ABSTRACT

Background & Objectives: Diabetes mellitus (DM) is a significant public health problem worldwide which is associated with hormonal, metabolic and micro vascular abnormalities. The angiopathic complications affect eyes, kidneys, nervous, cardiovascular and respiratory system, which are primarily due to biochemical alterations in connective tissue. Materials & Methods: In this study, we included 100 subjects, 50 Diabetic (25 Male and 25 Female) and 50 (25 Male and 25 Female) healthy individuals aged 30-55 years. The pulmonary function tests were performed by the computerized spirometer in the Clinical Physiology Lab, Department of Physiology, Dr. PSIMS & RF, Chinnavutapalli. Results: The results of our study showed a statistically significant reduction in FEF50%, FEF75% & FEV1 /FVC ratio in diabetic male subjects when compared with control male subjects (p< 0.0001) and diabetic female subjects showed a reduction in FEV1/FVC which is not statistically significant (p = 0.0004) but we observed a statistically significant reduction in FEF50% & FEF75% in diabetic female subjects when compared with control female subjects (p< 0.0001). On spirometry, Diabetic subjects showed a significant reduction in FEV1/ FVC ratio, FEF 50%, FEF 75% relative to non diabetic controls. Conclusion: We conclude from our study that diabetic subjects showed impairment in lung function. We found a decrease in FEV1/FVC ratio, FEF50% and FEF75% in diabetic subjects as compared to control subjects.

Keywords: Diabetes, Forced Vital capacity, Forced expiratory Volume, Forced Expiratory Flow

INTRODUCTION

Diabetes is a systemic disease that produces changes in the structure and function of several tissues. The pathogenesis of diabetic complications involves both microangiopathic process and non-enzymatic glycosylation of tissue proteins. This process results in biochemical alterations in connective tissue constituents leading to impaired collagen and elastin cross-linked with a reduction in strength and elasticity of connective tissue, also, due to a non-enzymatic glycosylation of proteins 1. Presence of an abundant connective tissue in the...
lungs and an extensive microvascular circulation can be the possible cause of lung to be a ‘target organ’ in diabetic patients. Due to increase in the incidence and prevalence of DM particularly in Asian Indians, it is essential to study pulmonary function in patients having type 2 DM and examine their correlation with microangiopathic complications. Several clinical studies have suggested a possible association between pulmonary function abnormalities and diabetic renal microangiopathy and retinopathy. Changes in pulmonary diffusing capacity for carbon monoxide (DLCO) as a manifestation of pulmonary microangiopathy have been reported. Defective pulmonary function in asymptomatic diabetic patients is more prevalent than generally recognized involving 60% of adult cases.

Autopsy findings in human diabetic subjects and experiments in rats with diabetes, have included thickening of the alveolar epithelia, pulmonary capillary basal lamina, centrilobular emphysema, and pulmonary microangiopathy. These anatomical changes may be due to the biochemical alteration of connective tissue constituents caused by a non-enzymatic glycosylation of proteins and peptides induced by chronic high circulating glucose. Tests of lung mechanical function include measurement of lung elasticity, airflow resistance, and forced spirometric pulmonary function tests. Diabetes has been inconsistently associated with spirometric abnormalities in a number of small retrospective cross-sectional studies, involving even fewer than 50 subjects. Alterations such as hyperglycaemia, oxidative stress from auto-oxidation of glucose, non-enzymatic protein glycosylation, and alterations of nitric oxide (NO) metabolism have been reported as metabolic markers of the diabetic state. The source of free radicals in diabetes is not fully understood, but glycation of proteins can lead to oxidative stress by direct release of O₂ and H₂O₂ and activation of phagocytes through a specialized receptor for advanced glycation end products. Oxidants include reactive oxygen species (ROS), reactive nitrogen species (RNS), sulfur centered radicals and others. Phagocytic cells generate large amounts of NO and other ROS. Peroxynitrite (ONOO⁻) is formed when NO reacts with superoxide (O⁻). This reaction occurs rapidly and promotes the nitration of biomolecules including protein tyrosine residues. Peroxynitrite anion and peroxynitrous acid (ONO/OH) can freely pass through lipid membranes and can mediate oxidation, nitration, or nitrosation reactions. Peroxynitrite is more than two orders of magnitude more potent than H₂O₂ in catalyzing lipid oxidation in vivo. During diabetes, there are also disturbances in antioxidant defense systems evidenced by alterations in antioxidant enzymes, impaired glutathione metabolism and decreased ascorbic acid levels.

The pathophysiologic connection between diabetes and lung function was explained by a possible pro-inflammatory stimulus of hyperglycemia causing impaired lung function through increased intrapulmonary inflammation and apoptosis. Another possible cause of impaired lung function could be increased sclerosis of bronchial arteries as a consequence of generalized arteriosclerosis in diabetes. Diaphragm elevation with increased closing volume and decreased FVC in absence of detectable bronchial obstruction is another possible cause of impaired lung function.

MATERIALS & METHODS

In this study, we included 100 subjects, 50 Diabetic (25 Male and 25 Female) and 50 healthy individuals (25 Male and 25 Female) aged 30-55 years, after obtaining their consent. An approval was obtained from Institutional Ethical committee. Individuals were classified as having diabetes (as per the criteria Adapted from American Diabetes Association Criteria 1997), if any of the following criteria were met: fasting glucose level of at least 7.0mmol/lit (126mg/dl); non fasting blood glucose level at least 11.1
mmol/lit (200mg/dl); current use of anti diabetic medication.

**Inclusion criteria:** The persons who had never smoked and without any self reported respiratory complaints or any history of respiratory diseases.

**Exclusion criteria:** Individuals with heavy smoking, Alcohol intake, Anemia, Malnutrition, productive cough, Exertional dyspnoea, and cardiovascular diseases, Individuals with chronic lung diseases (like pulmonary TB, Bronchial asthma, Chronic Bronchitis, etc), Individuals who had undergone Abdominal & Chest surgery, Kypho scoliosis, Pectus carinatum, Pectus excavatum, Occupational diseases like Pneumoconiosis.

Procedure: The pulmonary function tests were performed by Computerized Spirometer model RMS Helios 401 in the Clinical Physiology Lab, Department of Physiology, Dr. PSIMS& RF, Chinnavutapalli. First FVC was recorded using the Helios spirometer as per the instructions. For SVC test same procedure is followed but the subject is instructed to take a deep breath followed by deep exhalation. Both inhalation and exhalation should be performed to the maximum extent but slowly. After this patient was instructed to take few gentle and normal breaths. For MVV test patient was asked to breathe deeply and quickly through the mouthpiece for 12-15 sec. The maneuver should imitate rapid breathing during exercise. Fasting blood glucose levels are estimated by using NIPRO Diagnosis Blood Glucose Monitoring System.

**Statistical analysis:** The statistical analysis was performed using Graph Pad Prism – 5.0 Version. As the analysis is done between the groups, UNPAIRED T – TEST was used.

**RESULTS**

Table: 1. Comparison of Mean Values of FEV1/FVC, FEF50% and FEF75% in Male, female subjects

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>CONTROL</th>
<th>DIABETIC</th>
<th>P-value</th>
<th>CONTROL</th>
<th>DIABETIC</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1/ FVC</td>
<td>82.4± 1.63</td>
<td>79.5± 1.87</td>
<td>0.0001</td>
<td>80.4± 1.35</td>
<td>78.9± 1.40</td>
<td>0.0004</td>
</tr>
<tr>
<td>FEF50% (L/sec)</td>
<td>3.8± 0.31</td>
<td>3.0 ± 0.50</td>
<td>0.0001*</td>
<td>3.8± 1.24</td>
<td>2.6±0.33</td>
<td>0.0001*</td>
</tr>
<tr>
<td>FEF75% (L/sec)</td>
<td>1.26± 0.13</td>
<td>1.02±0.20</td>
<td>0.0001*</td>
<td>1.2±0.12</td>
<td>0.9± 0.11</td>
<td>0.0001*</td>
</tr>
</tbody>
</table>

When compared with Control male subjects, the Diabetic male subjects showed a reduction of mean FEV1/ FVC ratio by 3.51 % (i.e.,2.9) , a reduction of mean FEF50% by 21.05 % (i.e., 0.8 L/s) and a reduction in the mean FEF 75% by 19.04 % (i.e., 0.24 L/s ). When compared with Control female subjects , the Diabetic female subjects showed a reduction of mean FEV1/ FVC ratio by 3.48 % (i.e.,1.8) , a reduction of mean FEF50% by 31.57% (i.e., 1.2 L/s) and a reduction in the mean FEF 75 by 25% (i.e., 0.3 L/s ).

On spirometry, the Diabetic subjects showed a significant reduction in FEV1/ FVC ratio, FEF 50%, FEF 75% relative to non diabetic controls. The results of our study showed a reduction in FEV1 /FVC ratio in diabetic male subjects when compared with control male subjects which is statistically significant (p< 0.0001 ) and also ,

diabetic female subjects showed a statistically significant reduction in FEF50% (p value < 0.0001). The results of our study showed a statistically significant reduction in FEF75% in diabetic male subjects when compared with control male subjects (p< 0.0001) and the diabetic female subjects also showed a reduction in FEF75% (p< 0.0001) which is statistically significant. (Table-1)

DISCUSSION

A lot of studies dealing with the problem of lung dysfunction in diabetes mellitus are cross-sectional, with the inclusion of a small number of patients suffering either from insulin-dependent diabetes mellitus (type I) or type II diabetes mellitus. Diabetes mellitus has an impact on the mechanical and microvascular function of the lung and influences ventilatory control. Numerous studies of lung function in diabetic subjects have shown slightly decreased indices of forced expiration and lung volumes in both type I and type II diabetes mellitus. Lange P, Groth S, Kastrup J et al.,13 conducted study to find the relation between diabetes mellitus, forced vital capacity and forced expiratory volume in one second. They observed that diabetic subjects in all age groups showed an impairment of lung function. The forced vital capacity (FVC), forced expiratory volume in one second (FEV1) and forced mid-expiratory flow are reduced by 8–20% with a moderately restrictive defect without airway obstruction 14,15,16. Other studies failed to show significant differences between patients with diabetes and normal controls in spirometric lung function tests17, 18. The Cardiovascular Health Study19 in determining reference standards for a healthy population, found diabetes to be significantly associated with a decreased FEV1. In the Framingham Heart Study20, diagnosis of DM was associated with a greater reduction in FVC than FEV1, suggesting a restrictive pathology. On the contrary, when those with diabetes on therapy were excluded, higher levels of fasting blood glucose were associated with larger reduction in FEV1 than FVC. The resulting progressive decrement in residual FEV1/ FVC ratio with increasing level of blood sugar suggests that higher fasting blood sugar was associated with more obstructive physiology. In the Fremantle Diabetes Study 21 reduced spirometric lung function was observed in patients with type 2 diabetes. Goya wannametthee S, Gerald Sharper A, Ann Rumley et al 22 prospectively studied the relationship between lung function, risk of type-2 diabetes. They opined that inflammation may be the cause for these associations. They concluded that Restrictive rather than obstructive impairment of lung function is associated with incident type 2 diabetes. Ali M.O, Begum S, Begum N et al.,23 conducted studies to observe the relation between different lung function parameters in type 2 diabetic patients. They concluded that the ventilatory function of lung may be reduced in type 2 diabetes which may be related to the duration of the disease. Mohhamed Irfan, Abdul jabbar, Ahmed Suleman Haque et al 24 studied about the pulmonary function in Diabetics. They observed impaired lung function, independent of Smoking in diabetics. The results of our study were in accordance with this study. The decline of FEV1 and FVC in diabetic individuals is similar to that observed in non-diabetic subjects in certain longitudinal studies 25. Few studies have been conducted for investigating respiratory muscle function in diabetes mellitus. DLCO was used to study pulmonary vascular changes. Even though some studies showed no defects in diabetes mellitus 26, the majority of studies reported reduced diffusing capacity among diabetic patients 27. Carmela Maiolo, Ehab I Mohamed, Angela Andreoli 28 conducted studies to assess the relation between Body Fat Distribution & reduced pulmonary function in obese Type 2 Diabetic adult women. They concluded that the DLCO and respiratory muscle
function explain the relationship between pulmonary dysfunction and body composition. A potential mechanism that explains the finding of decreased lung function was decreased muscle strength in diabetic subjects because of defective muscle metabolism \(^2\) or it may be due to inflammatory origin.

**CONCLUSION**

The cause for the decline in lung function in diabetes remains unclear. Taking into consideration of increased prevalence of lifestyle-related chronic diseases like diabetes, the complications for patients with diabetes, with overt pulmonary diseases claim special attention. To study the possible pathophysiological mechanisms further research is needed. Our study has several limitations. First, there were less number of subjects. So we cannot generalize the result in different groups i.e., diabetic and control groups. Secondly, we did not measure DL\(_{CO}\) in our subjects. Several studies showed a reduction in DL\(_{CO}\) in diabetic subjects, also in subjects with normal spirometric values. Lung function should be monitored regularly to know the degree of impairment in diabetic or pre-diabetic subjects.

**ACKNOWLEDGEMENT**

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