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COMPARISON OF PULMONARY FUNCTIONS AND DIFFUSION CAPACITY IN TYPE 2 DIABETES MELLITUS WITH OR WITHOUT COMPLICATIONS : A HOSPITAL BASED STUDY IN EASTERN INDIA

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ABSTRACT

Background: Diabetes mellitus is a systemic disease that causes secondary metabolic changes involving kidney, eyes, nerve, heart and vasculature causing severe social burden. Considering large microvasculature and abundant connective tissues, pulmonary system is prone to be affected in diabetes.

Aims and Objectives: To compare the parameters of Pulmonary functions and diffusion capacity in Type2 Diabetes with or without complications.

Methods: A total of 60 T2DM patients with or without complications of age group 35-55years and 60 age and sex matched control were included after inclusion and exclusion criteria. All subjects were evaluated for PFT by RMS HELIOS 401 and Diffusion capacity (DLCO) by single breath technique- INSPIRE HD –PFT) and status of microangiopathies were evaluated by microalbuminuria for nephropathy, by clinical examination and autonomic studies for neuropathy and Ophthalmoscopy for retinopathy. $p<0.05$ was considered as significant.

Results: There was significant($P=0.0001$) reduction in FVC% in complicated T2DM and also reduction in diffusion capacity (DLCO% and DL/VA%) in Type2 diabetes cases having microangiopathic complications which is significantly (0.0001) comparable.

Conclusion: There was significant impairment of Vital capacity and diffusion capacity of lung with restrictive pattern in Type2 diabetes with microangiopathic complications compared to T2DM without complications.

INTRODUCTION:

Diabetes mellitus is a systemic disease that causes secondary metabolic changes in multiple organs and the pathophysiologic complications such as micro- and macroangiopathy involving kidney, eyes, nerve, heart and vasculature deteriorating these systems are responsible for large morbidity and mortality of the disease and also causing severe social burden [1,2]. The pathogenesis of diabetic complications are due to non-enzymatic glycosylation of tissue proteins of extracellular matrix, leading to microangiopathic process of vasculatures at elevated circulating glucose level [2,4,24] and a biochemical processes result in impaired collagen and elastin cross linkage with a reduction in the strength and elasticity [2,5,24]. The common microangiopathic complications are retinopathy, nephropathy and neuropathy. "Diffuse thickening of the basement membrane", the most consistent morphological change of DM are evident in the capillaries of skin, skeletal muscle, retina, renal glomerular and renal medulla[23,24]. The presence of an extensive microvasculature and abundant connective tissue raises the possibility that lung might also be a target organ due to diabetic complications[3,4]. It has also been suggested that pulmonary dysfunction is a non metabolic complication in T2DM and prone to damage microvasculature affecting ventilation and diffusion[4,5,6]. Diabetic nephropathy is due to hemodynamic alterations in the renal microcirculation (glomerular hyperfiltration, increased glomerular capillary pressure), and structural changes (increased extracellular matrix, basement membrane thickening, mesangial expansion, fibrosis)[1,12]. The pathophysiologic mechanisms invoked in nonproliferative retinopathy include loss of retinal pericytes, increased retinal vascular permeability, alterations in retinal blood flow, all of which lead to retinal ischaemia[1]. The appearance of neovascularization in response to retinal hypoxia is the hallmark of proliferative diabetic retinopathy[1,23,24]. The pathophysiological background responsible for impaired respiratory neuromuscular function in association with diabetic polyneuropathy has not yet been conclusively investigated. The neuropathic process in diabetic patients is predominantly due to axonal loss rather than demyelination [8,17]. The wide range of geographical and regional differences of lung functions and diffusion studies of lung exist in India with T2DM. We intended to assess and compare the pattern of changes of pulmonary functions between T2DM patients with or without microangiopathic complication.

AIMS AND OBJECTIVES

1. To compare the Pulmonary functions and diffusion capacity of lung in Type2 diabetes patients with or without microangiopathic complications.

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 collaboration with Dept. of Medicine, Dept. of Biochemistry in the year 2011. Eighty type 2 DM cases, were systematically selected from patients attending Diabetic clinic OPD, R.G.Kar Medical College. Among them 60 patients with or without complications were included following strict inclusion & exclusion criteria. Type 2 diabetes of age group between 35 to 55 years of both sexes with duration not <2 years 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].

For T2DM, age, family history, obesity, Basal insulin or C-peptide, CRP (in specific cases), complications at presentation were included.

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,

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)[9,10], glycated hemoglobin (HbA1C) level as an index of glycemic control (by Ion Exchange Resin method)[11]. Complete hemogram with hemoglobin level (as it influences on DLCO), serum urea, creatinine, Creatinine clearanc (by Cockcroft- Gault equation)[1] (in specific conditions), serum TSH, serum ANA, RF (for specific situations)

Special investigation for diabetic nephropathy:

Microalbuminuria estimation: Diabetic nephropathy was evaluated by Microalbuminuria in urine. Microalbuminuria is defined as 30–300 mg/d in a 24-h collection or 30–300 mg/mg creatinine in a spot collection (preferred method)[1,12]**.** In this study the albumin/creatinine excretion ratio was measured on morning spot urine in each subjects by using micoprotein kit (Pyrogallol Red method)[12].

Investigation for diabetic retinopathy:

Ophthalmoscopy: An experienced ophthalmologist performed the direct ophthalmoscopic examination on the patients. According to the ophthalmoscopic findings retinopathy was defined as mild to moderate nonproliferative, severe nonproliferative and clinically significant macular edema[1,23,24].

Diabetic Neuropathy was assessed by taking symptoms, neurological examination and autonomic neuropathy studies and criteria.

Pulmonary Function test: [Spirometry]

Pulmonary functions were measured by the flow sensitive and high performance electronic spirometer, model-RMS Helios-401 in accordance with the standards of lung function testing of the American Thoracic Society(ATS) [13]. Standard spirometric measures included, forced vital capacity (FVC), forced expiratory volume in one second FEV1, the ratio of forced expiratory volume in one second to forced vital capacity (FEV1/FVC), forced expiratory flow rates (FEF25%-75%) and peak expiratory flow rate(PEFR). Results of best of three maneuvers were taken. Normal value of FEV1 is above 80% and FEV1/FVC is 0.7-0.8.

Special investigation for diffusion of lung: (DLCO)

The Diffusion capacity for Carbon momoxide (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 analysed in SPSS software version17(IBM, Chicago, Illinois, 2008) [16] with P value of <0.05 was taken as significant with 95% confidence interval

RESULT AND ANALYSIS:

Table1: Distribution of patients according to the complication of diabetes.

Diabetes with complication (n=30)	Diabetes without complication (n=30)
50%	50%

We had taken equal no (n=30) of patients having microangiopathic complication and not having any microangiopathic complication.

Table2: Comparison of Lung function parameters in T2DM with complications and without complications.

PFT% predicted(pp) value	T2DM with microangiopathy	T2DM without microangiopathy	P value
FVC%%pred	**75 ±6.062**	**80.50 ± 3.559**	**0.0001**
FEV1%pred	80.36 ±4.350	82.26 ± 3.095	0.056
FEV1/FVC%pred	**107.33 ±5.856**	**98.60 ± 8.360**	**0.0001**
PEFR%pred	84.63 ±6.019	86 ± 4.152	0.310
FEF25-75%pred	82.20 ± 5.868	83.46 ± 3.775	0.324
DLCO%pred	**81.70 ± 7.470**	**107 ± 17.878**	**0.0001**
DL/VA%pred	**81.83 ± 8.554**	**97.10 ± 11.451**	**0.0001**

There is gross and significant(P=0.0001) decrease in FVC%pred., DLCO%pred. and DL/VA%pred. in T2DM with microangiopathic complications.There is also an increase in FEV1/FVC%pred. inT2DM with complications.

DISCUSSION

Diabetes mellitus (DM) is a metabolic disease characterized by absolute or relative insulin deficiency that causes secondary pathophysiological changes in multiple organ systems. The pathophysiological changes causing chronic complications are thought to involve both a microangiopathic process due to thickening of vascular endothelium and a non-enzymatic glycosylation of tissue proteins (AGEs) and extracellular matrix[1,4,5]. Diabetic microangiopathy in kidneys, nerves, eyes have frequently been studied but the pattern of pulmonary complications of diabetes have been poorly evaluated . As the prevalence of diabetes is increasing, and lung has an abundant vasculature, the potential implication to evaluate and compare the pulmonary complications demand further attention.

From this study, we could say that pulmonary function (decrease FVC%, increase FEV1/FVC) showing restrictive pattern and diffusion capacity (DLCO%, DL/VA%) impaired significantly in T2DM with microangiopathic complications compared to without complications.

The findings of this study were not almost same to previous studies[2,3,7,18]. But, in larger population based study, Davis M.E. Timothy et al, studied the pulmonary function and its association with Type-2 diabetes mellitus and showed an average decrease of 9.5%(68ml/year) in FVC, an average decrease of 10.5% (84ml/year)in FEV1 and an average of 8.5% (17ml/year)decrease in PEFR in T2DM study group[19]. An Indian study [7] reported that the mean value of uncorrected DLCO was significantly lower in patients with type-2 DM with microangiopathy as compared to those without microangiopathy and healthy controls. Few other studies[6,18] have observed only correlation between diffusing capacity and microalbuminuria. and spirometric values did not differ in the diseased and healthy controls. Asanuma *et al* [20], reported a significantly lower FVC in diabetics and a decreased diffusing capacity. In contrary, Bulbou *et al* [21] did not find any correlation between reduced diffusion capacity in diabetes with complications.

Diabetes mellitus causes abnormalities two structural components leading to the development of abnormalities in the pulmonary function such as a reduction in the vital capacity and ventilation, TLC, lung compliance, reduction of central and peripheral air flows [22]. Axonal loss of phrenic nerve in diabetic polyneuropathy, myopathic processes causing changes in muscle fibre composition, reduced capillary density in skeletal muscles[8,17,25]. All these lead to restricted ventilation in T2DM.

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[3,5,6].

In addition, autonomic neuropathy has been shown to affect respiratory function by impairing hypoxic ventilatory drive [25].

A small sample size and non-measurement of TLC, cross-sectional study with no follow-up are the limitations of the present study. Further, compliance measurements of the lung, and correlation with specific complication need to evaluate.

In conclusion, our study had shown an impairment of ventilation and diffusion capacity of lung in diabetic patients having microangiopathic complications.

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