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EVALUATION OF PULMONARY FUNCTIONS IN TYPE 2 DIABETES MELLITUS AND ITS AGE AND GENDER SPECIFIC CHANGES ON POPULATION OF URBAN AND SUBURBAN AREAS OF KOLKATA: A HOSPITAL BASED STUDY

Physiology

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ABSTRACT

Background: Diabetes mellitus is a metabolic disease that causes secondary changes and complications in multiple organs and It has been suggested that pulmonary dysfunctions may be one of the earliest measurable non metabolic alteration in T2DM, the potential alteration of lung function status in diabetic patients need further attention.

Aims and Objectives: Assessment of pulmonary functions in Type 2 DM and to compare (if any) according to age groups, both sexes and urban-suburban population.

Methods: A total of 60 T2DM patients of age group 35-55years and 60 age and sex matched control were included after inclusion and exclusion criteria again sub grouped into Gr. A (age 35-45yr) and Gr. B (>45yr) according to urban and suburban population. PFT and DLCO were done. The PFT parameters were compared and correlated according to age, sex and urban-suburban population. $p<0.05$ was considered as significant.

Results: There was significant impairment of DLCO% (P=0.023) and DL/VA%(P=0.001) in Gr.B age>45years) and also negative correlation of DLCO%(r=—0.377) and DL/VA%(r=—0.475) with age. But changes in urban patients were insignificant in relation to suburban.

Conclusions: Age and gender specific impairment of pulmonary function and diffusion capacity in T2DM when compared with their matched control but no significant changes when it is compared between cases from urban and suburban populations.

KEYWORDS

Pulmonary function, Type 2 diabetes mellitus , Urban & Suburban

Introduction:

There is an alarming increase in the incidence and prevalence of diabetes mellitus particularly in Asian Indians[1]. Diabetes mellitus (DM) is one of the most common metabolic disorders affecting the functions of majority of body systems. Prevalence of complications such as micro- and macroangiopathy involving heart, kidney, eyes is also increasing, causing severe economic and social burden[2]. It has been suggested that pulmonary dysfunction may be one of the non metabolic alteration in diabetes[7]. The pathogenesis of diabetic complications are thought to involve both a microangiopathic process and non enzymatic glycosylation of tissue proteins and peptides of extracellular matrix at elevated circulating glucose level[2,3] Isotani et al[19] showed independent changes in pulmonary as a manifestation of pulmonary microangiopathy. Several biochemical processes result in impaired collagen and elastin cross linkage with a reduction in the strength and elasticity of connective tissuewhich can cause both vascular and non-vascular complications[2,4,5].The presence in the lung of an abundant connective tissues and an extensive microvascular circulations raise the possibility that lung may be a 'target organ' in type2 diabetes[7] affecting ventilation and diffusion capacity. In a Japanese study, the incidence of pulmonary pathology was found to be 50% on autopsy[8]. Several pathological changes affecting lung functions in T2DM may vary due to environmental factors, ethnic and anthropometric variations and also to gender. There may be differences in pulmonary functions between the population of urban and suburban areas possibly due to differences in socioeconomy and lifestyle and effects of pollution.

Aims and objectives:

1. Assessment of pulmonary functions in Type 2 DM of different age groups and both sexes.
2. To compare (if any) the pulmonary functions in Type 2 diabetes of urban and suburban population.

Materials and methods:

After proper ethical clearance, a comparative cross sectional hospital based study was conducted at the Dept. of Physiology, R.G.Kar Medical college & Hospital in the year 2011. All the patients of T2DM in this study were from urban and sub urban areas around R.G.Kar Medical College and Hospital and surrounding municipal areas of Kolkata on the north and east portions of the municipality and corporations of the city and surroundings.

Operational definitions:

Urban areas:[19]

All statutory places with a municipality, corporations, cantonment board or notified town areas committee etc.

A place satisfying the following 3 conditions simultaneously:

1. Minimum population is 5000
2. At least 75% of male working population engaged in non agricultural pursuits.
3. Density of population of at least 400/Km^2 (1000/$mile^2$).

Suburban areas :[19]

Surrounding and peripheral to the urban municipal areas are called suburban areas.

Eighty type 2 DM cases, were systematically selected from patients attending Diabetic clinic OPD, R.G.Kar Medical College & Hospital. Among them 60 cases were included following strict inclusion & exclusion criteria. Age & sex matched 60 healthy controls were included according to inclusion criteria. Type 2 diabetes of age group between 35 to 55 years of both sexes with duration not <2 years were included. For T2DM, age, family history, obesity, Basal insulin or C-peptide, CRP (in specific cases), complications at presentation were included

Criteria for diagnosis of type 2 DM: The National Diabetes Data Group and World Health Organization have issued diagnostic criteria for DM based on the following premises [2,10]

Following patients were excluded from the study:

Smokers; history of respiratory diseases such as asthma, COPD, tuberculosis, ILD; H/O occupational exposure; H/O URTI & LRTI; Hypertension, H/O angina; CVA; Obesity (BMI>30 kg/m^2); known thyroid disorders, autoimmune disease like SLE, RA; Known kidney diseases, Hereditary peripheral neuropathy; individuals with unacceptable spirometric technique, due to various causes like obstruction of teeth or tongue, sub-maximal effort, air escape, effort sustained for less than 6 seconds duration, failure to attain a plateau on volume time curve, recent surgery .

Detailed history and clinical examinations were done and blood sample after overnight fasting was taken for the Fasting plasma glucose and post prandial plasma glucose (by Glucose Oxidase Peroxidase method using kit developed by Aspen Laboratories Pvt Ltd)[10,11], glycated hemoglobin (HbA1C) level as an index of glycemic control (by Ion Exchange Resin method)[12]. Complete hemogram with hemoglobin level (as it influences on DLCO), base line lipid profile, serum urea, creatinine, Creatinine clearanc (by Cockcroft- Gault equation)[2] (in specific conditions), serum TSH, serum ANA, RF (for specific situations)

Spirometry: With the help of computerised electronic spirometer, RMS–HELIOS 401[13], flow sensitive and high performance computer based electronic spirometer and results of best of three maneuvers were taken. Normal value of FEV1 is above 80% and FEV1/FVC is 0.7-0.8. All the lung function parameters i.e., FVC, FEV1, FEV1/FVC, MMFR (25-75)/FEF25-75 and PEFR, were read as normal or abnormal when compared to predicted values.

Special investigation for diffusion of lung: (DLCO)

The DLCO of the subjects of this study were measured by single breath ($DLCO_{sb}$) method using computerized DLCO measuring machine, -INPIRE- HD–PFT[14]. Best of three satisfactory readings was taken for analysis. The technique was validated in our laboratory and the prediction equations for normal Indian subjects had been derived and reported previously[14,15]. Normal values are based upon age, height, ethnicity, and sex. A value is usually considered abnormal if it is less than 80% of predicted value[14,15].

Statistical analysis: Data were analyzed in SPSS software- version 17 (IBM, Chicago, Illinois, 2008)[16] with P value of <0.05 was taken as significant with 95% confidence interval.

Results and analysis:

Table 1: Comparison of PFT parameters between cases and controls:

Lung functions parameters	Cases Mean ± SD	Control Mean ± SD	P value
FVC –PP	77.75 (±5.655)	96.50(± 9.523)	0.0001*
FEV1-PP	81.31(±3.864)	97.50(±9.590)	0.0001*
FEV1/FVC –PP	102.97(±8.402)	104.25(±5.435)	0.011*
PEFR-PP	85.31(± 5.173)	94.56(±7.770)	0.009*
FEF-PP 25-75	82.83(± 4.934)	91.76(±6.955)	0.01 *
DLCO-PP	94.35(±18.635)	108.53(±13.128)	0.002*
DL/VA –PP	89.47(±12.636)	98.68(±7.890)	0.0001*

N.B. PP= Percent predicted

Significant (p<0.05) impairment of PFT parameters (FVC%pred, FEV1%pred, FEV1/FVC%, PEFR%pred, FEF25-75%) and Diffusion capacity (DLCO% and DL/VA%) in T2DM cases than controls but maximum deterioration was seen in FVC%(P=0.0001), DLCO% (P=0.002) and DL/VA% (P=0.0001)[Table 1]. There was increase in FEV1/FVC% in cases of T2DM, which showed a restrictive pattern in T2DM

Table 2: Distribution and grouping of cases according to age:

Sub Groups	AGE of the patient (years)	No of patient
Gr. A	35 -45	n=36(60%)
Gr. B	>45	n=24(40%)

Table 2 showing that maximum number(n=36) (60%) of paients belonged to age group between 35- 45 years(n=36)[Group A].

Table 3: comparative studies of PFT parameters between Group A & Group B

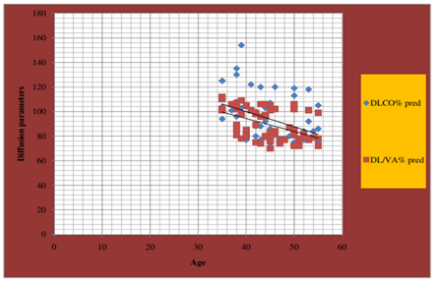
PFT parameters	Age Group of the Patients		P value
	Group A (35-45year)	Group B (>45year)	
FVC PP	78.75 (± 4.918)	76.25 (± 6.428)	0.094
FEV1 PP	81.88 (± 3.732)	80.45 (± 3.977)	0.162
FEV1/FVC PP	102.666 (± 8.298)	103.41 (± 8.717)	0.738
PEFR PP	86.02 (± 5.034)	84.25 (± 5.301)	0.195
FEF25-75 PP	83.08 (± 4.999)	82.45 (± 4.916)	0.635
DLCO PP	98.77 (± 19.170)	87.70 (± 15.965)	0.023
DL/VA PP	93.61 (± 12.290)	83.25 (± 10.608)	0.001

There is insignificant deterioration in PFT parameters (FVC%, FEV1%, FEV1/FVC%, PEFR% and FEF25-75%), where as DLCO% (P=0.023) and DL/VA%(P=0.001) were significantly decreased in Group B (age>45)(Table 3).

Table 4: Correlation of PFT parameters with Age of the patients

Age	Lung Function parameters						
	FVC-PP	FEV1-PP	FEVI/FVC-PP	FEF25-75-PP	PEFR-PP	DLCO-pp	DL/VA PP
Pearson correlation coefficient(r)	-.208	-.233	.038	-.223	-.225	-.377	-.475

Diagram1. Correlation of different variables related to pulmonary diffusion capacities with age



There were significant negative correlation of DLCO%(r=—0.377) and DL/VA%(r=—0.475) with increasing age

Table 5: Comparison of PFT among Female T2DM and Control

PFT parameters	Female		
	T2DM Cases Mean(± S.D.)	Controls Mean(± S.D.)	P value
FVC% pred	76.23(± 6.719)	90.833(±6.878)	<0.0001
FEV1% pred	80.36(± 4.334)	91.533(± 5.309)	<0.0001
FEV1/FVC%	106.03(± 6.95)	104(± 6.051)	0.232
PEFR% pred	85.66(± 5.535)	93.133(±5.649)	0.0001
FEF25-75%pred	82.9(± 5.267)	95.933(± 6.480)	<0.0001
DLCO% pred	95.8(+ 19.245)	110.666(±13.481)	0.001
DL/VA% pred	86.83(± 12.437)	97.133(± 7.125)	0.0002

Table 6: Comparison of PFT among Male T2DM and Control

PFT parmeters	Male		
	T2DM Cases Mean(±S.D.)	Controls Mean(± S.D)	P value
FVC% pred	79.26(± 3.894)	102.166(± 8.412)	<0.0001
FEV1% pred	82.26(± 3.117)	103.466(± 9.235)	0.0001
FEV1/FVC%pred	99.90(± 8.711)	104.5(± 4.833)	0.014
PEFR% pred	84.96(± 4.852)	96(± 9.310)	0.0001
FEF25-75% pred	82.76(± 4.665)	87.6(± 4.530)	0.0001
DLCO% pred	92.9(± 18.215)	106.4(± 12.628)	0.0015
DL/VA% pred	92.1(± 12.484)	100.23(± 8.418)	0.0045

There was significant(P<0.0001) deterioration of Pulmonary function and diffusion capacity comparable in T2DM female from control female and also T2DM male from control male(Table 5 & 6).

Diagram 2: Geographical distribution of patients (Urban and Suburban)

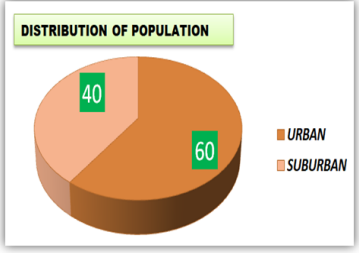


Table 7: Comparison of Pulmonary function parameters between Urban and Suburban Areas

PFT Parameters	Urban Patients	Suburban Patients	P value
	Mean±S.D.	Mean±S.D.	
FVC%predicted	76.83± 6.126	78.27±4.651	0.332
FEV1% predicted	80.94±4.326	82.13±2.833	0.240
FEV1/FVC%pred	101.83±9.656	104.95±5.652	0.159
DLCO%predicted	88.91±17.889	93.13±18.251	0.378
DL/VA%predicted	83.56±14.446	88.27±16.734	0.250

There were deterioration of lung function and diffusion capacity in urban from suburban T2DM patients, but insignificant (P>0.05)(Table 7).

DISCUSSION

The major findings of this study were significant alteration of pulmonary functions in Type 2 Diabetes and it was comparable among both male and female to matched control. Maximum number of paients belonged to age group between 35- 45 years..There were insignificant decrease in lung function with age and diffusion capacity was negatively correlated with age. There was insignificant impairment of PFT and diffusion capacity with urban T2DM patients also. Some studies[10,20] showed type 2 DM was more common in the age group of more than 40 years. The study conducted by Augusto A. Litonjua et al[21] found the decrease lung function with increase in age group which was consistent with our study. Ljubic S et al[4] also confirmed, the decrease in FEV1, FVC, FEF25-75 and DLCO with increase in age of diabetic patients which also support our study but Guvener N et al[22] concluded, an inverse correlation between diffusion of gases and increase age in diabetes. Gupta Bhavyesh et al,[23] who showed that the values of all lung functions were significantly ($P<0.01$) reduced in males diabetics but in females diabetics significant reduction ($P<0.05$) was observed only in PEFR and MVV.

The main pathophysiological mechanisms have established for underlying impaired Pulmonary functions in diabetes. Non enzymatic glycosylation of connective tissue, especially collagen and elastin, which might be responsible for end organ damage causing structural alterations including lung tissue (thickened alveolar epithelial and pulmonary capillary basal lamina) leading to reduced pulmonary elastic recoil, lung volume and limitation in airflow. Thus ventilation is affected[5,7].

Diabetic polyneuropathy impairs respiratory neuromuscular function, Phrenic nerve conduction time was comparable between diabetic patients and control in several studies and axonal loss of phrenic nerve is the most likely mechanism to explain the reduced diaphragmatic strength, thus affecting pulmonary volumes[9,17]. All these may contribute to impaired pulmonary function in a restrictive pattern.

Pulmonary diffusion capacity for carbon monoxide (DLCO) estimates the transfer of oxygen from alveolar gas to red blood cells. A combination of increased thickness of respiratory membrane and basal lamina, reduced pulmonary blood volume (V/Q mismatch), modification of surfactant activity and altered affinity of HBA1c to carbon monoxide may impair the diffusion capacity in diabetes[4,6].

Gupta Bhavyesh et al,[23] in their study showed a change in lung functions parameters in suburban and rural patients of Northern India. In our study, there was mild and insignificant change in PFT parameters in urban patients, probably the patients taken from urban and suburban areas were homogeneous in respect of age, sex, socioeconomic status and BMI. but, Diffusion capacity significantly deteriorates possibly due to increase disease burden in urban population, enrolment of maximum complicated T2DM patients in parts of urban areas of Kolkata, increase mechanical and epithelial injury to the lung due to environmental pollution, increased systemic inflammation reduction in antioxidant defenses and increase in oxidative injury of lung tissues[24].

But, how air flow limitation, other PFT parameters and DLCO correlated with duration of DM, HBA1c and microangiopathies remain to be ascertained in our population.In conclusion, There was age and gender specific impairment in pulmonary function and diffusion capacity in Type2 DM patients when compared with matched control. A significant impairment of pulmonary function and diffusion capacity established in T2DM with increase in age and a moderately negative correlation was seen with age of the patients but changes are insignificant between urban and suburban patients.

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