

## CHANGES IN LUNG FUNCTION TESTS IN TYPE-2 DIABETES MELLITUS

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### OBJECTIVES

☞ To study the ventilatory function of individuals with type 2 diabetes mellitus patient by performing spirometry.

☞ To compare the spirometric findings of persons with type 2 Diabetes mellitus with that of non-diabetic controls.

☞ To correlate the abnormalities of spirometry with duration of diabetes mellitus.

### METHODOLOGY

Design of the study:

A cross-sectional study, descriptive, prospective study of the lung function of diabetics compared with age and sex-matched non-diabetic controls.

Materials

Vitalograph 2170 pneumotach spirometer with Spirotrac IV software, Vitalograph calibration syringe, weighing scale, stadiometer, Microsoft Excel and SPSS Version 10 software.

### METHODOLOGY

Over a period of 2 years, patients with type 2 diabetes mellitus who were attending medical OPD of Dr.B.R.Ambedkar Medical College Hospital were included in the study. They were requested to attend a medical interview, and underwent physical examination including fundoscopy. Non-smoking diabetic patients who had no history of respiratory disease, and who gave informed consent were selected for this study, and underwent pulmonary function testing. Healthy, non-smoking, non-diabetics who were matched for age and sex were chosen as controls, and also underwent pulmonary function testing. The results were entered on a Microsoft Excel spreadsheet and were analyzed using SPSS version 10.0 software.

Inclusion criteria:

Type 2 Diabetes mellitus of at least 6months

duration, able to give informed consent. Diabetics who have never smoked, with no past history of lower respiratory

illness and who did not show at the time of the examination, symptoms related to respiratory illness. These included nasal itching, nasal congestion, running nose, dry throat, hoarseness, epistaxis, sneezing, pain suggestive of sinusitis, cough, expectoration and dyspnea.

Exclusion criteria:

Smokers

Present or past history of respiratory diseases that might affect lung function such as asthma, COPD, tuberculosis, bronchiectasis, interstitial lung disease.

History of occupational exposure to any substances that could affect lung function.

Individuals with current or recent upper respiratory or lower respiratory infection, that could pre-dispose to heightened airway reactivity.

Individuals with unacceptable spirometric technique. An unacceptable spirometry was that in which FEV<sub>1</sub> or FVC could not be correctly measured due to

- o Cough
- o Obstruction of teeth or tongue
- o Sub-maximal effort
- o Air escape
- o Effort sustained for less than 6 seconds duration
- o Failure to attain a plateau on volume time curve
- o Lack of understanding of the procedures
- o Recent surgery.

Vitalograph 2120 (with Spirotrac IV software), calibrated daily, was used for all pulmonary function measurements according to ATS performance criteria. The subjects' details including age, sex, and

height of the subject were recorded on the patient data sheet of Spirotrac software. The test procedure was explained to the subjects. The object of the test was to obtain reproducible records of the flow volume loop and a volume time curve. All efforts were made to secure three satisfactory and reproducible expiratory maneuvers, and the best results ("ATS best") recorded in an ATP (ambient, temperature and pressure, saturated) scale. The final spirometric reports were saved and analyzed

using Microsoft Excel worksheet and SPSS software.

## RESULTS

A total number of 130 cases were suitable for analysis. There were 74 diabetics (STUDY GROUP) and 56 non-diabetics (CONTROL GROUP).

### Age and gender distribution

There were 25 males (33.8%) and 49 females (66.2%) in the study group. There were 21 males (37.5 %) and 35 females (62.5%) in control group.

	Gender	Number	Minimum	Maximum	Mean	Standard deviation
Non diabetics	Males	21	42	71	55.86	8.72
	Females	35	33	72	51	9.80
Diabetics	Males	25	42	72	56.48	8.85
	Females	49	33	85	52.73	10.23

The mean age of male subjects in study group was 56.48 years (range 42-72 years) while the mean age of male subjects in control group was 55.86 years (range 42-71 years).

The mean age of female subjects in study group was 52.73 years (range 33-85 years) while the mean age of female subjects in control group was 51.00 years (range 33-72 years).

Subjects were closely comparable in their age distribution within groups, i.e., male diabetics against male controls and female diabetics with female controls. For details (table 1) Chart 1 and 2.

The mean height of males in the diabetic group was 165.3 cm (SD 6.58, range 148 - 174 cm), and in the control group was 164.95 cm (SD 6.17, range 153 - 175 cm). The mean height of females in the diabetic group was 151.88 cm (SD 7.21, range 137- 168 cm), and in the control group was 155.6 cm (SD 3.75, range 140 - 158 cm). Both groups were well matched in terms of height and weight

The duration of diabetes ranged from 6 months to 22 years, with a mean duration of 11years, median duration of 5 years).

Among males the duration of diabetes ranged from 18 - 144 months (mean

81.36 months, SD 37.71 months) while among females, the duration of diabetes ranged from 6 - 240 months (mean 86.24 months, SD 62.84 months). Blood glucose levels

Overall, the level of control of diabetes among the subjects appeared to be poor. The mean Fasting Blood Glucose (FBS) among males was 229.88 (range 86 -470, SD87.95), and among females 194.43 (range 70 - 408, SD 68.6).

The mean 2 hr post prandial Blood Glucose (PPBS) among males was 303.4 (range 166 - 525, SD 97.14), and among females 273.85 (range 140 - 496, SD 79.83).

One female patient did not return for her PPBS assessment.

Only 29 of the 74 study subjects had a glycosylated haemoglobin assessment done, but even this group showed evidence of poor control. Among the 11 male subjects, the mean HbA1c was 9.97 (range 7 - 14, SD 2.00). The 18 females who had a glycosylated haemoglobin estimation showed a mean HbA1c of 9.31 (range 7 - 12, SD 1.35).

The non-diabetic subjects did not have glycosylated haemoglobin done, and while blood sugars were done to rule out diabetes, the values were not used for the analysis.

**Spirometric results**

<b>Males</b>	<b>Diabetic (n = 25) Mean (SD)</b>	<b>Non-diabetic (n=21) Mean (SD)</b>	<b>P value</b>
FVC	2.66(0.56)	2.86(0.73)	0.32
FEV <sub>1</sub>	2.01(0.41)	2.19(0.60)	0.232
FEV <sub>1</sub> /FVC	75.56(9.35)	76.49(10.51)	0.763
PEFR	337.92(98.48)	397.38(138.37)	0.097
<b>Females</b>	<b>Diabetic (n = 49) Mean (SD)</b>	<b>Non-diabetic (n=35) Mean (SD)</b>	<b>P value</b>
FVC	1.89(0.45)	2.13(0.45)	0.017
FEV <sub>1</sub>	1.53(0.41)	1.65(0.32)	0.147
FEV <sub>1</sub> /FVC	80.72(14.83)	78.18(10.47)	0.385
PEFR	231.75(82.59)	287.27(84.69)	0.004

Spirometric values were consistently lower in diabetics than in non-diabetics. However, the differences were statistically significant only among females, and that too for the parameters of FVC and PEFR.

When diabetics with duration of diabetes greater than the median duration of 5 years (60 months) were considered, the same results were obtained, i.e., spirometric values were consistently lower in diabetics than in non-diabetics. However, the differences were statistically significant only among females, and that too for the parameters of FVC, FEV<sub>1</sub> and PEFR.

<b>Parameter Mean (SD)</b>	<b>Diabetic (n = 17) Mean (SD)</b>	<b>Non-diabetic (n=21)</b>	<b>P value</b>
FVC	2.78 (0.56)	2.86 (0.73)	0.73
FEV <sub>1</sub>	2.09 (0.40)	2.19 (0.60)	0.60
FEV <sub>1</sub> /FVC	75.83 (10.31)	76.48 (10.51)	0.85
PEFR	356.8 (89.24)	397.39 (138.36)	0.303

**DIABETICS WITH DURATION OF DIABETES GREATER THAN THE MEDIAN DURATION OF (60 MONTHS) MALES**

<b>Parameter Mean (SD)</b>	<b>Diabetic (n = 26) Mean (SD)</b>	<b>Non-diabetic (n=35) Mean (SD)</b>	<b>P value</b>
FVC	1.73 (0.27)	2.14 (0.45)	0.000
FEV <sub>1</sub>	1.41(0.29)	1.65 (0.32)	0.004
FEV <sub>1</sub> /FVC	82.35 (13.13)	78.18 (10.47)	0.172
PEFR	217.99 (60.07)	287.28 (84.69)	0.001

**FEMALES**

The mean decline in the spirometric values among diabetics as compared to non-diabetics was as follows. Values were also assessed as percentages of predicted, to overcome the variation in ages, heights and weights of the subjects, and still allow for comparison of a larger group. Here too, the diabetics had lower values than nondiabetics on FVC % predicted, though not on other measures. The highly effort dependent variables such as PEFR and FEF 25-75 showed a very variable effect with wide standard deviations.

It appears that the main effect of diabetes is on the Forced vital capacity, and much less so on other parameters.

## DISCUSSION

This study was undertaken to assess the ventilatory function of type 2 diabetes mellitus patients, and to compare it with those of non-diabetic healthy subjects. Few studies have focused on the relationship between pulmonary function and diabetes. Most such studies have been conducted on subjects with type 1 diabetes.

In this study, there was a larger number of females than males (66.2% vs 33.8%). The probable cause for this female preponderance was the fact that many males were excluded on account of their smoking history, while female diabetics were mostly eligible on account of their being non-smokers.

The different groups i.e., males and females, diabetic and non-diabetics were comparable in terms of age, height and weight. These being the major determinants of the spirometric values, the main determinants of ventilatory differences are likely to be the presence or absence of diabetes.

The groups were also homogeneous in respect of having no known respiratory disease, and all being non-smokers. In the study of Hiroshi Mori et al, smokers were included in the analysis, and this was therefore an additional confounding variable.

The few studies conducted have mainly focused on alterations in diffusing capacity ( $DL_{CO}$ ) and their relationship with duration of diabetes, in insulin dependent diabetes mellitus. They found that there was reduction in lung function that was slightly

more pronounced in insulin dependent than in non-insulin dependent diabetics.

As expected, for all parameters except FEV1/FVC males had higher mean values than females, among diabetics and non-diabetics. Non-diabetics had higher mean values on all parameters than diabetics.

When duration of diseases was compared with all parameters the following was observed:

1. There was a tendency for all parameters to fall with longer duration of diabetes. However, a multiple regression analysis showed that this was not significant. Clearly, those with a longer duration of diabetes also were older, and the effect of decline in lung function with age was a greater contributing factor.
2. FEV1 fall in values was more pronounced among females than among diabetic males.
3. Poor diabetic control was associated with poorer lung function. There was a rough association between greater declines in FVC and higher values of FBS and PPBS.
4. A similar inverse association was noted between higher HbA1c levels and lower FVC and FEV1 levels.

In the study of Marco Guzzi et al, absolute values and percentage of predicted normal values of FEV1, MVV, vital capacity and total lung capacity were reduced in NIDDM patient group.  $DL_{CO}$  showed a step wise highly significant reduction from normal to hyperglycemic.

In Hiroshi Mori<sup>2</sup> study people says %  $DL_{CO}$  was negatively correlated with duration of diabetes, but other PFTs like %VC, FEV1 or  $Pao_2$  did not show such a negative correlation.

Patients with microangiopathy had a slight decrease in %VC compared to patients without microangiopathy. Also, a decrease in diffusing lung capacity was noted in patients with diabetic nephropathy compared with those not having nephropathy. No relation was found between diabetic microangiopathy and FEV1, % $Pao_2$  or  $PaCO_2$ .

Patients treated with insulin had significant decrease in %  $DL_{CO}$  compared to those taking OHAs. No relation was noted between treatment with %VC, FEV1%,  $PaO_2$  or  $PaCO_2$ . No such difference

between insulin treated and OHA treated individuals was noted in our study, but the numbers were too small to draw any conclusions. Differences could be explained by the differences in duration of diabetes and diabetic control with insulin treated Type 2 diabetics likely to have had diabetes for a longer duration with higher sugars needing a change from OHAs to insulin.

In P Lange's<sup>3</sup> study, the diabetic subjects had slightly smaller height adjusted FEV1&FVC compare values of non-diabetic subjects, their regression analysis also, showed association between raised values of plasma glucose & reduction of the lung function was highly significant.

In a Letter to the Editor, B Ozmen<sup>5</sup> et al reported finding abnormal pulmonary function tests in their diabetic patients that were mild and unlikely to be of clinical significance. The most likely explanation is that single breath method may not be sensitive enough to detect pulmonary vascular microangiopathy. Low pulmonary vascular pressures determines only minor changes in pulmonary capillaries of diabetes mellitus subjects, and so the commonly used method of DLco might not discriminate between diabetics mellitus and normal subjects. The concluded that doing a longitudinal study may help to identify a temporal pattern of lung involvement and relation to other organ involvement. In our study, we did not look at diffusing capacity. However, a similar explanation may account for our observation that the spirometric abnormalities though being consistently noted in diabetics, did not reach levels of statistical significance. In SK Rajan's<sup>8</sup> study, spirometric readings of study group patients revealed that 60% showed an obstructive pattern, 30% showed a restrictive pattern, and there was a mixed obstructive-restrictive pattern in 23%.

In our study, we found a predominantly restrictive pattern, with 100% of males having a FVC less than 80% of the predicted value, while only 36% of females had FVC < 80% of predicted. An obstructive pattern, indicated by an FEV1/FVC ratio less than 70% was seen in 28% of men and 8.2% of women. Possibly, the predicted values, based on

## CONCLUSIONS

1. Spirometric values were consistently lower in subjects with Type 2 diabetes mellitus than in non-diabetics. The differences reached statistical significance only for the forced vital capacity, but the trend was seen across all parameters.
2. Males with diabetes tended to be affected more than females, attaining lower levels of their percentage of predicted values.
3. The effect on the FVC was even more pronounced in diabetics who had duration of disease longer than 5 years, and the effect was not explained by the difference in age alone.
4. There was a mean decline of FVC of 200 ml among diabetic males. And a decline of 240 ml among diabetic females as compared to diabetic controls. There was a decline of FEV1 of 180 ml among men and 120 L among women.
5. Subjects with poorer diabetic control have worse spirometric function.
6. Non-enzymatic glycosylation of connective tissue, especially the collagen, may be responsible for reduced lung functions.
7. There is scope for further intensive work in the same area, extending the study to a larger group, and including diffusion studies as part of the protocol.

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