www.jmscr.igmpublication.org
Index Copernicus Value: 79.54
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v7i5.150

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Case Control Study on Pulmonary Function in People with Type 2 Diabetes Mellitus

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Abstract

Introduction and Objectives: *T2DM affects various organs of body causing micro and macrovascular disease. It is known to affect eyes, kidneys, heart, nerves and blood vessels, but its effect on lung which is a highly vascular organ, is not yet thoroughly studied. Previous studies have reported that PF are compromised in T2DM and histopathological changes have been observed in lungs in T2DM. The current study was planned to assess PF (FEV1, FVC, FEV1/FVC, PEFR, MMEFR) in T2DM patients using spirometry and to compare them with age and gender matched HV.*

Methods and Materials: *This was observational case control study in which 200 T2DM and 200 age and gender matched HV were enrolled. Subjects with history of smoking, any acute/chronic medical illness or on drugs which can alter PF were excluded from the study. Following detailed history, examination and routine investigations, all enrolled subjects underwent spirometry test to evaluate PF as mentioned above. Data analysis was done using SPSS software and data is presented as Mean ± SD. P value <0.05 was considered statistically significant.*

Results: *Data of 192(M:F::40:152) T2DM and 191(M:F::50:141) was analysed. Mean age of study subjects was 49 ±12; BMI was 25 ±6.0, waist circumference (M:F:: 93.10±11.16: 94.13±13.78). 35.92% patient had T2DM of 5-10 years duration and 48.5% had moderate glycemic control. Among T2DM, 45.83% had normal PF as assessed by spirometry,44.26% had restrictive, 3% had obstructive and 7% had mixed pattern of PF. HbA1c and duration of T2DM were found negatively correlated with PF.*

Conclusion: *The present study suggests that PF are deranged in T2DM and should be assessed with advancing T2DM to detect early PF changes in these patients. Future prospective study should be planned for involvement of lungs in T2DM independent of any lung disease.*

Keywords: *Pulmonary Functions (PF), Type 2 Diabetes Mellitus (T2DM), Healthy Volunteers (HV), Forced Expiratory Volume In 1 Sec (FEV1), Forced Vital Capacity (FVC), Peak Expiratory Flow Rate (PEFR), Maximum Mid Expiratory Flow Rate (MMEFR).*

Introduction

Diabetes mellitus is a chronic metabolic disorder of multiple etiologies. It is a major, rapidly growing public health care problem. According to WHO survey conducted in 2016, diabetes affects 422 million people in the world. The number is expected to double in 2030. T_2 DM contributes to 85-90% of the cases.

India holds second position after China with 69 million persons affected by diabetes and lays a daunting challenge to the sustainable development of the nation as almost every tenth adult (9.3%) in India is estimated to be affected by diabetes.[1] A recent report of WHO showed that every 26 per 100,000 persons die due to diabetes in India though it declined marginally and for males increased between 2000 and 2012.[2]

Diabetes affects various organ of body by micro and macro vascular diseases. It has a proven effect on eyes kidneys heart blood vessels and nerves[3,4]. Its effect on lungs (being a highly vascular structure) is not yet proved. Although various studies[5] have been conducted on patients with T_2 DM to study the effect of diabetes on lung function. The mechanism by which impaired glycemic control may lead to a defect in lung function is not certain, though it has been suggested in studies that the increased systemic inflammation associated with diabetes may result in pulmonary inflammation causing air way damage[6]. Therefore it is hypothesized that lung can also be a target organ in patients with diabetes.

Although pulmonary complications due to type 2 diabetes mellitus are not reported in diabetics but it has been seen in various studies that PF are compromised in patients with long standing T2DM[7]. The abundance of microvasculature in lungs makes it more prone for non enzymatic glycosylation of tissue protein as a result of tissue hyperglycemia which causes histopathological changes in basal lamina leading to impairment of diffusion through basement membrane in patients with type 2 diabetes mellitus[8]. Moreover duration of type 2 diabetes mellitus and glycemic control have varied impact on PF of these patients. In histopathological reports it has been shown that in diabetics basal lamina is thickened and fibrosed. There is impaired diffusion due to reduced pulmonary capillary blood volume and thickening of the basement membrane.

In Type 2 DM PF have been studied frequently in other countries, while from India there are not many studies on lung function abnormality in type 2 diabetes. Some authors have reported normal PF[9] while others have shown abnormal pulmonary function test in the form of obstructive or restrictive defects.

There is limited data concerning nature of abnormal PF in people with type 2 diabetes mellitus with conflicting results. Here hypothesized that Pulmonary Function Tests are impaired in people with Type 2 DM in Indian population. Therefore this study was planned to assess the PF in people with type 2 diabetes using spirometry and to compare the results with age and gender matched healthy controls.

Materials and Methods

This was a cross sectional case control study conducted in the department of medicine, Gandhi Medical College and associated Hamidia Hospital, Bhopal. The aim of study was to compare PF of patients with T2DM and age and gender matched healthy controls and to correlate the PF with duration of diabetes and HBA1c.After informed consent and detailed history and clinical examination, 200 diabetes and 200 healthy individuals were enrolled in the study.

Inclusion Criterion

1) Cases- Patients with type 2 diabetes mellitus
2) Controls- healthy individuals free from any other debilitating illness

Exclusion Criterion

1) Type 1 diabetes mellitus
2) Chronic smokers.
3) Type 2 diabetes mellitus patients with complications.

Interpretation of data and Statistical analysis

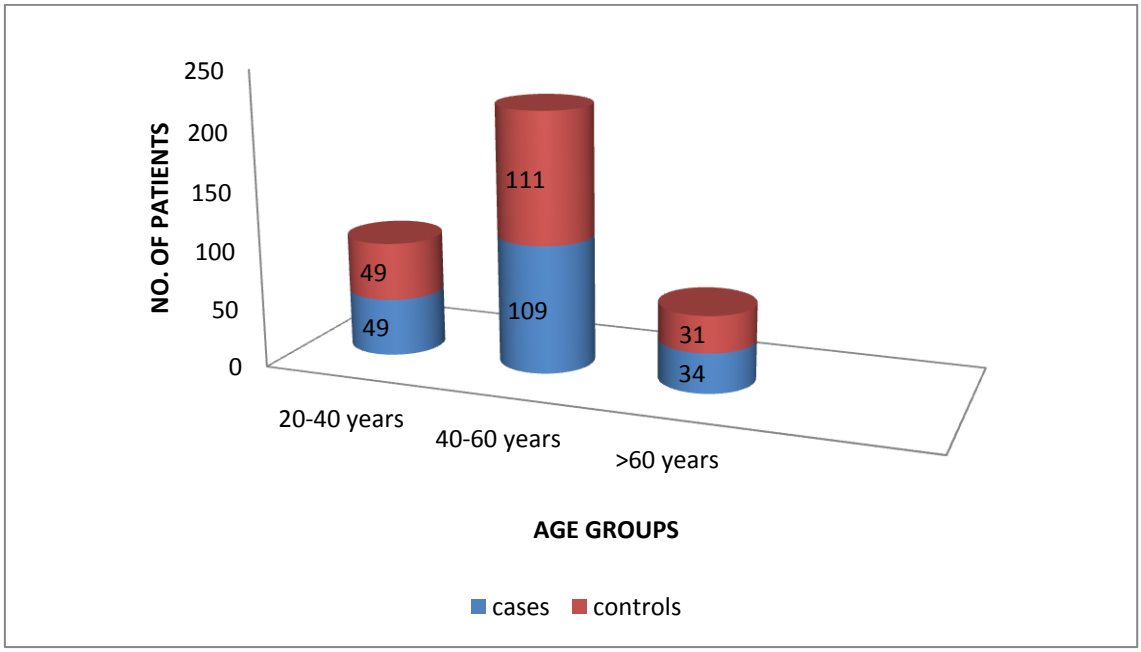
The subjects were selected for study after ruling out any coexisting illness (through history and routine investigation) which might affect PF. After that anthropomeric parameters like Height, weight, waist circumference and waist hip ratio was recorded and all individuals in case as well as in control groups performed spirometry using helios 401 spirometer. Descriptive summary

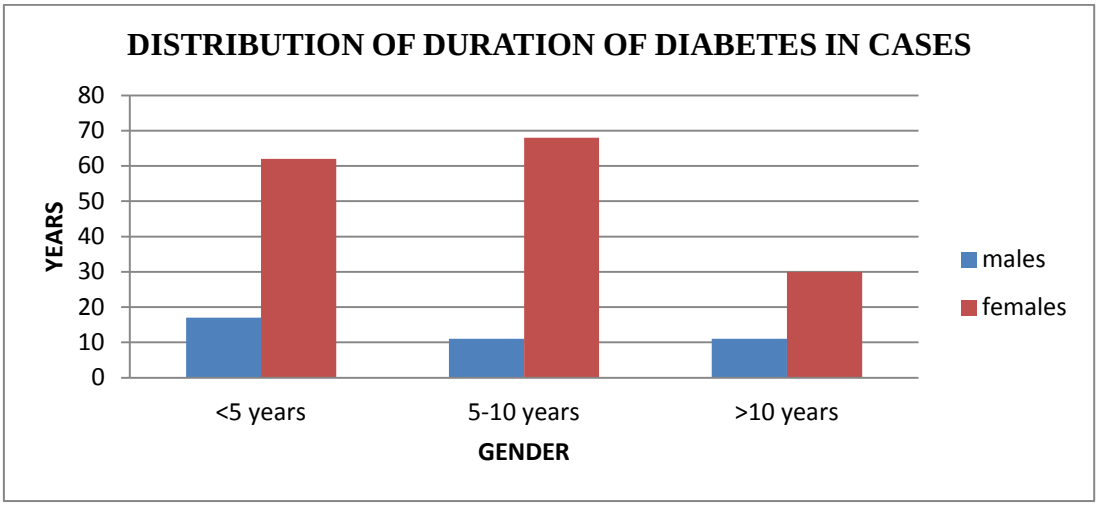
statistics were reported as mean and standard deviation for continuous variables, frequency and proportion for categorical variables. Pearsons Chi Square and Chi Square for trend were used to find the association between the categorical variables. Paired and unpaired t-test was used to find the associations for continuous variables. Correlation coeffiecient (r) was used to find out the correlation between lung function parameters and anthropometric measures like waist circumference and BMI. Scatter diagrams were used to visualise the correlation between these variables. The alpha was set at 0.05 with a power (beta) of 80%. A p-value of 0.05 was considered to be statistically significant. The data was entered in Microsoft Excel and was analysed using Statistical Package R

Results

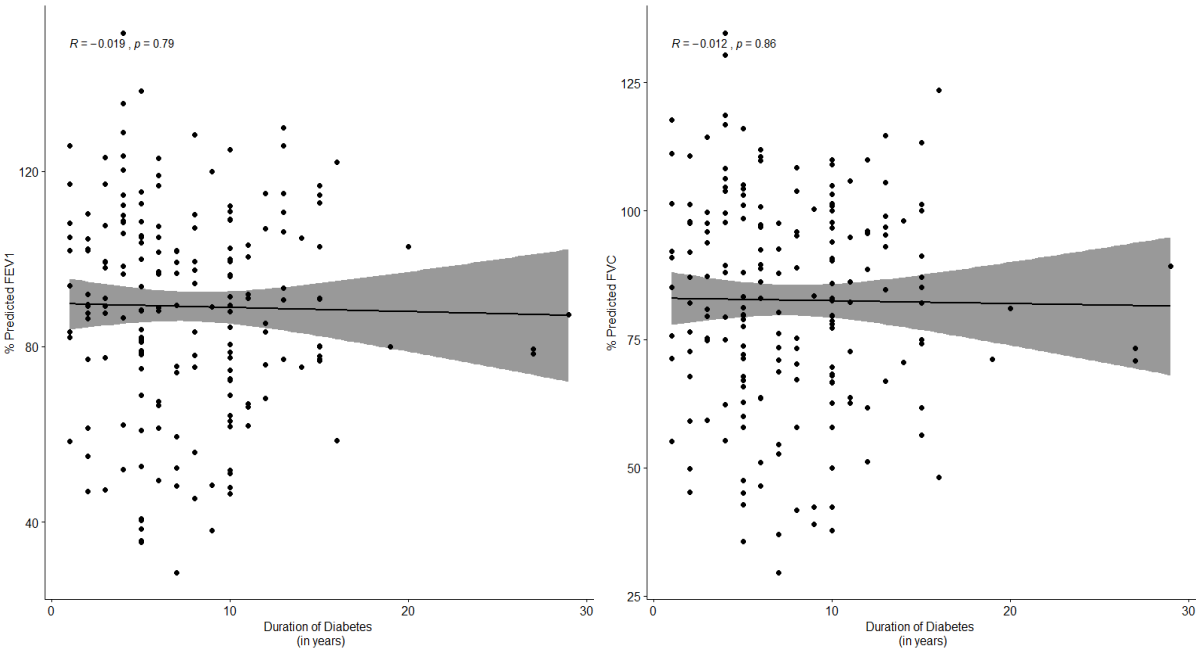
In the present study, Mean age of the patients in Cases and Control was 49.51±12.09 years and 48.42±12.15 years respectively (p=0.865). The distribution of gender among both the groups was comparable (P>0.05). BMI was higher among Cases (25.05±6.00) as compared to Control group (24.62±6.01kg/m2) (p=0.506). Maximum number of patients had T2DM for 5-10 years (male- 8.85%; female- 32.29%) followed by those who had diabetes for <5 years (male- 5.72%; female- 30.20%). Also maximum patients had Moderate control (6.5-8.5%) of HbA1c [97 (48.5%)] followed by good control [85 (42.5%)] whereas 18 (9%) patients had poor HbA1c control. Comparison of FEVI and FVC of both the groups revealed that in % predicted mean FEV1 was significantly lower among cases as compared to controls (p<0.001). Comparison of FEVI/FVC ratio among both the groups revealed that mean FEVI/FVC ratio was significantly higher among Cases (81.15±15.49) as compared to control (75.89±24.21) (p=0.014) suggesting restrictive pattern. Among cases 45.8% PF within normal limits. Remaining 44.2% of patients had restrictive changes, 3% had obstructive changes where as 7% of patients were found to have mixed blockage pattern of pulmonary functions. In this study FEV1(r=-0.421, p<0.001) and FVC (r=0.471, p<0.001) was negatively correlated with HbA1c.

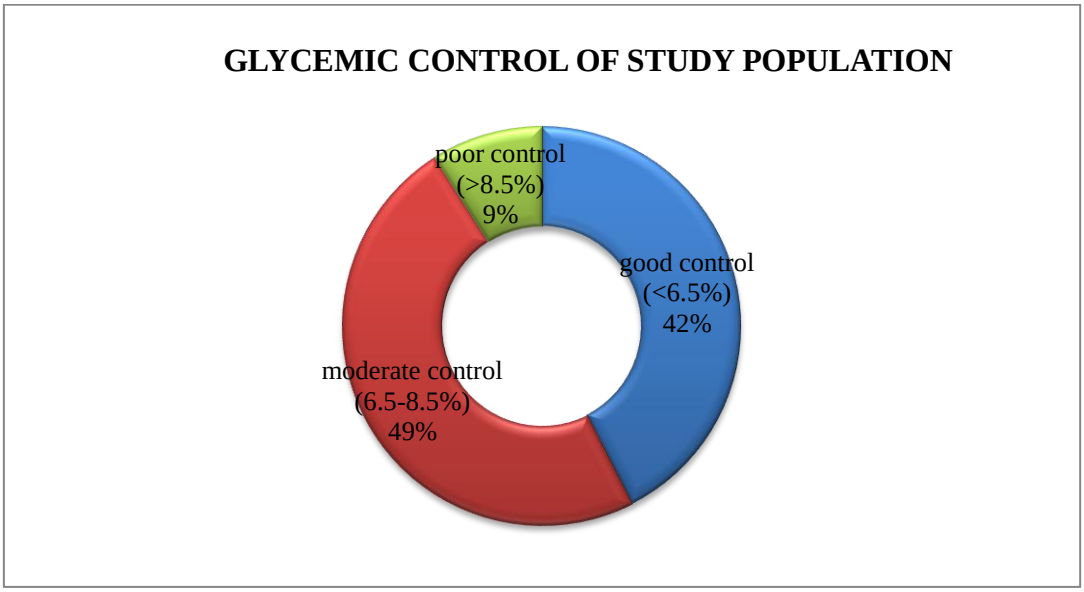
Age Wise Distribution of Participants in Case and Control Groups



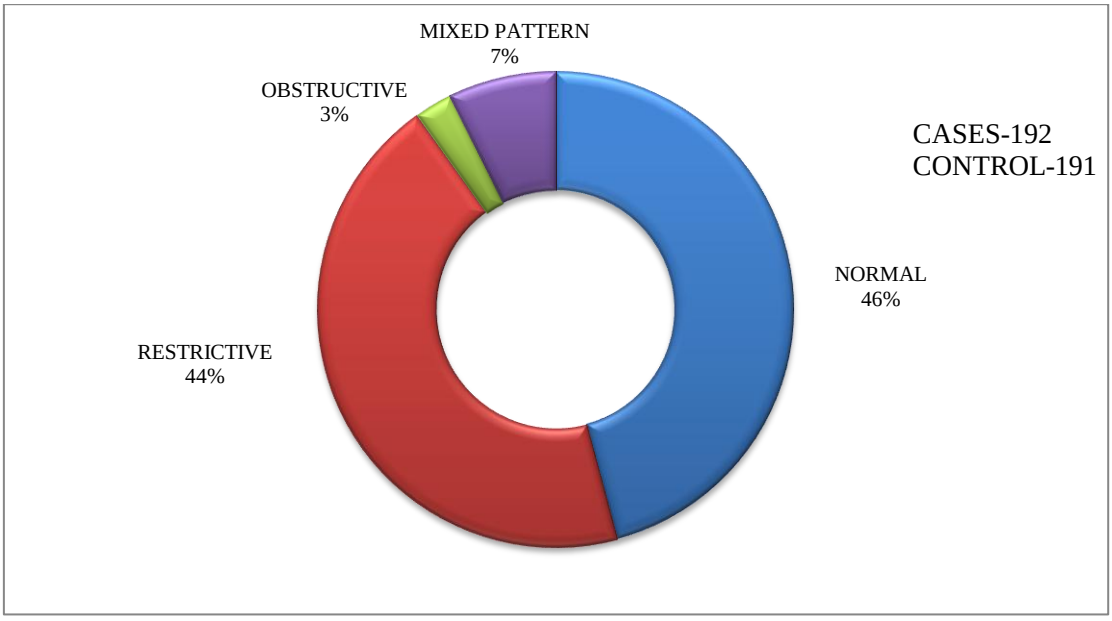


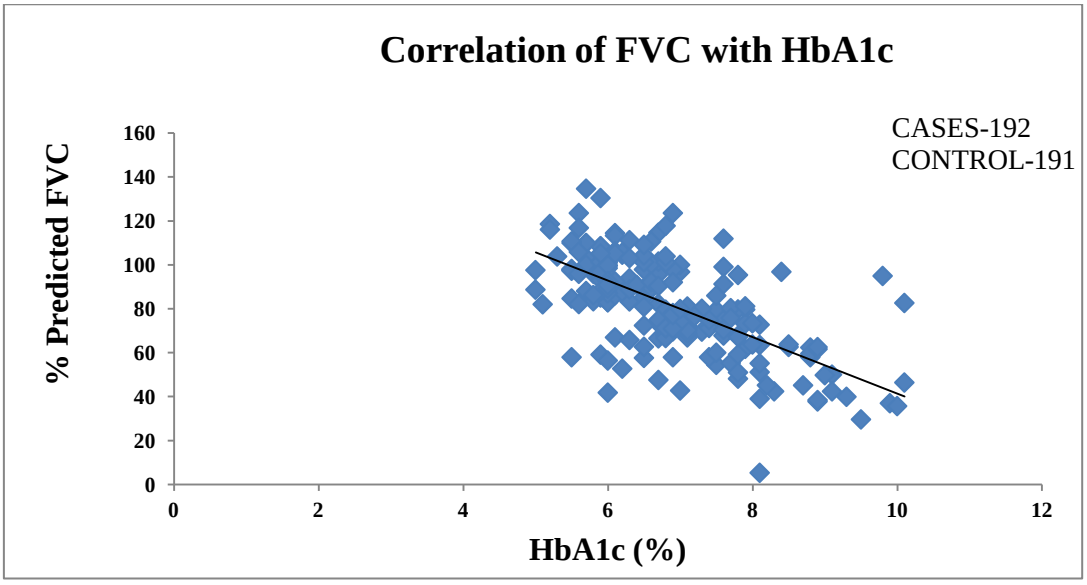
Distribution of duration of diabetes

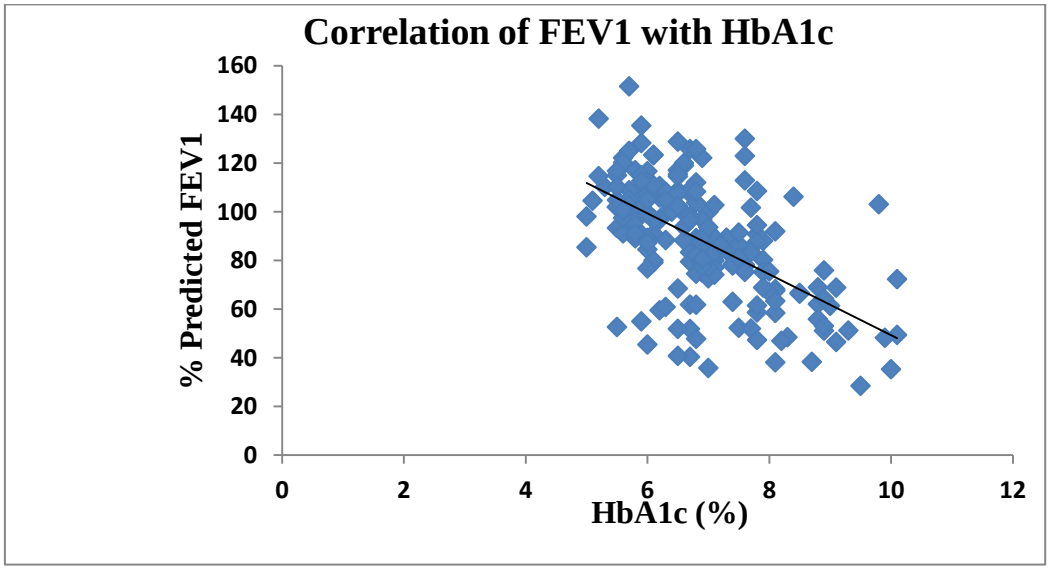




Pulmonary functions in patients with type 2 diabetes







Discussion

T2DM is long known for its effect on vascular organs of the body but lungs even though being highly vascular has not received any attention for affect of T2DM. In our study it was hypothesized that T2DM causes changes in the lung functions in the form of restriction, obstruction or mixed pattern or lung function may also remain normal. This was based on various studies performed which showed restrictive changes. The aim of our study was to assess lung functions of T2DM patients and to compare them with age and gender matched controls.

Age related decrease in the PF is observed in general population therefore it was necessary to match age of the two groups so that this confounding variables do not effect the results. In our study mean age of the patients in Case and Control group was 49.51±12.09 years and 48.42±12.15 years respectively, (p=0.865). In present study, among Cases and Control maximum were females [152 (72%) vs. 141 (72.77%)]. The distribution of gender among both the groups was comparable (P>0.05).

Maximum number of participant had normal range of BMI and it was comparable in both the groups. Aparna et al 2013[10] in their study had age and BMI matched participants in case and control groups. Comparable BMI in two groups nullify their variable affect on the study. Mean waist circumference of male (cases- 93.10±11.16; control-93.31±10.02) as well as female (cases-94.13±13.78; control-93.98±13.38) participants is in normal range. In Indian population waist circumference is more accurate marker of obesity as central obesity is more common in Indian population.

Cases in this study were classified on the basis of duration of diabetes. Maximum number of cases had diabetes for <5 years (female- 32.5%; male-8.8%) , followed by those who had diabetes for 5-10 years (female- 30%; male 7.2%).only 15% females and 7 % male cases had diabetes for more than 10 years

Cases in our study were classified on the basis of HbA1c level into good control (<6.5%) moderately controlled (6.5-8.5%) and poorly controlled (>8.5%). Maximum participants [94(48.5%)] had moderate control of HbA1c followed by good control [85 (42.5%)] whereas 17 (9%) patients had poor HbA1c control.

All the participants in the study performed spirometry to assess the PF. Patients with diabetes had decreased mean % predicted value of FEV1 in case group (male:female::87.21 ± 2.44:88.35 ± 23.96) compared to controls (male: female::103.76 ± 12.93:106.72 ± 15.57). The difference of value between cases and controls was significant (p<0.05).Asanuma et Al (1985)[11] have reported significantly reduced FEV1 in patent with T2DM compared to healthy individuals similarly sreekumar et al (2017)[12] who compared the mean FEV1 of 100 T2DM patients with controls also concluded significantly reduced FEV1 among patients with diabetes.

Mean observed FVC values are more than 80% predicted in both the groups but there's a significant reduction in FVC values in patients with T2DM compared to healthy controls suggesting reduced forced vital capacity in patients with diabetes (male-cases:controls:: 83.47 ±23.04:78±13.02;female-cases:control:: 80.93±21.55 :99.78± 12.31). Our observations are in agreement with Khan et al (2012)[13] who reported that both IDDM and NIDDM were associated with a slight reduction in FVC. Significant reduction in FVC among T2DM participants also reported by sreekumar et al (2017)[12] in their study. Present study results are in agreement with the findings of Sreekumar et al[12]. El-Azeem et al (2013)[7] also reported reduced FVC in patients with T2DM.

Ratio of the above mentioned values, FEV1/FVC in cases was higher than the predicted ratio in both the genders (male-cases:control::78.52 ± 11.21: 78.87 ± 22.55; female-cases:control::84.11 ± 9.82: 74.56 ± 26.40) . Difference between the two values of cases and control was highly significant (p<0.0001). The inference which can be drawn

from this was that those participants with diabetes had reduced lung capacity as compared to control group which goes more in favour of restrictive changes in the lung of diabetes individuals. Similar results were seen In a study performed by Boulbou et al (2003)[14] who studied type 1 diabetes patients and compared them with healthy controls for PF abnormalities and reported that the ratio of FEV1/FVC was reduced in diabetic patients than in controls subjects. Likewise many studies were done like Fimognari et al (2007)[15], Nakagima et al (2008)[16], El-Azeem AA (2013)[7] in which the reduced FVC and normal FEV1/FVC were reported and concluded the presence of restrictive pulmonary function but not the obstructive pattern might be associated with metabolic disorders and the metabolic syndrome. Aparna et al (2013)[10] reported that FEV1/FVC was increased in type 2 diabetics as compared to that in controls and the increase was statistically significant. Kinney et al (2014)[17] have observed a moderate reduction in FVC, FEV1 and diffusing capacity for carbon monoxide of the lung in patients with type 1 and type 2 diabetes.

In present study mean of % predicted PEFR value was lower among cases as compared to control [Cases:control (male-72.05 ± 22.69: 81.49 ± 25.77; female- 75.02 ± 72.80: 82.51 ± 18.86] and the difference is significant (p_{male}=0.18; p_{female}=0.23). our study was in agreement with study perfomed by El-Azeem et al (2013)[7] who reported that mean PEFR was significantly low among Cases as compared to Control group (p<0.001) on the other hand David et al (2004)[18] performed a prospective study in which he studied diabetic patients and recorded baseline values. A subset of 125 patients were studied after 7 years, who showed a significant reduction in the FEV1, FVC, PEFR .

In present study comparison of MMEFR among both the groups revealed that mean MMEFR was lower among cases as compared to controls [male-Cases:control::52.47 ± 25.7: 68.16 ± 23.35; female-cases:control::62.60 ± 105.68: 66.98 ± 24.62)] (p_{male}=0.002 ; p_{female}= 0.63).The findings of our study were in accordance with some previous studies. (Davis WA 2004, Asanuma Y 1985)[18,11]

On interpreting the results of PF it was seen in our study that although maximum no of participants in case group [88(45.83%)] had PF within normal limit but nearly equal number of cases [85(44.26%)] had restrictive changes in their lung. Remaining participants were found to have obstructive pattern [5(2.6%)] and mixed blockage pattern [14(7.29%)] of pulmonary functions. This makes clear from our study that pulmonary functions are significantly compromised in those with diabetes.

In our study correlation between duration of study and PF came out to be negative (FEV1 r= -0.027; FVC r= -0.023) which indicates that in those with longer duration of diabetes PF were more compromised .Some other studies showed no significant correlation between PFTs and duration of disease. (Benbassat CA 2001)[19] While some have reported a strong negative correlation of pulmonary tests with duration. (Barrett-Conor E 1996, Davis TM 2000)[21]

In present study, FEV1 and FVC are negatively correlated with HbA1c (p<0.001). suggesting poor glycemic control may cause impairment in PF in patients with T2DM. It was observed in a study performed by Singh et al (2015) that all the parameters of PF in type 2 diabetes mellitus with uncontrolled glycemic status had lower mean compared to T2DM with controlled glycemic status. On group comparison, mean difference between these groups was statistically significant for FEV1, FVC and DLCO respectively (P <0.05) which is in agreement to present study where there was a negative correlation between FEV1 and FVC with HbA1c.Asanuma Y et al (1985)[11] and Lange et al (1989)[23] also reported that FVC and FEV1 were reduced in type 2 diabetic subjects as compared to those in control subjects. On contrary, Benbassat (2001)[19] showed that FVC and FEV1, were within the predicted values in type 2 diabetics. The most probable reason for this contradiction was that Benbassat had studied PF

in a group of patients with type 2 diabetes, but they had not compared their results with a matched control group. The results of our study were identical to studies conducted by Davis et al (2004)[18] and Mckeevear et al (2005)[24] as they found significantly reduced PF (FEV1 and FVC) in diabetes with uncontrolled glycemic status. Baba et al (2017)[25] measured PFT and HbA1c of 1019 subjects and reported that participants with HbA1c >5.6% showed a significantly lower FEV1/FVC compared to participants with lower Hb1Ac levels.

This correlation suggest that glycemic control affect the poor pulmonary function as a result of micro and macrovascular changes. Occurring in various other organs like retina kidney etc. hence attainment of good glycemic control in patients with T2DM will prevent determination in lung function in these patients

Conclusion

The findings of this study are in sync with the findings of others, which strongly suggest that type 2 diabetes mellitus adversely affects the PF predominantly of restrictive pattern. Nevertheless, the findings of present study conclude that lung is a target organ for damage in diabetes and that the glycaemic exposure is a strong determinant of reduced PF in type 2 diabetics. Thus, an intensive glycaemic management may reduce the risk of death through an improved ventilatory function which is independent of other beneficial effects. Also, as pulmonary dysfunction may be one of the earliest and easily measurable non– metabolic alterations in diabetes, the patients with diabetes are suggested to undergo PF testing along with other investigations. It is advisable, therefore, that diabetic patients must undergo periodic Spirometry tests to assess the severity of lung function impairment. These measures will help in preventing lung damage in initial stage, and thus contribute to reduction in morbidity and mortality in type 2 diabetes patients.

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