] This protein glycation and formation of advanced glycation end products (AGEs) is a major cause in development and progression of different diabetic complications and has an important role in the pathogenesis including nephropathy, retinopathy, neuropathy and cardiomyopathy along with some other diseases such as rheumatoid arthritis, osteoporosis and aging. [30, 31] Lung has abundant connective tissue and dense capillary network which makes it very likely to get affected by diabetes mellitus. [5, 6] The glycation of proteins (AGEs) alters the normal functions by disrupting molecular conformation, altering enzymatic activity, and interfering with receptor functioning.[30] Collagen is a major component of ECM and a prominent target of nonenzymatic glycation [32]. It is likely that persistent inadequate blood glucose control over a period of time which is more likely with longer duration of diabetes, may alter the regulation of inflammatory pathways that are involved in pulmonary function impairment; mainly restrictive impairment and reduction in diffusing capacity to carbon monoxide [33]. The complications in lung, kidneys, and eyes needs to be compared in severity as all three have identical aetiopathogenesis. The development of complications in the three, maybe the nonenzymatic glycosylation of proteins due to chronic hyperglycemia which brings about changes in connective tissue (collagen and elastin), as well as microangiopathy [34, 35]. The involvement of lungs as compared to kidney and retina doesn't seem to be alarming in our study.

The pulmonary abnormalities may remain subclinical in diabetic patients mainly because of the great microvascular reserve in alveolar-capillary system.[36] In spite of the presence of a large capillary network in the lung and its acknowledgement as one of the organs involved in diabetes, pulmonary function tests in diabetes are frequently disregarded and not conducted as a regular follow up. But this loss of microvascular reserve in the lung may become clinically important in case of acute or chronic pathological lung conditions like pneumonia, chronic obstructive pulmonary disease, asthma and heart failure and hence should not be disregarded. [37]

## CONCLUSIONS

The intensity of lung involvement in type 2 diabetic subjects as compared to microvascular complications nephropathy and retinopathy was not significant. This may be due to the large micro-vascular reserve in alveolar capillary system. All type 2 diabetics with retinopathy should be thoroughly investigated for nephropathy as both the microvascular complications in type 2 diabetes mellitus seem to go hand in hand. The treatment modality in those with onset of retinopathy if intensified could deter further worsening of retinopathy in diabetic patients and serve to check the onset and progress of nephropathy and thus may help to reduce the morbidity in type 2 diabetic patients.

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