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*Original Research Article*

# Study of Pulmonary Functions in Adolescents with Type 1 Diabetes Mellitus

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## ABSTRACT

**Background:** Hyperglycaemia is an important factor in initiation and progression of metabolic and microvascular complication in Type 1 Diabetes Mellitus (T1DM). Since pulmonary functions and gas exchange depends partly on the integrity of connective tissue and microcirculation within lungs, changes involving these structural components could lead to lung dysfunction and impaired gas exchange.
**Aim:** To assess the pulmonary functions in adolescent with Type 1 Diabetes Mellitus.
**Methods:** Thirty cases of T1DM of either sex (age range 10-19 year), age and sex matched thirty-three healthy subjects as controls were selected. The pulmonary function tests including diffusion study and ABG (arterial blood gas) analysis were done.
**Results:** All the absolute values of spirometry parameters FVC (Forced Vital Capacity), FEV1(Forced expiratory volume in 1 sec), FEV1/FVC ratio (FEV%), PEF(peak expiratory flow), MEF(Mid Expiratory Flow), MEF25%, MEF50%, MEF 75%, SVC(Slow Vital Capacity) and their values expressed as percentage of predicted values in T1DM group were lower as compared to healthy subjects. The difference was highly significant (p value<0.000). All the absolute values of diffusion study parameters DLCO (diffusion capacity of lung for carbon monoxide), KCO or DLCO/ Va (Transfer coefficient or diffusion constant) in T1DM group were lower as compared to healthy subjects. The difference was highly significant (p value<0.000).
**Conclusion:** All the absolute values of spirometry values and diffusion study parameters in T1DM group were lower as compared to healthy subjects. The difference was highly significant (p value<0.000). But there was no significant correlation observed with HbA1c and duration of disease in T1DM.

***Key words:*** Type 1 Diabetes Mellitus (T1DM), pulmonary function, adolescent, hyperglycaemia.

## INTRODUCTION

Diabetes Mellitus (DM) is a chronic progressive disease that has profound consequences for individuals, families and society.

T1DM is a chronic autoimmune disorder of multifactorial origin which precipitates in genetically susceptible individuals. The body's own immune system attacks the beta cells in the Islets of Langerhans of the pancreas, destroying or damaging them sufficiently to reduce and eventually eliminate insulin production leading to hyperglycemia. Hyperglycemia is an important factor in the initiation and progression of metabolic &microvascular complications in T1DM. [1]

Non-enzymatic protein glycosylation induced by chronic hyperglycaemia has been proposed as one of the determinant mechanisms leading to systemic diabetic microangiopathy. This leads to systemic involvement leading to coronary artery disease, nephropathy, retinopathy, neuropathy and probably pulmonary dysfunction. Owing to its abundant connective tissue and diffuse microvascular circulation, the lung too is thought to be a target organ for diabetics where it is referred to as diabetic pulmonary microangiopathy. [2]

Pulmonary damage in diabetic patients can arise from several other mechanisms, including biochemical changes in connective tissue, especially in collagen and elastin. Since pulmonary function and gas exchange depends partly on the integrity of the connective tissue and microcirculation within the lung, changes involving these structural components could lead to mechanical lung dysfunction and impaired blood gas exchange. [2]

Another important aspect to long term diabetes complications is Diabetic Autonomic Neuropathy (DAN) which causes dysautonomia in almost every organ and also lungs. It has been shown that dysfunction of cholinergic system and adrenergic denervation are significant parts of the clinical picture of diabetic neuropathy. [3]

To the best of our knowledge the reports on pulmonary functions in Indian adolescent patients with T1DM are very few. Most of the studies in India have been conducted in adult population with T2DM. In paediatric and adolescent groups, limited numbers of studies have been carried out and that too with conflicting results as compared to the studies in adults.

## LACUNAE IN EXISTING KNOWLEDGE

1. Limited studies are available on pulmonary functions in T1DM in adolescents age group, both in India & abroad.
2. Paucity of studies investigating pulmonary functions in terms of spirometry, DLCO and arterial blood gas analysis in T1DM adolescents in India and the comparison of the same with that of healthy adolescents.

## RESEARCH QUESTION

Do Type 1 Diabetes Mellitus adolescents when compared to control groups show decrease in pulmonary functions?

## HYPOTHESIS

There is impairment of pulmonary functions in Type 1 Diabetes Mellitus adolescents.

## AIM

The aim of this study was to assess pulmonary functions in terms of spirometry, arterial blood gas [ABG] analysis & diffusion lung capacity of carbon monoxide [DLCO] in adolescents with TIDM.

## OBJECTIVES

In order to fulfill the aim, following objectives had been formulated-

- To study pulmonary functions (spirometry, ABG analysis and DLCO) in adolescents with T1DM.
- To compare the above-mentioned parameters in age and sex matched control group.
- To look for any correlation of the pulmonary functions with the duration of disease and glycemic control in T1DM patients.

## MATERIALS AND METHODS

**VENUE OF STUDY:** The present study was conducted in the Department of Physiology, VMMC & Safdarjung hospital, New Delhi. The study was commenced after obtaining clearance from the institutional Ethical Committee.

**PERIOD OF STUDY:** November 2016 to February 2018.

**STUDY DESIGN:** A case control study was carried out.

**STUDY POPULATION:** For cases of T1DM adolescents already diagnosed with T1DM and attending Endocrinology Out Patient Department of Safdarjung Hospital for follow-up visits were worked up for the study. For controls, otherwise healthy adolescents attending medical Out Patient Department in VMMC & Safdarjung hospital for minor illnesses were followed up and, after recovery from illness, were included in the study.

**SAMPLE SIZE:** Thirty adolescents with T1DM and thirty-three, age and sex matched, controls were selected.

**STUDY GROUPINGS: INCLUSION CRITERIA**

GROUP A: thirty diagnosed cases of T1DM, both males and females in the age group 10-19 years with disease duration of more than 2 years.

GROUP B: thirty-three controls (age and sex matched) i.e. healthy subjects both males & females.

**EXCLUSION CRITERIA FOR BOTH GROUPS**

1. Subjects suffering from any acute respiratory infection within previous 6 weeks.
2. Subjects with any diagnosed chronic respiratory diseases, cardiovascular disease, congenital heart disease, thyroid disease, anemia and chronic allergies.
3. Subjects on any medication known to effect pulmonary functions like (beta agonist, beta blocker, antihistaminic).
4. Adolescents with acute complications of Diabetes mellitus like diabetic ketoacidosis, hypoglycemic coma or any other medical or surgical condition.
5. Adolescents with diagnosed chronic complications like diabetic neuropathy, nephropathy and retinopathy.
6. Subjects having any physical deformity that may affect lung function (like kyphoscoliosis, pectus excavatum and pectus carinatum etc.), neuromuscular disease
7. Smokers or drug users.

**PROTOCOL OF THE EXPERIMENT**

All the subjects were called to the department of Respiratory Medicine in morning hours and all the investigations were performed in between 9 a.m. and 11:30 a.m. in the Pulmonary Function Test laboratory. All the subjects were explained the prerequisites for PFT. The temperature of the PFT lab was maintained between 23°C to 25°C.

All the subjects and controls were tested under similar laboratory conditions. The nature of the tests was explained to the subjects beforehand. Each participant was provided with a patient information sheet in either English or Hindi language as per preference. An informed written consent in either English or Hindi language was obtained from each participating subject for enrolment.

A detailed history was taken. Routine investigations like Complete blood count with ESR, glycated hemoglobin (HbA1c), Kidney function test and Thyroid Function Test, complete lipid profile as available inpatient records were noted in a proforma. For HbA1C wherever available average of three previously recorded values was taken. The anthropometric parameters (height in cm and weight in kilograms) were recorded. Body Mass Index in $kg/m^2$ and Body surface area in $m^2$, were calculated.

Each subject was interviewed to collect relevant information on educational status, menstrual history, socio-economic status, medical history, family history, exposure to industrial smoke/soot/dust/pets etc.

A detailed clinical examination including the general physical examination was done.

**METHODS**

***1 .Anthropometric measurement:***

For all measurements, subjects wore light clothing and were barefoot. The following parameters were measured

(a) Height (ht)(cm): Height was measured to the nearest 0.1 cm using a stadiometer.

(b) Weight (wt)(kg): body weight was measured to the nearest 0.1 kg using a standardized machine.
(c) Body surface area (BSA)(kg/$m^2$): was calculated from height and weight.
(d) BMI: was calculated using the formula:
BMI = [wt (in kilograms)/{ht}$^2$(in square meters)].

### *2. PULMONARY FUNCTION TEST (PFT)*

Following pulmonary function were recorded on BODY BOX 5500 Medisoft ExpAir Software in the Department of Pulmonary, Critical Care and Sleep Medicine. To provide accurate spirometry data American Thoracic Society [ATS]/European Respiratory Society [ERS] 2005 recommendations [4] on equipment and calibration procedures were followed. All measures recommended by the ATS/ERS Task Force to prevent transmission of infection to patients during pulmonary function testing were applied in this study.

*Test procedure:*

Subject was asked to loosen tight-fitting clothing if any and was made to relax before starting the test. He/she was demonstrated to how to hold the mouthpiece and create a good seal around the mouth piece. He/ She was also demonstrated the various respiratory excursions and manoeuvres for recording various parameters.

He/she was then made to sit straight, with head erect, nose clip in place and holding the mouthpiece tightly between lips to get a good seal around the mouthpiece of spirometer.

Initially, as demonstrated earlier, he/she was made to breath in and out at the tidal volume (normal quiet breathing).

Then, for recording

1. SVC, thesubject after 3-4 normal breathing was asked to inhale rapidly and maximally (‘breath in all the way’) and without delay blow out as slowly and continue to exhale (‘keep going…. Keep going’) until subject was not able to blow any more. This was repeated until at least three technically acceptable manoeuvres were completed to ensure reproducibility in order to meet quality control criteria (American Thoracic Society or ATS criteria).
2. FVC, the subject after 3-4 normal breathing was made to inhale rapidly and maximally (‘breath in all the way’) and without delay blow out as hard and as fast as possible (‘blast out’) and continue to exhale (keep going…. keep going) until subject can blow no more. This was repeated until at least three technically acceptable manoeuvres were completed to ensure reproducibility in order to meet quality control criteria (American Thoracic Society or ATS criteria).
3. DLCO Single breath method, the subject after few 3-4 normal breathing was made to exhale maximally and then without delay was asked to do rapid maximum inhalation from a bag containing a diffusion gas mixture (0.3%CO, 10%He, 21%$O_2$, balanced nitrogen). Breath was then held for 10 seconds and then the subject exhaled rapidly.

   Severe respiratory impairment is defined as a DLCO below 45 percent of the predicted value. [5]

Lung volume and capacities show wide range in the normal population depending on the age, sex, and height of the subject. Indian population shows significant lower values as compared to their western counterparts. Predicted normograms are available based on these variable factors. Therefore, here we have taken % predicted values according to regression equations available Indian population. Formulae for calculating % predicted values of PFT parameters were different for $\leq$ 17 year and >18 year. [6] All formulae are given in Table 1.

**TABLE 1: INDIAN PREDICTION EQUATIONS FOR SPIROMETRY**

**A. Spirometry Adults (18 years & above)** [4]

**Enter age in years, height in cm and weight in Kg rounded off to nearest integer**

**1. MALES**

*Grey Highlighted parameters are log transformed, to be entered as EXP*

FVC = -5.048-0.014*age+0.054*ht +0.006*wt; SEE 0.478
FEV1= -3.682-0.024*age+0.046*ht SEE 0.402
FEV1/FVC = 74.866-0.233*age+0.107*ht-0.075*wt SEE 5.58
PEFR: =EXP(0.346-0.004*age+0.011*ht+0.5*0.158*0.158) SEE 0.158
FEF25-75 (or MEF25-75): =EXP(-0.091-0.019*age+0.011*ht+0.5*0.271*0.271) SEE 0.271
FEF50 (or MEF50): =EXP(0.573-0.016*age+0.008*ht+0.5*0.262*0.262) SEE 0.262
FEF75 (or MEF25):=EXP(-0.789-0.057*age+0.017*ht-0.007*wt+0.000344*age*age+0.5*0.350*0.350) SEE 0.350

**LLNs (Lower limit of normal: 5th percentile)**

FVC = -5.048-0.014*age+0.054*ht +0.006*wt - (1.645*0.478)
FEV1= -3.682-0.024*age+0.046*ht - (1.645*0.402)
FEV1/FVC = 74.866-0.233*age+0.107*ht-0.075*wt - (1.645*5.58)
PEFR: =EXP(0.346-0.004*age+0.011*ht+0.5*0.158*0.158-1.645*0.158)
FEF25-75 (or MEF25-75): =EXP(-0.091-0.019*age+0.011*ht+0.5*0.271*0.271-1.645*0.271)
FEF50 (or MEF50): =EXP(0.573-0.016*age+0.008*ht+0.5*0.262*0.262-1.645*0.262)
FEF75 (or MEF25): =EXP(-0.789-0.057*age+0.017*ht-0.007*wt+0.000344*age*age+0.5*0.350*0.350-1.645*0.350)

**ULN (Upper limit of normal: 95th percentile)**

FVC = -5.048-0.014*age+0.054*ht +0.006*wt + (1.645*0.478)
FEV1= -3.682-0.024*age+0.046*ht + (1.645*0.402)
FEV1/FVC = 74.866-0.233*age+0.107*ht-0.075*wt + (1.645*5.58)
PEFR: =EXP(0.346-0.004*age+0.011*ht+0.5*0.158*0.158+1.645*0.158)
FEF25-75 (or MEF25-75): =EXP(-0.091-0.019*age+0.011*ht+0.5*0.271*0.271 +1.645*0.271)
FEF50 (or MEF50): =EXP(0.573-0.016*age+0.008*ht+0.5*0.262*0.262+1.645*0.262)
FEF75 (or MEF25): =EXP(-0.789-0.057*age+0.017*ht-0.007*wt+0.000344*age*age+0.5*0.350*0.350+1.645*0.350)
Range of normal values: LLN to ULN

2. **FEMALES**

FVC = 20.07-0.010*age-0.261*ht+0.000972*ht*ht SEE 0.315
FEV1= -2.267-0.019*age+0.033*ht SEE 0.286
FEV1/FVC = 73.539-0.330*age+0.151*ht-0.074*wt SEE 5.08
PEFR =EXP(-0.829+0.0137*ht+0.026*age-0.000402*age*age+0.5*0.198*0.198) SEE 0.198
FEF25-75 (or MEF25-75): EXP(-0.116+0.011*ht-0.0223*age+0.5*0.308*0.308) SEE 0.308
FEF50 (or MEF50): EXP(-0.051+0.010*ht-0.015*age+0.5*0.292*0.292) SEE 0.292
FEF75 (or MEF25) =0.423-0.090*age+0.000799*age*age+0.017*ht SEE 0.372

**LLNs (Lower limit of normal: 5th percentile)**

FVC = 20.07-0.010*age-0.261*ht+0.000972*ht*ht- (1.645*0.315)
FEV1= -2.267-0.019*age+0.033*ht- (1.645*0.286)
FEV1/FVC = 73.539-0.330*age+0.151*ht-0.074*wt - (1.645*5.08)
PEFR: =EXP(0.346-0.004*age+0.011*ht+0.5*0.198*0. 0198-1.645*0.198)
FEF25-75 (or MEF25-75): EXP(-0.091-0.019*age+0.011*ht+0.5*0.308*0.308-1.645*0.308)
FEF50 (or MEF50): EXP(0.573-0.016*age+0.008*ht+0.5*0.292*0.292-1.645*0.292)
FEF75 (or MEF25): = 0.423-0.090*age+0.000799*age*age+0.017*ht -(1.645*0.372)

**ULN (Upper limit of normal: 95th percentile)**

FVC = 20.07-0.010*age-0.261*ht+0.000972*ht*ht + (1.645*0.315)
FEV1= -2.267-0.019*age+0.033*ht + (1.645*0.286)
FEV1/FVC = 73.539-0.330*age+0.151*ht-0.074*wt + (1.645*5.08)
PEFR: =EXP(0.346-0.004*age+0.011*ht+0.5*0.198*0.198+1.645*0.198)
FEF25-75 (or MEF25-75): EXP(-0.091-0.019*age+0.011*ht+0.5*0.308*0.308+1.645*0.308)
FEF50 (or MEF50): EXP(0.573-0.016*age+0.008*ht+0.5*0.292*0.292+1.645*0.292)
FEF75 (or MEF25): = 0.423-0.090*age+0.000799*age*age+0.017*ht +(1.645*0.372)
Range of normal values: LLN to ULN

**B: Pediatric age groups 6 to 17 years** [7]

| Parameter | Equation | SEE |
|---|---|---|
| **1.Males** | | |
| (FVC) | =EXP(-1.687+0.016*ht+0.022*age+0.5*0.111*0.111) | 0.111 |
| (FEV1) | =EXP(-1.748+0.015*ht+0.031*age+0.5*0.115*0.115) | 0.115 |
| PEFR | =EXP(-0.319+0.009*ht+0.051*age+0.5*0.131*0.131) | 0.131 |
| $FEF_{25-75}$ | =EXP(-0.951+0.011*ht+0.035*age+0.5*0.181*0.181) | 0.181 |
| $FEF_{50}$ | =EXP(-7.641+1.594*Ln(ht)+0.322*Ln(age) +0.5*0.230*0.230) | 0.230 |
| $FEF_{75}$ | =EXP(-2.008+0.011*ht+0.049*age+0.5*0.327*0.327) | 0.327 |
| FEV1/FVC | 74.866-0.233*age+0.107*ht-0.075*wt | 5.58 |
| **2.Females** | | |
| (FVC) | =EXP(-9.989+(2.018*Ln(ht))+(0.324*ln(age)) +(0.5*0.117*0.117)) | 0.117 |
| (FEV1) | =EXP(–10.055+(1.990*Ln(ht))+(0.358*Ln(age)) +(0.5*0.115*0.115)) | 0.115 |
| PEFR | =EXP(-6.341+(1.362*Ln(ht))+(0.469*Ln(age)) +(0.5*0.142*0.142)) | 0.142 |
| $FEF_{25-75}$ | =EXP(-7.89+(1.641*Ln(ht))+(0.317*Ln(age)) +(0.5*0.176*0.176)) | 0.176 |
| $FEF_{50}$ | -2.258+(0.027*ht)+(0.125*age) | 0.691 |
| $FEF_{75}$ | =EXP(-9.139+(1.676*Ln(ht))+(0.468*Ln(age)) +(0.5*0.323*0.323)) | 0.323 |
| FEV1/FVC | 73.539-0.330*age+0.151*ht-0.074*wt | 5.08 |

LLN for log transformed variables: = $\exp^{(\text{predicted - (1.645*SEE)})}$
ULN for log transformed variables: = $\exp^{\text{predicted + (1.645*SEE)})}$
Range of normal values: LLN to ULN

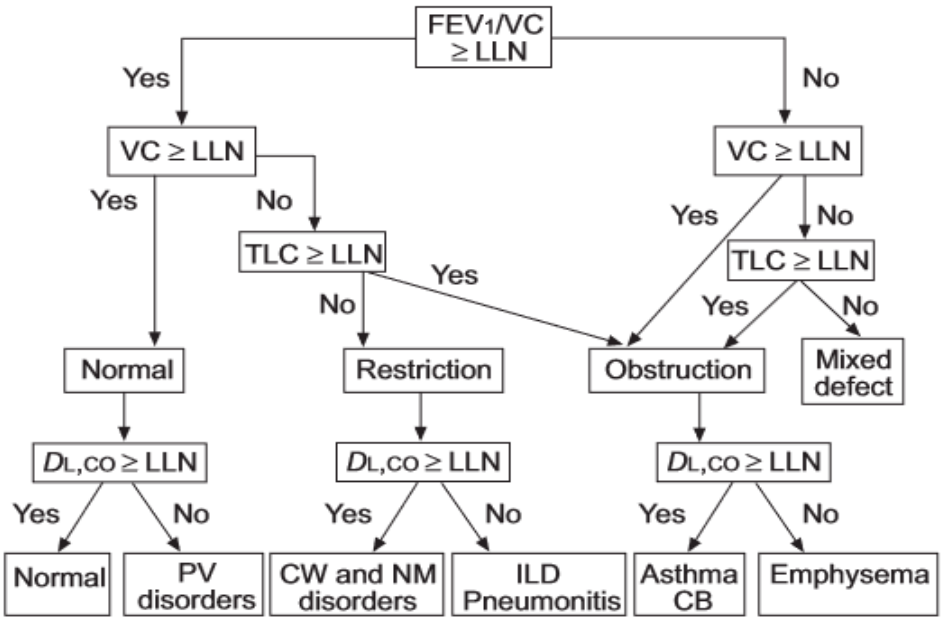


**Figure1: Interpretation of PFT according to ATS/ERS criteria 2005** [8]

Figure 1: A simplified algorithm that may be used to assess lung function in clinical practice. It presents classic patterns for various pulmonary disorders. As in any such diagram, patients may or may not present with the classic patterns, depending on their illnesses, severity and lung function prior to the disease onset (e.g. did they start with a vital capacity (VC) close to the upper or lower limits of normal (LLN)). The decisions about how far to follow this diagram are clinical, and will vary depending on the questions being asked and the clinical information available at the time of testing. The forced expiratory volume in one second (FEV1)/ VC ratio and VC should be considered first. Total lung capacity (TLC) is necessary to confirm or exclude the presence of a restrictive defect when VC is below the LLN. The algorithm also includes diffusing capacity for carbon monoxide (DLCO) measurement with the predicted value adjusted for haemoglobin. In the mixed defect group, the DLCO patterns are the same as those for restriction and obstruction. This flow chart is not suitable for assessing the severity of upper airway obstruction. PV: pulmonary vascular; CW: chest wall; NM: neuromuscular; ILD: interstitial lung diseases; CB: chronic bronchitis.

**Overview of recorded measures:**

- Forced Vital Capacity [FVC]
- Forced Expiratory Volume in 1 second [$FEV_1$]
- $FEV_1$ % [$FEV_1$/FVC%]
- Peak Expiratory Flow [PEF]
- Maximum Mid Expiratory Flow Rate [MMEF] or Forced Expiratory Flow 25-75%[FEF25-75%]
- Mid Expiratory Flow Rate 25% [MEF 25%] or Forced Expiratory Flow 75%[FEF75%]
- Mid Expiratory Flow Rate 50 %[MEF50%] or Forced Expiratory Flow 50%[FEF50%]
- Mid Expiratory Flow Rate 75%[MEF75%] or Forced Expiratory Flow 25%[FEF25%]
- Slow Vital Capacity [SVC]
- Diffusion study:
  - Transfer Factor for Carbon Monoxide or Diffusion Capacity of the Lung [TLCO or DLCO]
  - Alveolar Ventilation [VA]
  - Transfer Co-efficient or Diffusion Constant [KCO or DLCO/VA]

### 3. ARTERIAL BLOOD GASES ANALYSIS (ABG):

Arterial blood sample of 1 ml from the radial artery was withdrawn under all aseptic condition and ABG was performed on RADIOMETER ABL 800- BASIC in Department of Pulmonary, Critical Care and Sleep Medicine.

The following were measured and recorded:

1. pH
2. Partial pressure of oxygen [ $PO_2$ ]
3. Partial pressure of carbon dioxide [$PCO_2$ ]
4. $PO_2$(A-a) [difference of partial pressure of oxygen in alveolar and arterial blood]
5. $PO_2$ (a/A) [Ratio of partial pressure of oxygen in arterial blood to alveolar blood]

### STATISTICAL ANALYSIS

The data was analyzed by statistical software SPSS version 22. Chi square test was used for the association between sex and study group. Differences of mean values of age, height, weight, BMI and BSA between two study groups were assessed through t test. All the recorded PFT parameters and the derived parameters like Percent Predicted were checked if they followed normal distribution using Kolmogorov-Smirnov test. Differences of mean values of those parameters that were normally distributed between case and control groups were assessed through t test. Mann-Whitney U test was used to test the between study group differences in the distribution of the parameters that did not follow normal distribution. However, for the sake of simplicity mean values along with standard deviation were presented for both, normally distributed and non-normally distributed parameters. Pearson's rank correlation coefficients were used to study the correlations in normally distributed parameters and Spearman's rank correlation coefficients were provided to test the strength of correlation between all the non-normative parameters. Correlations of PFT indices measured with age, BMI, BSA, HbA1C and duration of diabetes were sought for. P value of <0.05 was taken as significant.

## OBSERVATIONS AND RESULTS

For this study sixty-three subjects including both males and females in the age group of 10-19 years were assessed with due consideration to inclusion and exclusion criteria. Out of these 33 were normal healthy subjects and 30 were diagnosed cases of TIDM.

The number of males and females in control group and that of in the diabetic group is shown in Table 2.

**Table 2: Sex wise distribution in case and control group**

| | CONTROL(n=33) | | T1DM (n= 31) | | p value |
|---|---|---|---|---|---|
| **SEX** | N | % | N | % | |
| **MALE** | 20 | 66.66 | 18 | 60.00 | 0.96 |
| **FEMALE** | 13 | 39.39 | 12 | 40.00 | |

The age, height, weight, BMI and BSA were recorded in both the groups and mean value of HbA1c and the duration of disease in T1DM patients shown in Table 3.

**Table 3: Age and anthropometric data of healthy controls and type 1 diabetics**

| | Parameters | Controls n = 33 | T1DM n = 30 | P value |
|---|---|---|---|---|
| | | [Mean ± SD] | [Mean ± SD] | |
| 1 | Age [years] | 16.70 ± 1.66 | 16.63 ± 1.49 | 0.874 |
| 2 | Weight [Kg] | 52.42 ± 4.77 | 50.89 ± 9.55 | 0.433 |
| 3 | Height [cm] | 156.91 ± 4.47 | 154.64 ± 7.47 | 0.156 |
| 4 | BMI [$Kg/m^2$] | 21.25 ± 1.20 | 21.03 ± 3.40 | 0.736 |
| 5 | BSA [$m^2$] | 1.50 ± 0.08 | 1.46 ± 0.15 | 0.195 |
| 6 | HbA1c [%] | 9.81 ± 0.24 | ---- | ---- |
| 7 | Duration [years] | 5.06 ± 3.12 | ---- | ---- |

*p value < 0.05 Significant, **p value < 0.01 Highly Significant, ***p value < 0.001 Very Highly Significant

The mean resting heart rate[RHR], systolic blood pressure [SBP] & diastolic blood pressure[DBP] were recorded in both the groups as shown in Table 4.

**Table 4: Resting blood pressure and heart rate of controls and type 1 diabetics**

| PARAMETERS | CONTROLS (n= 31) | T1DM (n=33) | P value |
|---|---|---|---|
| HR (bpm) | 76.80 ± 12.23 | 86.76 ± 13.27 | 0.001** |
| SBP (mm of Hg) | 117.94 ± 10.88 | 110.79 ± 9.39 | 0.327 |
| DBP (mm of Hg) | 73.23 ± 8.68 | 69.61 ± 8.79 | 0.599 |

*p value < 0.05 Significant, **p value < 0.01 Highly Significant, ***p value < 0.001 Very Highly Significant

## COMPARISON OF PULMONARY FUNCTION TESTS BETWEEN CASE AND CONTROL GROUP

Since the prediction equations for spirometry and diffusion studies are different for males and females and also for subjects less than equal to 17 years and more than equal to18 years, both the control and T1DM groups were divided into 4 subgroups each as shown below.

| AGE [Years] | T1DM (n=30) | | CONTROL (n=33) | |
|---|---|---|---|---|
| | MALES (n=18) | FEMALES (n=12) | MALES (n=20) | FEMALES (n=13) |
| ≤17 | 9 [30%] | 9 [30%] | 8 [24.24%] | 8 [24.24%] |
| > 17 | 9 [30%] | 3 [10%] | 12 [36.36%] | 5 [15.15%] |

## SPIROMETRY

The mean recorded values of FVC, FEV1, FEV1/FVC %, PEF, MEF (MMEF25-75%), MEF 25%, MEF 50%, MEF 75% and SVC of both the groups are shown in Table 5 and Figure 2, 3&4. The recorded values of clinically relevant parameters FVC, FEV1, FEV1/FVC %, PEF, MEF (MMEF25-75%), MEF 25%, MEF 50% were also expressed as the percentages of their predicted values and are shown in Table 5. All the absolute values of spirometry parameters and their values expressed as percentage of predicted values in the T1DM group were lower as compared to the healthy subjects. The difference was highly significant (p value<0.000).

**Table 5: Recorded, predicted and %predicted values of spirometry of controls and T1DM.**

| | Parameters | Controls n = 33 | | | T1DM n = 30 | | | P value |
|---|---|---|---|---|---|---|---|---|
| | | Recorded [Mean ± SD] | Predicted [Mean ± SD] | % of predicted [Mean ± SD] | Recorded [Mean ± SD] | Predicted [Mean ± SD] | % of predicted [Mean ± SD] | |
| 1 | FVC [L] | 3.92 ± 0.75 | 3.24 ± 0.43 | 118.16 ± 13.77 | 2.71 ± 0.54 | 3.16 ± 0.53 | 86.27 ± 10.95 | 0.0001*** |
| 2 | $FEV_1$ [L/s] | 3.49 ± 0.7 | 2.90 ± 0.37 | 117.98 ± 14.59 | 2.10 ± 0.64 | 2.83 ± 0.46 | 74.03 ± 17.30 | 0.0001*** |
| 3 | $FEV_1$/FVC [%] | 89.11 ± 3.07 | 87.16 ± 1.69 | 102.26 ± 3.79 | 76.53 ± 12.05 | 86.94 ± 1.81 | 88.02 ± 13.74 | 0.0001*** |
| 4 | PEF [L/s] | 6.16 ± 1.21 | 6.68 ± 1.00 | 90.62 ± 9.96 | 3.73 ± 2.12 | 6.597 ± 1.10 | 55.71 ± 27.94 | 0.0001*** |
| 5 | MEF[L/s] | 4.96 ± 0.84 | 3.69 ± 0.28 | 132.20 ± 17.60 | 2.49 ± 1.30 | 3.64 ± 0.39 | 67.54 ± 31.77 | 0.0001*** |
| 6 | MEF25%[L/s] | 3.38 ± 0.90 | 1.85 ± 0.18 | 180.07 ± 40.24 | 1.59 ± 0.71 | 1.82 ± 0.24 | 87.40 ± 36.55 | 0.0001*** |
| 7 | MEF50%[L/s] | 4.96 ± 1.16 | 4.16 ± 0.64 | 117.37 ± 19.09 | 2.79 ± 1.42 | 4.07 ± 0.67 | 67.73 ± 28.51 | 0.0001*** |
| 8 | MEF75%[L/s] | 5.86 ± 1.06 | ---- | ---- | 3.44 ± 2.10 | ---- | ---- | 0.0001*** |
| 9 | SVC [L] | 3.79 ± 0.76 | ---- | ---- | 2.53 ± 0.69 | ---- | ---- | 0.0001*** |

*p value < 0.05 Significant, **p value < 0.01 Highly Significant, ***p value < 0.001 Very Highly Significant

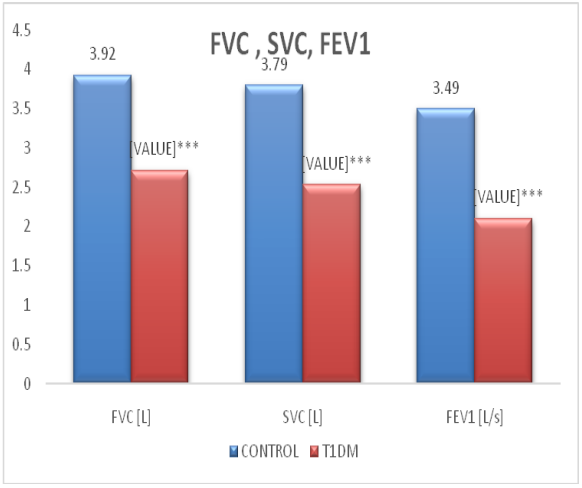


**Figure 2 : Recorded values of FVC, SVC, FEV1 in controls and T1DM**

*p value < 0.05 Significant, **p value < 0.01 Highly Significant, ***p value < 0.001 Very Highly Significant

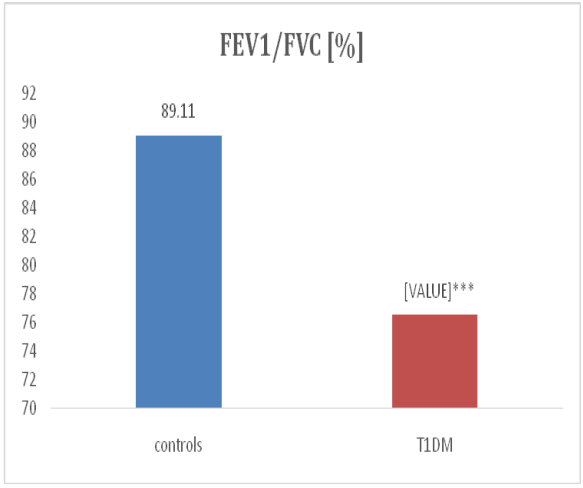


**Figure 3: Recorded values of FEV1/FVC in controls and T1DM.**

*p value < 0.05 Significant, **p value < 0.01 Highly Significant, ***p value < 0.001 Very Highly Significant

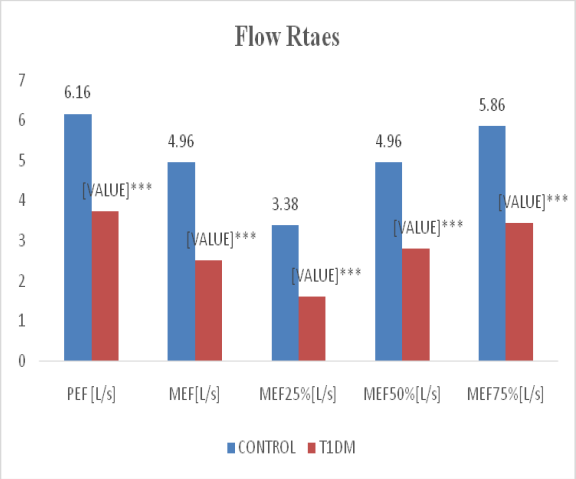


**Figure 4: Recorded values of flow rates in controls and T1DM.** *p value < 0.05 Significant, **p value < 0.01 Highly Significant, ***p value < 0.001 Very Highly Significant

The values of Lower Limit of normal for different parameters were calculated for all the subjects of both the groups. All the spirometry values in males and females of different age groups were more than the lower limit of normal [LLN] values of different parameters in the control group.

In this study we have inferred the diabetic group to be having obstructive, restrictive or mixed pattern of spirometry on the basis of taking the cut off value as lower limit of normal [LLN] or 5$^{th}$ percentile, calculated for each individual case from the predicted values. Accordingly, we have observed values which are suggestive of obstructive spirometry pattern in five, restrictive spirometry pattern in five, and mixed respiratory pattern of obstructive and restrictive in ten patients. Ten patients demonstrated to be having normal pattern. [6,7,4] It has been strongly recommended to abandon the fixed cut offs and switching to a statistically valid LLN to define abnormality as given in ATS/ERS guidelines. [8] Therefore, percent predicted values can quantify the lung function parameters with respect to predicted values but can be misleading in making a diagnosis about the qualitative (normal, obstructive, restrictive or mixed disorder) nature of lung function. [6] The same are summarized in Table 6 and Figure 5.

**Table 6: T1DM cases showing different spirometry pattern according to their LLN**

| Spirometry pattern | | | | |
|---|---|---|---|---|
| **Obstructive** | **Restrictive** | **Obstructive +Restrictive** | **Normal** | **Total number of subjects [n]** |
| 5 | 5 | 10 | 10 | 30 |
| 16.16% | 16.16% | 33.33% | 33.33% | 100% |

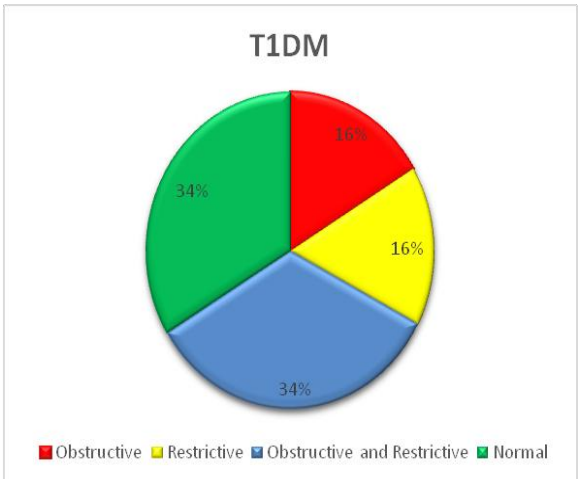


**Figure 5: T1DM cases showing different spirometry pattern according to their LLN**

## Diffusion Studies and Arterial blood gas analysis

The absolute values of TLCO, VA, KCO of both the groups are shown in Table 7 and Figure 6. The predicted values and the percentages of predicted values of TLCO, VA, KCO could not be calculated for adolescents less than 18 years as regression equations for predictive values for children and adolescents less than 17 years are not available for North Indian population. Therefore, absolute values of both the groups were compared. All the absolute values of diffusion study parameters in the T1DM group were lower as compared to the healthy subjects. The difference was highly significant (p value<0.000).

The Arterial blood gas studies showed pH and $PCO_2$ values in T1DM to be comparable to the control [p>0.05]. While $PO_2$, and $PO_2$(a/A) were significantly lower [p <0.000] but P $O_2$(A-a) were significantly higher in T1DM group as compared to the

control [p <0.05]as shown Table 7 and figure 7.

**Table 7: Recorded values of diffusion study and arterial blood gases**

| | Parameters | Controls n=33 | T1DM n=30 | P value |
|---|---|---|---|---|
| | | Recorded [Mean ± SD] | Recorded [Mean ± SD] | |
| 1 | TLCO[ml/mmHg/min] | 28.77 ± 4.46 | 22.75 ± 5.44 | 0.0001*** |
| 2 | VA [L] | 4.47 ± 0.68 | 3.84 ± 0.82 | 0.002** |
| 3 | KCO[ml/mmHg/min/L] | 6.47 ± 0.79 | 5.90 ± 0.61 | 0.002** |
| 4 | pH | 7.41 ± 0.21 | 7.41 ± 0.19 | 0.824 |
| 5 | $PO_2$ [mmHg] | 90.65 ± 4.03 | 84.55 ± 5.71 | 0.0001*** |
| 6 | $PCO_2$ [mmHg] | 41.93 ± 1.31 | 41.76 ± 1.36 | 0.615 |
| 7 | $PO_2$(A-a) [mmHg] | 15.63 ± 2.76 | 18.87 ± 6.45 | 0.015* |
| 8 | $PO_2$(a/A) | 87.11 ± 3.13 | 81.98 ± 5.64 | 0.0001*** |

*p value < 0.05 Significant, **p value < 0.01 Highly Significant, ***p value < 0.001 Very Highly Significant

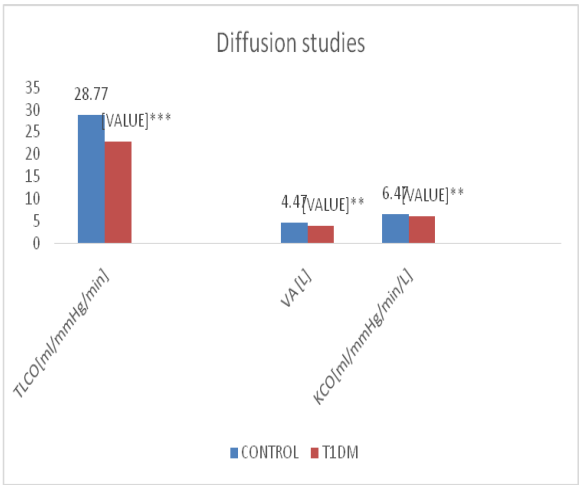


**Figure 6: Recorded diffusion studies values in T1DM and controls**
*p value < 0.05 Significant, **p value < 0.01 Highly Significant, ***p value < 0.001 Very Highly Significant

## DURATION OF DISEASE AND PFT

There was no statistically significant correlation of any of the pulmonary function tests with duration of disease when calculated for the T1DM group.

However, to further analyze the relationship between duration of disease and PFTs in TIDM, the group was divided on the basis of duration of disease into two groups, ≤ 5 years and >5 years, as shown in Table 8, 9,10.

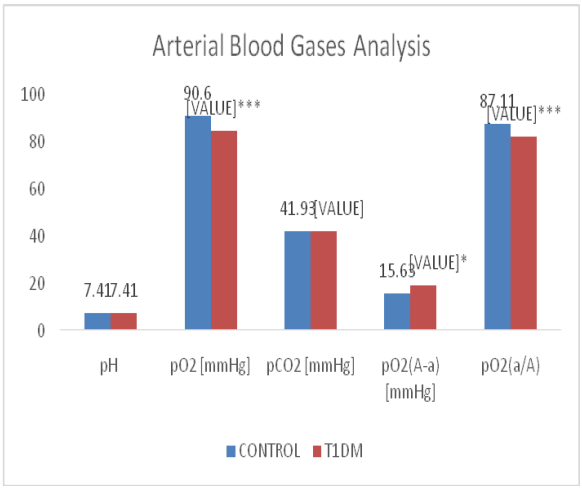


**Figure 7 : Recorded Arterial blood gases analysis values in T1DM and controls**
*p value < 0.05 Significant, **p value < 0.01 Highly Significant, ***p value < 0.001 Very Highly Significant

**Table 8: Anthropometry parameters, HbA1c and duration of disease in subgroups made on the basis of HbA1c in ≤ 5 years and > 5 years in T1DM.**

| | Parameters | T1DM duration ≤ 5 year n=19 | T1DM Duration > 5 year n=11 | P value |
|---|---|---|---|---|
| | | [Mean ± SD] | [Mean ± SD] | |
| 1 | Age [years] | 16.68 ± 1.42 | 16.55 ± 1.69 | 0.298 |
| 2 | Height [cm] | 153.89 ± 7.16 | 155.94 ± 8.16 | 0.876 |
| 3 | Weight [Kg] | 50.43 ± 9.28 | 51.69 ± 10.42 | 0.841 |
| 4 | BMI [$Kg/m^2$] | 21.24 ± 3.35 | 21.20 ± 3.58 | 0.754 |
| 5 | BSA [$m^2$] | 1.46 ± 0.14 | 1.49 ± 0.17 | 0.515 |
| 6 | HbA1c | 10.14 ± 2.45 | 9.27 ± 2.32 | 0.342 |
| 7 | Duration | 3.16 ± 0.90 | 8.36 ± 2.84 | 0.287 |

*p value < 0.05 Significant, **p value < 0.01 Highly Significant, ***p value < 0.001 Very Highly Significant

**Table 9: Spirometry parameters in subgroups made on the basis of duration of disease in ≤ 5years and > 5 years in T1DM.**

| | Parameters | T1DM duration ≤ 5 year n=19 | T1DM Duration > 5 year n=11 | P value |
|---|---|---|---|---|
| | | [Mean ± SD] | [Mean ± SD] | |
| 1 | FVC [L] | 2.71 ± 0.50 | 2.72 ± 0.64 | 0.652 |
| 2 | $FEV_1$[L/s] | 2.14 ± 0.59 | 2.05 ± 0.75 | 0.853 |
| 3 | $FEV_1$/FVC [%] | 77.79 ± 12.19 | 74.37 ± 12.07 | 0.746 |
| 4 | PEF[L/s] | 4.09 ± 1.60 | 3.77 ± 1.71 | 0.816 |
| 5 | MEF[L/s] | 2.63 ± 1.32 | 2.27 ± 1.28 | 0.295 |
| 6 | MEF 25%[L/s] | 1.63 ± 0.69 | 1.53 ± 0.80 | 0.165 |
| 7 | MEF50%[L/s] | 2.91 ± 1.41 | 2.60 ± 1.50 | 0.274 |
| 8 | MEF75%[L/s] | 3.70 ± 2.19 | 3.00 ± 1.98 | 0.638 |
| 9 | SVC [L] | 2.65 ± 0.73 | 2.54 ± 0.78 | 0.719 |

*p value < 0.05 Significant, **p value < 0.01 Highly Significant, ***p value < 0.001 Very Highly Significant

**Table 10:** Diffusion parameters and arterial blood gases parameters in subgroups made on the basis of duration of disease in ≤ 5years and > 5 years in T1DM.

| | Parameters | T1DM duration ≤ 5 year n=19 | T1DM Duration > 5 year n=11 | P value |
|---|---|---|---|---|
| | | [Mean ± SD] | [Mean ± SD] | |
| 1 | TLCO[ml/mmHg/min] | 22.10 ± 4.63 | 23.88 ± 6.72 | 0.762 |
| 2 | VA [L] | 3.71 ± 0.61 | 4.10 ± 1.10 | 0.830 |
| 3 | KCO[ml/mmHg/min/L] | 5.94 ± 0.61 | 5.84 ± 0.64 | 0.439 |
| 4 | pH | 7.42 ± 0.02 | 7.42 ± 0.02 | 0.856 |
| 5 | $PO_2$ [mmHg] | 83.67 ± 5.38 | 86.08 ± 6.20 | 0.385 |
| 6 | $PCO_2$ [mmHg] | 41.35 ± 1.22 | 42.46 ± 1.35 | 0.492 |
| 7 | $PO_2$(A-a) [mmHg] | 20.02 ± 6.17 | 16.91 ± 6.76 | 0.782 |
| 8 | $PO_2$(a/A) | 80.78 ± 5.29 | 84.06 ± 5.89 | 0.925 |

*p value < 0.05 Significant, **p value < 0.01 Highly Significant, ***p value < 0.001 Very Highly Significant

The percent predicted values of all PFT parameters were lower in TIDM subgroup with duration of disease > 5 years as compared to that of with duration of disease ≤5 years, but this was not statistically significant (p>0.05).

**Table11: Correlation of HbA1c with spirometry parameters in T1DM subgroups with disease duration > 5 years**

| | **DURATION** | **HbA1C** |
|---|---|---|
| **Spirometry Parameters** | | |
| **FVC [L]** | **NS** | **NS** |
| FEV1 [L] | r= - 0.7215 p= 0.0148* | NS |
| FEV1/FVC% | r= - 0.7608 p= 0.0086*** | NS |
| MEF [L/s] | r= - 0.7808 p= 0.0066*** | |
| MEF25%[L/s] | r= - 0.6655 p= 0.0293* | NS |
| MEF50%[L/s] | r= - 0.7973 p= 0.0047*** | NS |
| MEF75%[L/s] | NS | NS |
| SVC [L] | NS | NS |

*p value < 0.05 Significant, **p value < 0.01 Highly Significant, ***p value < 0.001 Very Highly Significant

There was no significant correlation found between the percent predicted PFT parameters with duration of disease and HbA1C in the T1DM subgroup with disease duration ≤5 years. However, in T1DM subgroups with duration of disease > 5 years there was a significant negative correlation of HbA1c was observed with FEV1, FEV1/FVC%, MEF, MEF25%, MEF 50% and MEF75%.

## HbA1c LEVELS AND PFT

There was no statistically significant correlation of any of the pulmonary function tests with levels of HbA1c when calculated for the T1DM group. However, to analyze the relationship between HbA1c and PFTs in TIDM, the group was divided on the basis of HbA1c into two groups, those with HbA1c levels ≤ 8% years and > 8%.

The percent predicted values of FEV1, FEV1/FVC%, PEF, MMEF (25%-75%), MEF (50%) were lower in subgroup with HbA1c levels > 8%, when compared with subgroup HbA1c levels ≤ 8%, however the difference was not significant (>0.05).Also, there was no significant correlation found between the percent predicted PFT parameters with duration of disease and HbA1c in both the T1DM subgroups with HbA1c ≤ 8% and > 8%.

There was no significant correlation found between the diffusion study parameters with spirometry parameters. However, in T1DM group there was a significant positive correlation of KCO was observed with SVC as shown in Table 12

**Table 12: correlation of SVC with Diffusion parameters in T1DM**

| | SVC |
|---|---|
| Diffusion Parameters | |
| TLCO[ml/mmHg/min] | NS |
| VA [L] | NS |
| KCO[ml/mmHg/min/L] | r= 0.042<br>p= 0.02* |

## DISCUSSION

Type 1 Diabetes Mellitus (T1DM) is one of the most common chronic endocrine disorders of childhood and adolescence. There is paucity of data from the Indian subcontinent in this regard more so in the younger (children and adolescents) population.

**Anthropometric Parameters:**

We have observed lower values of anthropometric parameters (height, weight and BMI, BSA) in T1DM group as compared to the controls. However, the difference was not statistically significant.

**Resting heart rate and systolic and diastolic blood pressure:**

In our study we observed a significantly higher resting heart rate in T1DM.Increased resting heart rate [RHR] is a well-documented finding in diabetes mellitus. Resting tachycardia and a fixed heart rate are late findings in diabetic patients with vagal impairment. [9]

Increased RHR in T1DM indicates a decreased parasympathetic activity that leads to decreased vagal inhibition of heart. As a result of this there is a sympathetic overdrive leading to the increased resting heart rate in almost all age groups. [10]

**PULMONARY FUNCTION TEST**

Based on this study, it was evident that the pulmonary functions were decreased in T1DM individuals in comparison with age and sex matched non-diabetic subjects.

**Spirometry**

T1DM patients had significantly lower absolute and percent predicted values of FVC, FEV1, FEV1/FVC%, PEF, MEF25%, MEF50%, MEF75% and SVC in comparison to their matched normoglycemic group. These results were similar to the observations made in other studies which documented decreased spirometry parameters of PFT in patients of T1DM. [11-13]

A number of studies have been done in children and adults. In some of the studies the range of age group of diabetics included in various studies is very broad. Omer M Al Tayeb et al have studied lung functions in age group 5 years to 20 years without classifying their findings for children, adolescents and adults. Similarly, Suresh V et al [14] have studied lung functions including diabetics of age group from 7 to 28 years. In another study by Sankarasubbu et al [15] the patients included in the study were in the age group from 15 to 40 years. Qazi Rais Ahmed et al [16] included patients in the age group of 19 to 68 years and reported a restrictive pattern of decrement. However, in our study we have included only adolescent subjects (10 to 19 years), [17] to study the effect of DM on their lung functions.

Most of these studies have classified their diabetic patients as having an obstructive, restrictive or mixed spirometry pattern on the basis of values of FEV1 and FVC taken as less than 80% of predictive and FEV1/FVC ratio < 0.7 [14]

In this study in T1DM group, comparisons and interpretations of FVC, FEV1 and FEV1/FVC% and various flow rates with their respective LLNs, were suggestive of obstructive pattern in five, restrictive pattern in five and a mixed pattern of both obstructive and restrictive disease in ten diabetic subjects. Ten diabetic subjects showed spirometry parameters above the LLN values and a normal spirometry profile.

**Duration of disease, HbA1c and Spirometry:**

In our study, we observed no significant difference in the spirometry parameters measured in subgroup of patients having duration of disease ≤ 5 years and those having duration of disease >5 years. Both the subgroups had HbA1c levels more than 8% indicating towards a poor glycemic control. [18] In subgroup with disease duration > 5 years the lower PFT values were observed than those with disease duration ≤ 5 years. Though not significant statistically this does indicate towards a subclinical deterioration of PFTs which is setting in as disease duration increases.

No significant correlation was observed of duration of disease with any of the PFT values in both subgroups, as calculated independently. The reason for this could be due to a small sample size in both subgroups (n=19 in ≤5 year and n=11 in >5 year). Similar finding has been documented in a study by Maria Martin Frias et al, [5] and Salvatore Cazzato et al. [19] Both the studies have documented lower spirometry values in diabetic children as compared to controls but no significant correlations of PFTs with disease duration or HbA1c levels.

Interestingly, in subgroup of diabetic patients with disease duration > 5 year, we observed a statistically significant negative correlation of HbA1c with FEV1, FEV1/FVC%, MEF(25-75%), MEF 25% and MEF75%. Maria Martin Frias et al, [20] attributed the absence of correlation between duration of disease and glycemic control with PFTs, due to a good glycemic control and shorter duration of disease in her study group. As mentioned earlier the glycemic control was poor in both the subgroups of our studies and this could have been the reason of the correlation, despite of the sample size.

This is an important finding and indicates that with progression of disease with time subclinical derangement of PFTs is less in diabetics with lower levels of HbA1c or in other words a better metabolic control.

The same correlation between HbA1c and PFTs was not observed in patients with disease duration with less than 5 years.

In diabetic subgroups with HbA1c≤ 8% and > 8 %, there was no difference in the percent predicted values of any of the spirometry parameters. Ismail L Mohamad et al. [21] in their study of 60 T1DM and 50 normal children found lower values of FEV1 in children with poor glycemic control(HbA1C>8 %), as compared to those with good glycemic control. We could not document similar findings which could be attributed to a smaller sample size in our subgroups (n=9 in ≤8% and n=21 in >8%).

The duration of disease in the subgroup with HbA1c>8 % was not significantly different than the subjects with HbA1C <8 %. However, no significant correlation was found between HbA1c and duration of disease with any of the spirometry parameter in both the subgroups when analyzed separately. This again could be attributed to a small sample size in both subgroups.

**Diffusion Parameters and Arterial Blood gas analysis:**

DLCO, VA and KCO which determines the alveolocapillary permeability of the lung were significantly reduced in the diabetic group which revealed decline in pulmonary gas exchange in the diabetic group. This was consistent with the findings of other studies. [22,23] However, there is paucity of studies on diffusion parameters in Indian adolescents and in most of the studies they have been assessed in adults and T2DM cases only. [24-26] In other studies, wider age ranges have been included. [18,27-29]

There was no significant correlation found between the PFT parameters with diffusion studies in T1DM cases but we observed negative correlation of SVC with KCO in T1DM cases. It may be due to higher decrease in VA as compared to the decrease in TLCO in T1DM patients which results in increase in KCO. Decrease in VA could be due to the decreased lung volumes

and capacities and deranged recruitment of alveoli with inflation due to changes in lung mechanics in DM [21,22]

The $PO_2$ of arterial blood though within the normal range was significantly lower in T1DM group as compared with the normal. $PO_2$(A-a) was significantly higher and $PO_2$(a /A) was significantly lower in diabetic group. To the best of our knowledge hardly any studies have recorded the arterial blood gas parameters along with diffusion parameters while assessing the diffusion capacity of the lung. However, a lower $PO_2$ of arterial blood and $PO_2$(a /A) along with higher $PO_2$(A-a) has been reported by Vis Niranjan et al [30] while studying glycemic control and cardiopulmonary function in T1DM patients in adults in the USA.

The lower values of DLCO, VA and KCO along with a higher $PO_2$(A-a) as observed in our study are suggestive of decreased transfer of $O_2$ from alveoli to the arterial blood in adolescent diabetics. A lower $PO_2$of arterial blood and $PO_2$(a /A) also indicates towards the same.

No significant correlation was found of duration of disease and HbA1c levels with any of the diffusion parameters and the $PO_2$(A-a) and $PO_2$(a /A) in the group as a whole. The diffusion parameters and $PO_2$(A-a) and $PO_2$(a /A) were no different in subgroups made on the duration of disease (< 5 years and > 5years) and level of glycated Hb (≤ 8 % and > 8 %). The presence or absence of any correlation in diffusion studies with respect to duration or glycemic control in our study could be because we have analyzed the recorded values and not the percent predicted values due to non-availability of prediction equations in children less than 17 years for our demographic region due to paucity of data in diffusion studies in this age group. Another reason for no significant correlations could be due to small sample size of the main group and subgroups. Also, HbA1c reflects the glycemic level of the patient for the last 3 to 4 months this lack of correlation may not be surprising. As all the previous level of HbA1c were not available for a number of patients therefore it is difficult to comment about the quality of glycemic control of the group as a whole.

However, our study does indicate that diffusion parameters along with arterial blood gas parameters like alveolar-arterial gradient and ratio of partial pressure of oxygen are deranged in T1DM adolescents.

The obstructive, restrictive and mixed parameters observed in spirometry parameters. Altered lung mechanics due to restrictive changes in lung parenchyma and chest wall are well documented. [31] Pulmonary microangiopathy and altered alveolar membrane thickening as a result of collagen and elastin metabolism due to long term biochemical changes induced by chronic hyperglycemia are well documented. [32] Altered function and weakness of muscles of respiration like diaphragm and intercostal muscles due to altered muscle metabolism which may lead to restrictive spirometry patterns in diabetics from a very early stage. [33] Another very important factor which may cause an imbalance in normal bronchial tone and its reactivity is DAN which affects almost all organs and lungs are no exception. Spirometry may show decline within diabetic autonomic neuropathy as concluded by Peter Durdik et al [34] in their study on pulmonary function tests in T1DM adolescents with diabetic autonomic neuropathy.

Lower diffusion capacity parameters have also been documented and explained on the basis of long-term effects of hyperglycemia in T1DM cases. A deranged diffusion membrane due to thickening of alveolo-capillary membrane, along with compromised alveolar ventilation and decreased blood volume in the pulmonary capillaries can lead to a higher alveolar-arterial gradient of $PO_2$(A-a)and lower values of $PO_2$ and a lower arterial/alveolar $PO_2$(a/A) in arterial blood. [30] Obliteration of capillaries from microangiopathy reduces capillary blood flow volume and the surface area available for oxygen transfer. Post

mortem finding of centrilobular emphysema, patchy atelectasis, microangiopathy in septal capillaries and in alveolar and pleural arterioles indicate towards areas of ventilation-perfusion mismatch in diabetic lung. [35,36]

Thus, it can be said that though less investigated and less documented, DM affects the pulmonary system, as it affects any other organ in the body. The patients may not present clinically for symptoms specific to pulmonary system due to large reserve of lung function, but subclinical assault goes on, on the vasculature and parenchyma of the lung affecting the functions of the lung in terms of mechanics of breathing and diffusion of gases.

## CONCLUSION

All the absolute values of spirometry parameters and their values expressed as percentage of predicted values in the T1DM group were lower as compared to the healthy subjects. The difference was highly significant (p <0.000).But there is no significant correlation observed of spirometry parameters with HbA1c and duration of disease in T1DM.

All the spirometry values in males and females of different age groups were more than the LLN values of different parameters in the control group. However, in the T1DM group, comparisons and interpretations of FVC, FEV1 and FEV1/FVC% and various flow rates with their respective LLNs were suggestive of obstructive pattern in five, restrictive pattern in five and a mixed pattern of both obstructive and restrictive disease in ten diabetic subjects.

All the absolute values of diffusion study parameters and their values expressed as percentage of predicted values in the T1DM group were lower as compared to the healthy subjects. The difference was highly significant (p value<0.000). But there was no significant correlation observed with HbA1c and duration of disease in T1DM.

The Arterial blood gas studies showed pH and $PCO_2$ values in T1DM were comparable to the control [p>0.05]. $PO_2$, and $PO_2$(a/A) were significantly lower [p <0.000] but $PO_2$(A-a) were significantly higher in T1DM group as compared to the control.[p value<0.000]

There was no significant correlation found between the percent predicted PFT parameters with duration of disease and HbA1c in the T1DM subgroup with disease duration ≤5 years. However, in T1DM subgroups with disease duration > 5 years shows significant negative correlation of HbA1c with FEV1, FEV1/FVC, MEF, MEF 25% and MEF 75%.

The percent predicted values of PFT were not significant in subgroup with HbA1c levels > 8%, when compared with subgroup HbA1c levels ≤ 8% (>0.05).

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