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Pulmonary Functions In Patients With Type 2 Diabetes Mellitus & Correlation With Microvascular Complications

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Abstract
Background: *The macrovascular and microvascular complications of type 2 diabetes mellitus (T2DM) diabetes involving various organs are well studied. However, the impact of diabetes on vasculature in the lung and its consequent effect on pulmonary function is less well characterised.*
Objectives: *This study was done with the primary objective of comparing pulmonary function in individuals with diabetes based on glycemic control duration of diabetes, age and microvascular complications.*
Material and methods:*20 patients were selected as study group all of were with T2DM and divided in to 2 groups-group III and group II, each group with 10 patients. Group III had T2DM subjects with retinopathy and/or diabetic nephropathy and/or neuropathy, whereas group-II had T2DM patients without any complications. In addition,10 age and sex matched controls without diabetes were selected from general population as group I*
Results: *The mean value of FEV1 (% predictive) of group-III (91.4±10.8), group-Il group-II (99.6±2.716) and group-I (96.4±4.9) has no significant difference with p value of > 0,05.The mean FVC (% predictive) values of group-III (81.5±8.15), group-II (91.3±8.88) and group-I (91.3±4.57) were not significantlydifferent (p>0.05). The mean values of FEV1/FVC of group-III (0.81±0.41), group-II (0.789±0.40), and group-I (0.797±0.020) were similar.The man values of PEFR of group-I (73.1±18.28), group-II (70.1±18.07) and group-III (69.5±18.07) were* ***not significantly different (p>0.05).***
Conclusions: *In conclusion, the present study showed there is no significant association between glycemic control, duration ofdiabetes, micro-angiopathy, and age with spirometry associated lung functions*
Keywords: *Diabetes, Microangiopathy, FEV1, FVC ,PEFR*

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I. Introduction:

Diabetes mellitus (DM) comprises a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM exist and are caused by a complex interaction of genetics, environmental factors, and life-style choices[1]

Depending on the etiology of the DM, factors contributing to hyperglycemia may include reduced insulin secretion, decreased glucose utilization, and increased glucose production.[1]

The metabolic deregulation associated with DM causes secondary path physiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system.[1]

In the Asian Indians, Diabetes Mellitus is the leading cause of endstage renal disease (ESRD), non-traumatic lower extremity amputations, and adult blindness. With an increasing incidence worldwide, DM will be a leading cause of morbidity and mortality for the foreseeable future.[1]

Chronic Complications of Diabetes Mellitus [1,2]
Micro vascular:
• Eye disease 1. Retionopathy 2. Macular edema
• Neuropathy 1. Sensory and motor (Mono and poly neuropathy)
2. Autonomic
3.Nephropathy

Macro vascular
• Cardio vascular disease
• Peripheral vascular disease
• Cerebra vascular disease
Others:
• Gastrointestinal (gastro paresis, diarrhea)
• Genitourinary (uropathy/sexual dysfunction)
• Dermatologic
• Infectious
• Cataracts
• Glaucoma

Pathogenesis of Micro vascular Complications:[1,2,3,4,5]
1. Formation of advanced glycosylation end products (AGES)
2. Hyperglycemia increases glucose metabolism via the sorbitol pathway
3. Hyperglycemia increases the formation of diacylglycerol leading to activation of protein kinase C (PKC).
4. Hyperglycemia increases the flux through the hexosamine pathway, which generates fructose-6-phosphate, a substrate for O-linked glycosylation and proteoglycan production.

The purpose of this study pose of this study was to evaluate pulmonary functions in type Diabetes Mellitus and to determine their correlations with bropometric profile, glycemic control and microangiopathic diabetic complications.

Material and Methods
The patients with T2DM were selected from the outpatient Department of Medicine, and Endocrinology Department, Government General Hospital,Vijayawada.

Period of Study:
The patients with T2DM were selected from the outpatient department (OPD) of the Department of Medicine, and Endocrinology Department, Government General Hospital, Vijayawada during period of two years i.e 2014 August to 2016 August.

Selection of patients & Sample size:
20 patients were selected as study group all of were with type II DM and divided in to 2 groups, each group contains 10 patients
Group-I n = 10 (males-7; females3) were T2DM subjects with retinopathy and/or diabetic nephropathy and/or neuropathy.
Group-II n=10 (males-8; females-2) were T2DM patients without any complications.
10 age and sex matched controls were selected from general population with out any diabetes randomly and included asGroup I n=10 (males-8; females-2).
Informed written consent was obtained from all subjects. The respiratory, cardiac and neuro-muscularsystems were ems were clinically normal as examined by a specialist. All patients had BMI < 30 Kg/m 2

Selection Criteria:
None of the patient is a smoker
Patients with positive history of respiratory symptoms or disease were excluded.
Persons with a history of allergic disorders and bronchial asthma were excluded.
Patients with BMI > 30 Kg/m^2 were excluded

Study Protocol:
Informed written consent was taken from all subjects after explaining the study protocols. A detailed history was taken from patient including the history various risk factors like hypertension, smoking, alcohol intake. A detailed general examination including height, weight, BMI, vital data including pulse, blood pressure were noted. Detailed systemic examination was done to rule out any other systemic diseases.
Chest skiagram was done to exclude the presence of structurally obvious pulmonary disease
All the exclusion criteria were taken into consideration and relevant data recorded in the proforma.

Evaluation of patients:
Biochemical investigations:
Blood samples were obtained after 12hr overnight fast for the estimation of levels of blood glucose, Blood urea, serum creatinine, electrolytes, complete urine examination urine for microalbuminuria and 24 hrs urinary protein values were performed.
Definitions and cut-offs:
Diabetes mellitus was diagnosed according to the World Health Organization criteria[8]
Normal lipid levels were defined according to the criteria of National cholesterol Educational Program, Adult Treatment Panel III [6]

Evaluations for the complications ofT2DM:
Diabetic retinopathy: An experienced ophthalmologist performed the direct ophthalmoscopic examination on the patients. Retinopathy was defined as mild to moderate non-proliferative, severe non-proliferative and clinically significant macular edema.
Diabetic nephropathy: Excretion of >300 mg of albumin in urine over 24 h was defined as the presence of overt diabetic nephropathy after excluding urinary tract infection and other causes of renal disease. Creatinine clearance was calculated using the following formula: {[140-age (yr) x weight (kg)/72] x serum creatinine}[20]
Diabetic peripheral neuropathy : Peripheral neuropathy was evaluate cli**nic**ally and was defined as > or = 2 missing deep tendon reflexes in legs, diminished distal touch (assessed by cotton wool), pinprick or pressure sensation, distal vibratory sensation (assessed by graduated tuning fork of 128 Hz) and joint position sense. Other potential causes of peripheral neuropathy were excluded before attributing the peripheral neuropathy to diabetes.
Methods of performing Pulmonary Function Tests
All the patients were taken to AP chest Hospital., Irrumnuma, Hyderabad, the place where the pulmonary function lab is present. Lung functions were evaluated in patients and controls from maximal expiratory flow volume curves recorded on vitalograph t, dry spirometer. Pulmonary functions including forced vital capacity (FVC), forced expired volume in one second (FEV1) and peak expiratory flow rate (PEFR) were measured by spirometer according to the American Thoracic Society criteriaThe variables were reported in absolute volume as well as the per cent predicted based on the regression equations. Maximal static inspiratory (MIP) and expiratory pressure (MEP) were measured in the sitting position. The MIP was measured near residual volume and MEP was measured near total lung capacity.. A minimum of three successive curves were obtained from each subject and the flow volume curve with greatest sum of FEV 1 and FVC was selected for analysis.
Forced Vital Capacity:
The patient was asked to sit comfortably infront of the spirometer and he was instructed to take deep inspiration after which the patient was told to exhale as rapidly and completely as possible during which the EVC spirogram is recorded on the vitalograph. So the total volume of the gas exhaled after full inspiraton is expressed as FVC in liters.
Forced Expiratory Volume in One Second (FEV1)
This was calculated from the FVC spirogram and is expressed a the volume of gas exhaled in 1 second during the execution of the forced vital capacity. This is expressed in liters per second.
FEV 1 /FVC % :- This is calculated as the ratio of the forced expiratory volume in 1 second to forced vital capacity expressed as percentage.
Forced Mid Expiratory Flow (FEF 25 – 75 %):- This was calculated from the FVC spirogram. This is obtained by dividing the volume between 75% and 25 % of vital capacity by the corresponding elapsed time.

Graph for HbA1C LEVELS OF DIFFERENT AGE GROUPS

Table 1

Column1	Column2	Column3	Column4
	group-1	group-2	group-3
HbA1C levels	5.7	8.7	8.6

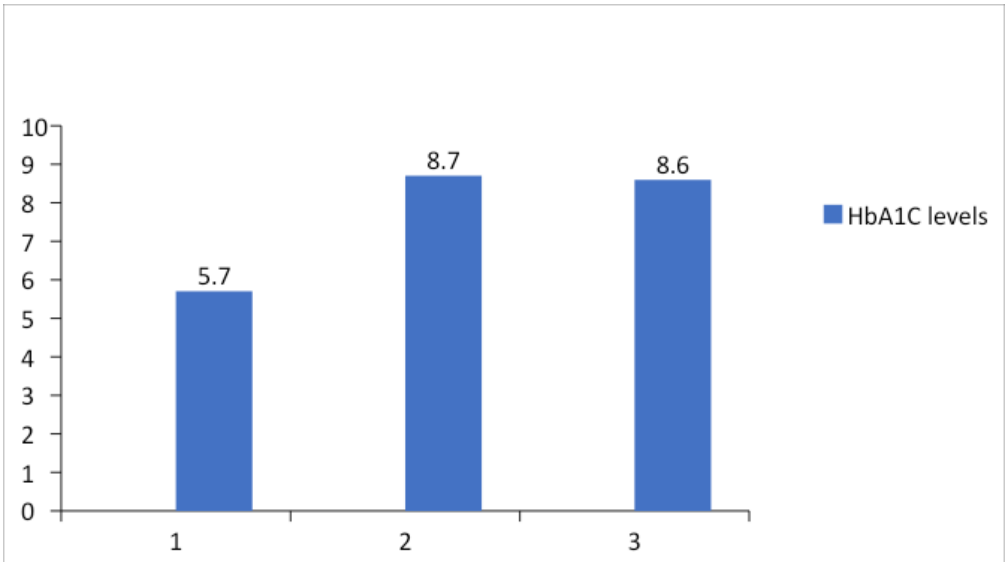


Table 2 for FBS & PLBS of different groups

Column1	Group-1	Group-2	Group-3
FBS	79.7	127.1	144.8
PLBS	122.5	177.2	203.1

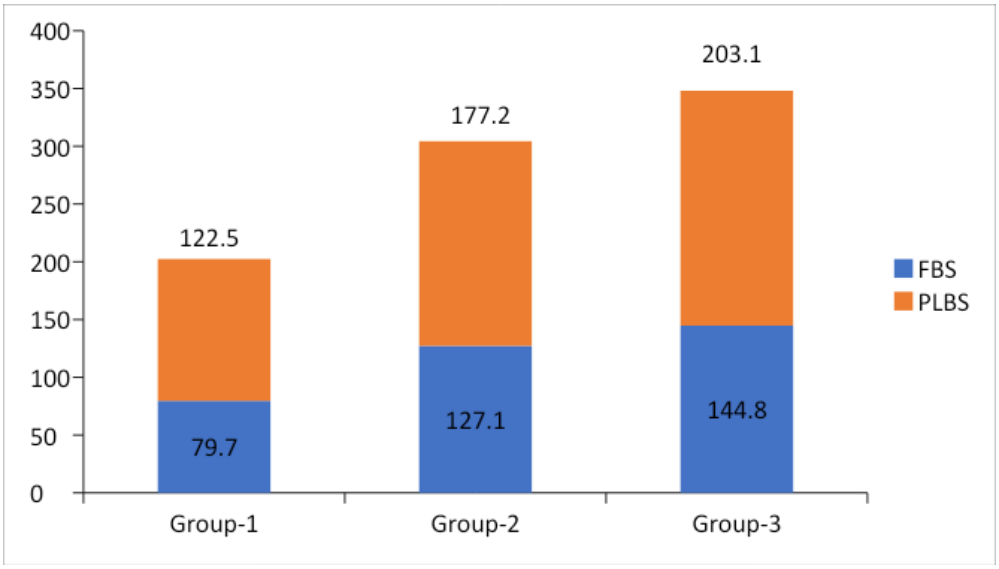
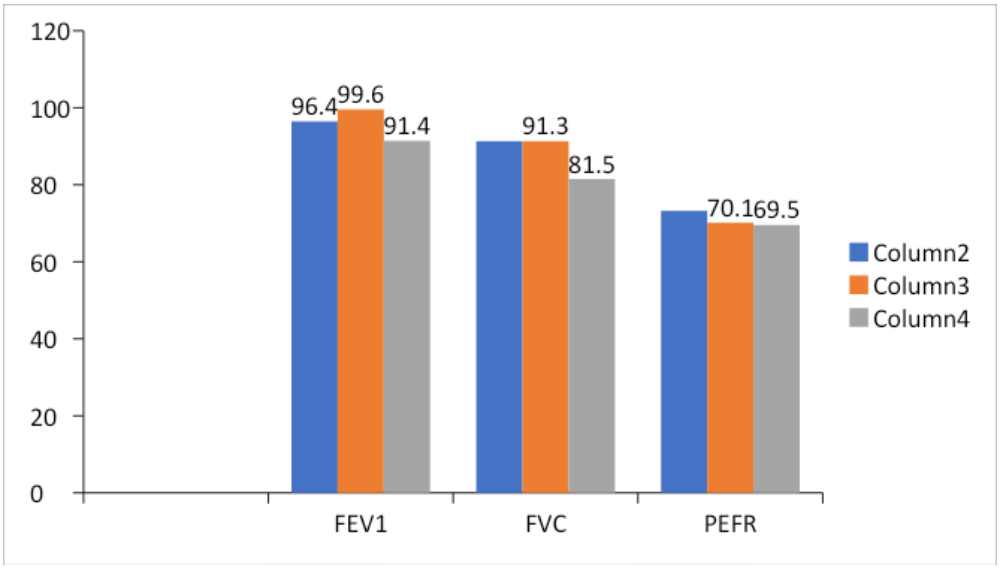


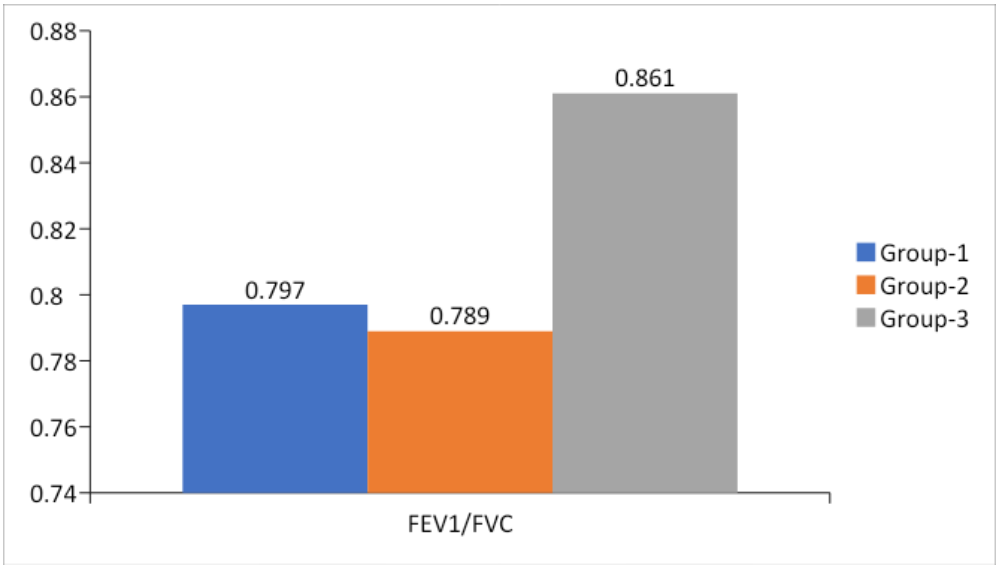
Table3 for pulmonary functions in different groups

Column1	Column2	Column3	Column4
	Group-1	Group-2	Group-3
FEV1	96.4	99.6	91.4
FVC	91.3	91.3	81.5
PEFR	73.2	70.1	69.5



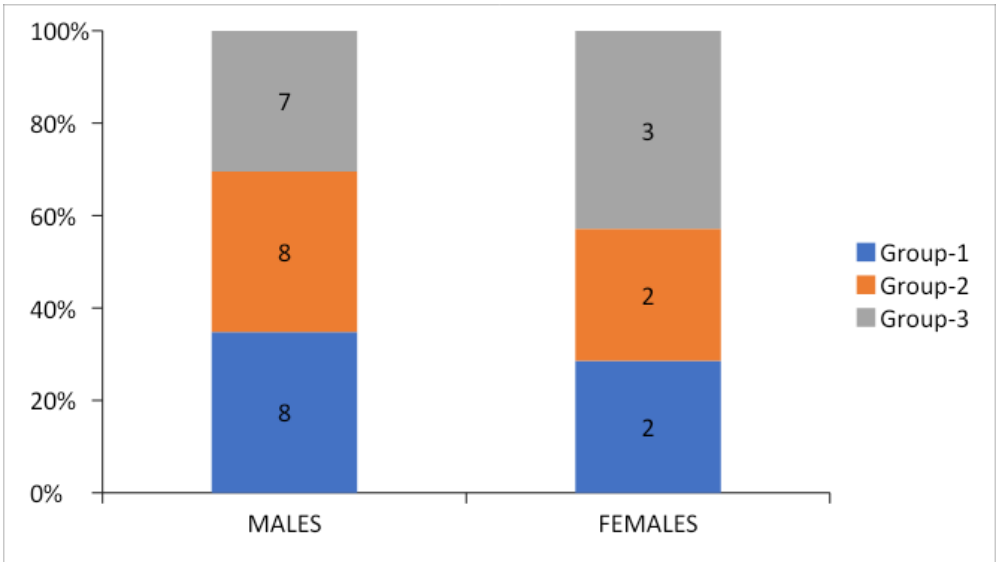
Graph for FEV1/FVC IN DIFFERENT GROUPS

Column1	Group-1	Group-2	Group-3
FEV1/FVC	0.797	0.789	0.861



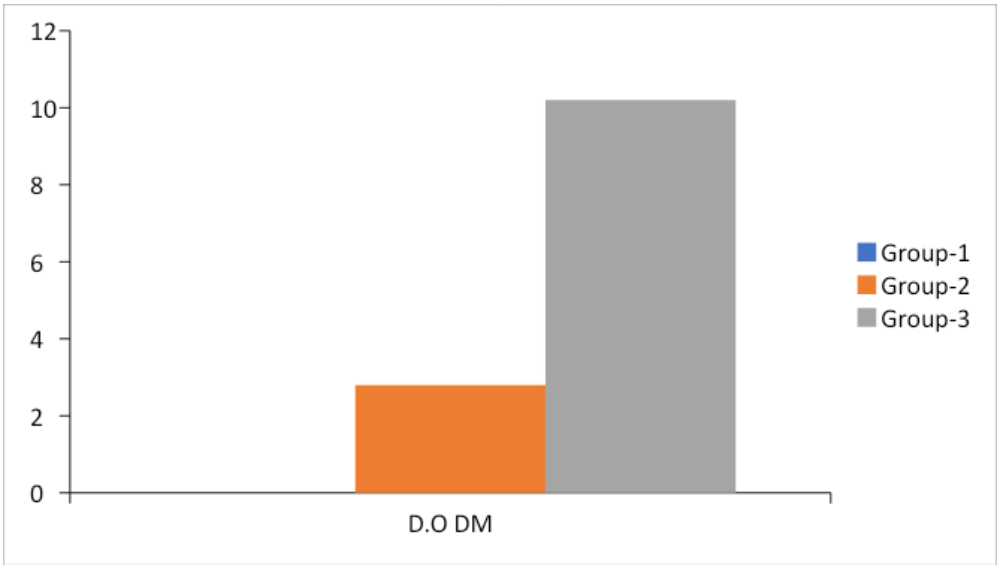
Graph for number of males and females

Column1	Group-1	Group-2	Group-3
MALES	8	8	7
FEMALES	2	2	3



Graph for duration of diabetes in different groups

Column1	Group-1	Group-2	Group-3
D.O DM	0	2.8	10.2



II. Results And Observations:

The data on 30 patients with 23male (76.66%) and 7 female (23.33%) and 20 with diabetes(66.66%) and 10 with out diabetes (33.33%) patients were analysed. The mean age was 45.9 (±3.071) in healthy rols and 47.7 (±2.263) years in patients with type Il diabetesus without microvascular complications and 49:(2.673) years in patients with type Il diabetes mellitus with microvascular complications.. None of the patient had coronary vascular disease, cerebral vascular disease or peripheral vascular disease. 7 patients (23.33%) were hypertensive, 7patients (23.33%) had retinopathy.3 patients (10%) had nephropathy 5 patients (16.66%) had nephropathy.

Biochemical profile analysis:

The mean levels of fasting blood glucose(144.8±12.43,p<0.001), postprandial blood glucose(203±24.9,p<0.001), blood urea(31.30±6.21, p<0.001), serum creatinine(1.20±0.22, p<0.05) and HbA1C(8.7±1,p<0.001) were significantly higher in group-Ill as compared to the other two groups.

Diabetic micrangiopathies :

7 patients (23.33%) had retinopathy, 3 patients (10%) had
Nephropathy, 5 patients (16,66%) had neuropathy.

Pulmonary functions analysis :

The mean value of FEV1 (% predictive) of group-III (91.4±10.8), group-Il (99.6±2.716) and group-I (96.4±4.9) has no significant difference with p value of > 0,05 but values of group-Ill when compared to other two groups were little lower.

The mean FVC (% predictive) values of group-III (81.5±8.15), group-II (91.3±8.88) and group-I (91.3±4.57) were showing some difference which were not significant with p value of >0.005. These values were lower in group-III when compared to other two groups

The mean values of FEV1/FVC of group-III (0.81±0.41), group-II (0.789±0.40), and group-I (0.797±0.020). The difference among these values were not significant with p values of >0.05. These values were little higher in group-III than other groups but these values were not significant. The individual values of FEV1/FVC in group-I than group-II are in between 0.7 to 0.8 with in the range of normal. In group-III 3 patients (33.33%) showing values in the spectrum of mild restrictive Pattern, but these values were not much significant and none of these patients were symptomatic at any time.

The main values of PEFR of group-I (73.1+/-18.28), group-II (70.1±18.07) and group-III (69.5±18.07) were showing some difference in values but were not significant with p values of >0.05. These values were little lower in group-Ill when compared to other groups, even though they were not significantly lower the underlying cause for this not understood one of these patients had neuropathy involving the respiratory muscle weakness.

III. Discussion:

The spirometry study in 20 patients with type-11 diabetes mellitus showing no significant difference in spirometry values with respect to healthy controls except in mild decrease in FEV1, FVC, PEFR and mild increase in FEV1/FVC values. However these values were not significant.

Study conducted by Benbassat CA et al (Am i Med Sci 2001:322:127-32) showed that there was no correlation between pulmonary function tests and the presence of microangiopathy or glycemic control.[7]

Study conducted by Sinhaet al., on pulmonary functions and type-Il diabetes with anthropometry showed that there was no correlation between glycemic control, microangiopathy and pulmonary functions. [7]

The same study showed that significant correlation between microangiopathy and diffusion capacity of lung for carbon monoxide which was not included in this study. The possible pathophysiological mechanisms remain speculative and requires further studies. Since Pulmonary bed has as extensive capillary bed, it could get affected in diabetes and causes thickening of alveolar epithelium and pulmonary capillary basallamina and same are observed in postmortem examination[8]

The studies of schanapf et al., have shown decrease in FEV1, FVC and FEV^1/FVC in diabetic patients but were not significant.

The pulmonary functions data of schernathaner et al1977 did not show significance difference in spirometry, or lung volumes in diabetes.

Isotani et al[9] showed independent changes in pulmonary diffusing capacity for carbon monoxide (Dico) 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. As anthropometry was taken in account in to study as a parameter which effect the pulmonary functions for evaluation the percentage predective values were taken in consideration to prevent the anthropometry as a confounding limiting factor.

The limitation of the present study was small number of subjects in each group and other lung functions like diffusion capacity of lung for carbon monoxide was not studied as such facilities were not available. These e the main factors affected in diabetes.

This preliminary observation of this study i.e. no significant association between glycemic control, microangiopathy and spirometry remains to bestudied in future studies, particularly in view of high prevalence of diabetes in Asian India.

IV. Conclusions:

There was no relationship between duration of diabetes, glycemic control, age, microangiopathy with pulmonary functions. In conclusion, the present study showed there is no significant association between glycemic control, duration of diabetes, micro-angiopathy, and age with spirometry associated lung functions.

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