

RESTRICTIVE PULMONARY DYSFUNCTION IN PATIENTS WITH TYPE-2 DIABETES MELLITUS

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ABSTRACT

Objective: To evaluate the frequency of restrictive pulmonary dysfunction in patients with Type-2 diabetes Mellitus, irrespective of their Body Mass Index, profession and anti-Diabetic Medication.

Material and Methods: This descriptive, cross sectional, single center study was conducted in department of medicine, Khyber Teaching Hospital, Peshawar, Pakistan from March 2012 to March 2013. Total 460 patients, with mean age of 50 ± 1.26 years, were enrolled in the study by non-probability consecutive sampling. After taking informed consent and recording the demographic profile of the patients, diagnosis of restrictive pulmonary dysfunction was established by performing pulmonary function tests using digital spirometer. Data was entered into Microsoft excel 2007 and analyzed using SPSS.

Results: Among 460 patients, 320 (70%) were male and 140 (30%) were female. Restrictive pulmonary dysfunction was recorded in 120 (26%) patients, while 340 (74%) patients had no dysfunction in study group. Out of 120 patients with restrictive pulmonary dysfunction, 88 were male and 32 were female. Mean duration of Type-2 diabetes Mellitus was 22 ± 2.14 years and there was a clear correlation of restrictive pulmonary dysfunction with the duration of diabetes, having p-value of 0.003.

Conclusion: Restrictive pulmonary dysfunction is a well-known significant complication of Type-2 diabetes mellitus.

Key Words: Type-2, Diabetes Mellitus, Restrictive, Pulmonary, Dysfunction, Spirometer.

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INTRODUCTION

Type- 2 DM is the most common type of Diabetes and account for more than 92%, which is caused by insulin deficiency, insulin resistance or both¹. It effects every organ in the body and now there has been growing evidence "that pulmonary dysfunction occurs in diabetes mainly with the course of the disease". Many Respiratory factor like Vital Capacity (VC) may play role in insulin resistance and need serious consideration in future. This has been confirmed in Fremantle Diabetes study, which shows "that in a cohort of 125 follow-up cases with type-2 Diabetes mellitus (T2DM), 23.2% had Forced Expiratory Volume in 1 second (FEV 1) values <70% and VC value <80% without evidence of any prior respiratory diseases."^{2,3}

In patients with T2DM, there is significant decrease in Peak Expiratory Flow (PEF), FEV1 and Forced Vital Capacity (FVC) with the duration of disease being compared with their normal matched control⁴. In the same way, patient having T2DM had significantly lower FVC (97 vs. 104%, $P < 0.001$) and FEV1 (93 vs. 97%, $P < 0.001$) than those having no diabetes. It has been seen in the result of another study "that FVC decrease faster in adults with T2DM than in their normal counterparts (65 vs 59 ml/year, $P = 0.01$)⁵. It is concluded that reduction in different Spirometric value in T2DM and expression of adhesion molecule which causing stiffness of pulmonary vasculature and endothelial damage is quite significant and may be future predictors of death in these patients.⁶

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In spite of such significant effects of T2DM on PFTs, there is very limited research data available both nationally and internationally. To fill this gap, this study was conducted to correlate the duration of T2DM with PFTs. By this we can enhance patients care and reduce their morbidity by protecting lung from the adverse effects of T2DM as their potential target organ.

MATERIAL AND METHODS

This detailed study was conducted in Medicine Department, KMC/KTH, Peshawar, from March 2012 to March 2013. Total 460 patients, having T2DM for a minimum period of 11 and plus years were selected by non-probability consecutive sampling. The group age were 25 and plus years, comprising seventy percent males and thirty percent females patients. To avoid confounders, all patients with Kyphoscoliosis, gross chest deformity, concomitant interstitial lung disease, advanced malignancy; chronic renal and cardiac diseases were excluded from the study. The study design was descriptive- cross sectional.

After getting informed consent, total 460 patients with T2DM, which were fulfilling the criteria for inclusion and exclusion, who visited to the Medical Outdoor of Khyber Teaching Hospital, Peshawar were enrolled in the study in a consecutive manner. Approval was obtained from ethical committee in advance. Demographic information like names, gender and age were recorded and all information regarding patients were kept confidential. After explaining the risk and benefits to the subjects, PFTs was done using digital Spirometer. All patients having FEV1/FVC ratio > 80% and FVC < 80% of predicted values were labeled as having restrictive pulmonary dysfunction. All information and Data was put into Microsoft Office Excel 2007 and analyzed, by using SPSS statistical program. The data was expressed as mean and shown in tabulated form.

RESULTS

In these 460 studied cases, there was 320 (70%) male and 140 (30%) female, having mean age of 50±1.26 years with minimum age of 25 years. Out of these 460 patients, 36(8%) patients were 25-35 years old, 70(15%) patients were 36-45 years old, 184(40%) patients were 46-55 years old, 138(30%) patients were 56-65 years and 32(7%) patients were above 65 years of age.

Spirometric Value of all these was analyzed by measuring FEV1/FVC showing that 340(74%) patients have FEV1/FVC ratio was <80, and 120 (26%) patients have FEV1/FVC ratio >80. The Mean duration of T2DM was 22 years with standard deviation of ± 2.14, and relation of RPDs with duration of T2DM is shown in Table 1. RPDs was present in 120(26%) of the patients, while 340(74%) patients had no RPDs.

Associations of RPDs with different age group show that in all these 120 patients with RPDs, 18 were in age group of 36-45 years range, 56 were in age group of 46-55 years range and 46 were in age group of 55-65 years range. In all these 120 patients with RPDs, 86 were male patients 34 were female. Presence of RPDs in different sex is presented in Table 5.

Table 1: Correlation of RPDs with age

Age	Frequency and percentage
25-35 years	36(8%)
36-45 years	70(15%)
46-55 years	184(40%)
56-65 years	138(30%)
> 65 years	32(7%)
Total	460(100%)

Table 2: FEV1 / FVC Observation in study population

FEV1 / FVC Observation	Frequency and percentage
< 80	340(74%)
> 80	120(26%)
Total	460(100%)

Table 3: RPDs Association with duration of T2DM

RPDs Presence	11-21 Years	22-31 Years	>32 Years	Total
Yes	50	38	32	120
No	136	106	98	340
Total	186	144	130	460
P-value				0.003

Table 4: Correlation of RPDs, with different age groups

RPDs	25-35 years	36-45 years	46-55 years	56-65 Years	> 65 years	Total
Present	0	18	56	46	0	120
Absent	36	52	128	92	32	340
Total	36	70	184	138	32	460
P-value						0.002

Table 5: Restrictive Pulmonary Dysfunctions (RPDs) in different sex group

RPDs	Male	Female
Present	86	34
Absent	234	106
Total	320	140

DISCUSSION

Restrictive pulmonary Dysfunction as complication of T2DM is an emerging target for many researchers around the globe. Till now, many national and international cross-sectional studies have consistently

proved, "that adults with diabetes have less vital capacity than their non diabetic counterparts".⁸ In all 26% patients of our study with RPDs, about 09% had severe, 05% had moderate and 12% had mild dysfunction respectively, which were close to the study findings of Yeh, et al.⁵ Another study, conducted in a small cohort with age range of 45-64 years, to test the hypothesis, "that diabetes is associated with reduced lung function independently of known risk factors". While doing cross-sectional analyses, it was observed, "that middle-aged adults with type 2 diabetes had significantly lower FEV1/FVC, FVC% and FEV1% predicted compared with their non-diabetic counterpart". In prospective analyses, FVC declined faster in T2DM patients compared with age matched non-diabetic persons. These findings of our study are generally closely similar to another prior cross-sectional study by Ceglia et al.⁷. According to their findings, "FVC and FEV1 are significantly lower in T2DM as compared to normal population with the same age and sex. This is lower in those patients, who have prolonged duration of T2DM with complications requiring insulin treatment". Furthermore, in Non-diabetic population with same age and sex, they observed "that low value of FVC and FEV1 have some association with impaired Fasting Blood Sugar, hyper insulinemia and insulin resistance". Another study, conducted in Copenhagen Denmark by Lange Pet al followed 17506 Danish adults in the Copenhagen city heart study for 15 years.⁸ It was observed, "that at baseline FVC and FEV1 were consistently lower in diabetic individuals, with more than 8% difference between diabetic and non-diabetic". FVC declined in diabetic individuals annually at the rate of 24 ml and 39 ml in women and men respectively. In another nested case-control study by Lazarus R et al conducted on 352 T2DM male patients and 352 male normal individual with same mean age in Normative Aging study.⁹ The study showed that "individuals with diabetes had lower FEV1 and FVC at all time points and had annual 5.4 ml greater declines compared to control subjects". Another study conducted in Australia by Tiengo et al by monitoring 125 patients with T2DM from different states of Australia for a mean of 7 years.¹⁰ In this study "FVC and FEV1 continued to decline at annual rates of 68 and 71 ml respectively". Declines in FVC and FEV1 were more rapid in patients with higher baseline HbA1C. However, in this study there was no non-diabetic control group for direct comparison. Most of the studies in this connection are cross sectional. Some prospective studies, including the ARIC (the Atherosclerosis Risk in Communities) have been conducted which demonstrated that "reduced lung function is an independent predictor of T2DM incident".¹¹ It was shown that "associations between diabetes status and lung function were more significant cross-sectional than prospective". It also became evident from these results

that "abnormalities in lung function precede diabetes and then continue after its onset".

After the approval of inhaled insulin therapy for Diabetes Mellitus, this correlation between T2DM and RPDs is further highlighted. The meta-analysis of large RCTs for a minimum of 12 weeks period demonstrates greater decrease in FEV1 from baseline, among those taking inhaled insulin than the comparison group^{12,13}.

How T2DM causes RPDs is still debatable, but different clinical and pathological studies conducted in this connection have some reasonable explanation. These include, "hardening of basal lamina, thickening of mucous secretions, predisposition to chest infection and non-enzymatic glycosylation of chest and bronchial tree proteins". Oxidative stress present in T2DM patients can decrease respiratory and bronchial muscle working capacity, leading to RPDs¹⁴. This stress mechanism suggest that "The effects could be mediated by pro-inflammatory master regulator molecules which themselves might be subject to further inflammation by hyperglycemia and oxidative stress"^{15,16}.

Development of RPDs in diabetic patients is multifactorial. Some other very important factors like BMI¹⁷, generalized obesity¹⁸, waist circumference¹⁹, body composition and abdominal obesity²⁰, have shown profound affects on the pulmonary functions in different patients with diabetes, which has been confirmed by a number of studies and still needs further evaluation.

Limitations

Keeping in mind the demographic profile of the study population, "this study has certain limitations, which need to be addressed in a large community based studies as these may act as a confounder factor and may cause certain degree of Pulmonary Dysfunctions". Of these, currently some of them like BMI, waist circumference, Central obesity, life style and profession are very important and need large comparative studies. (Lecube A et al, 2010).

CONCLUSION

Type 2 DM is a chronic disorder of metabolism, affecting almost every system of the body including Respiratory system and RPDs are a well-known significant complication of T2DM".

RECOMMENDATIONS

Further clinical, physiological, pathological, genetic and molecular studies are needed to answer few commonly asked questions about the true nature and cause of RPDs in T2DM. Lungs should be considered as potential target organ for T2DM". However, future study is recommended.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

- Nizamuddin:** Data collection and typing.
Din JU: Idea and operating surgeon.
Khan B: Bibliography.
Wazir ZM: Statistics.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.