EFFECT OF GLYCAEMIC CONTROL (HBA1C) ON PULMONARY FUNCTION TESTS (SPIROMETRY) IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

BACKGROUND

Diabetes mellitus is a metabolic disorder affecting almost all the organs by its micro and macrovascular complications. Like other organs the respiratory system is also affected by diabetic complications like microangiopathy. Very few studies investigated the complications and the relationship with the duration of the diabetes and glycaemic status. So in this point of view, we planned to study the effect of pulmonary function in our type 2 diabetic patients.

AIMS AND OBJECTIVES

To study the influence of glycaemic control (based on HbA1c levels) on pulmonary function tests and the correlation between spirometric abnormalities and duration of diabetes in type 2 diabetic patients.

MATERIALS AND METHODS

55 type 2 diabetic patients who gave informed consent were recruited. History regarding duration of diabetes, treatment, history suggestive of complications like neuropathy, retinopathy, nephropathy, regular sugar monitoring, exercise, etc. were recorded. BMI was calculated. Chest x-ray was taken for all patients. They underwent spirometry and the predicted and measured values of FEV1, FVC, FEV1/FVC, PEFR, FEF 25-75 for all the patients were recorded. After spirometry, HbA1c estimation was done using ion exchange resin method. Oneway ANOVA, correlation, paired and unpaired-t-test were used for analysis.

RESULTS

There was significant difference between the mean predicted FVC, FEV1, PEFR, and FEF 25-75, and measured values. The mean of measured spirometric values decreases as the HbA1c increases. There was reducing trend of the spirometric values as HbA1c increases, this was not statistically significant. The incidence of restrictive pattern was more common among the male patients compared with female patients but this was not statistically significant.

DISCUSSION AND CONCLUSION:

Restrictive pattern was more with increase in duration of diabetes. Out of 55 patients, 33 had probable restriction, 5 had moderate obstruction and 1 had severe obstruction. This may be due to underlying obstructive airway disease and they might have concealed smoking or other history which may attribute to obstruction. Our studies show that increase in HbA1c % values were associated with reduced spirometric values.

KEYWORDS

Diabetes, Microangiopathy, Pulmonary Function Tests, Glycosylated Haemoglobin.

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INTRODUCTION: Diabetes mellitus is a metabolic disorder affecting almost all the organs by its micro and macrovascular complications. Practically every system is affected by the micro and macrovascular complications of diabetes. The respiratory system is mostly neglected except for recognition of increased prevalence of infectious diseases like tuberculosis.

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Like other organs the capillary network in the alveoli also gets affected by microangiopathy.[1] But because of the large surface area and pulmonary reserve, substantial loss of vascular bed can be tolerated for long periods without clinical symptoms. Moreover, by this time, patients develop other complications and they might succumb. Hence pulmonary microangiopathy is under recognised clinically in diabetics.[2] In our country, there are only a few studies regarding these changes and their relationship with the duration of the disease and glycaemic status. Hence, this study is done to add to the experience in our patients with type 2 diabetes.

AIMS OF THE STUDY

1. To study the ventilatory pulmonary function in type 2 diabetic patients by performing spirometry.
2. To study the influence of glycaemic control (based on HbA1c levels) on pulmonary function tests.
3. To study the correlation between spirometric abnormalities and duration of diabetes in type 2 diabetic patients.

MATERIALS AND METHODS:

Study Design: An analytical type of cross-sectional study. Ethical committee approval was obtained from Institutional Ethical Committee.

Source of Data: 55 type 2 diabetic patients who were already registered in the Outpatient Department of Mahatma Gandhi Memorial Govt. Hospital attached to K.A.P.V. Govt. Medical College, Tiruchirapalli were included in the study.

Inclusion Criteria:

- Patients diagnosed as type 2 diabetes mellitus with minimum duration of 2 years.
- Nonsmokers – those who never smoked.
- Patients who were willing and able to give consent.
- Without any history of respiratory tract diseases in the recent past.
- Without symptoms of respiratory diseases during the study.
- Patient with normal chest x-ray.

Exclusion Criteria:

- Smokers – both present and previous.
- Present or past history of respiratory illness that may impair lung function (Asthma, COPD, ILD, TB, Malignancy).
- Presence of kyphosis, scoliosis, pectus excavatum, pectus carinatum.
- History of occupational exposure to silica cotton, jute dust, asbestos that can affect lung function.
- Presence of signs or symptoms suggestive of upper/ lower respiratory tract infection and cardiac disease.
- Instances where spirometric readings are unacceptable like air escape, inadequate effort, failure to reach a plateau, effort sustained for less than 6 seconds[3].
- History of Rheumatoid Arthritis/Ankylosing Spondylitis.
- History of ingestion of drugs like Amiodarone, Bleomycin & Methotrexate.

Period of Study: From January 2015 to November 2015.

Materials: Easy one spirometer with mouth piece, weighing scale, stadiometer, HbA1c kit using ion exchange resin method.

Spirometer: EasyOne spirometer. It is a portable type of spirometer based on ultrasonic flow sensor method. The advantage of this spirometer is disposable flow tube can be inserted between transducers which prevents cross contamination[4]. Since the tube acts a transparent barrier separating the airflow and transducer it does not require calibration. Another advantage of this spirometer is that it is not affected by the composition of gas.

Methodology: Type 2 diabetic patients who were registered in diabetic OP and who gave informed consent were recruited. History regarding duration of diabetes, treatment, history suggestive of complications like neuropathy, retinopathy, nephropathy, regular sugar monitoring, exercise, etc. were recorded. Height, weight and BMI was calculated. They underwent spirometry and the predicted and measured values of FEV1, FVC, FEV1/FVC, PEFR, FEF 25-75 for all the patients were recorded. Minimum of three performances and maximum of eight performances done for each patient till we get a best value for all parameters based on guidelines from American Thoracic Society.[5]

After spirometry, HbA1c estimation was done using ion exchange resin method. The values were entered in an excel spread sheet and statistical analysis done with SPSS software. Oneway ANOVA, correlation, paired and unpaired-t-test were used for analysis. Each patient's measured spirometric data was compared with the predicted value for that patient which was calculated by the spirometer.

If the FEV1 is reduced compared to FVC value with the FEV1/FVC ratio less than 70% an obstructive pattern of ventilatory abnormality was considered.

If both FEV1 and FVC are reduced with FEV1/FVC ratio equal to or more than 70% a restrictive pattern of ventilatory abnormality was considered.[6]

RESULTS: A total of 55 diabetic patients (30 males, 25 females) between the age group 30 and 60 yrs. were included in the study. The mean age was 47.47+/-8.38. The mean duration of diabetes was 88.45+/-35.75 months. The mean HbA1c % was 8.8 +/- 1.37.

With respect to duration of diabetes, most of the subjects had duration between 5 to 10 yrs. 10 patients came under 5 yrs. duration and 9 patients had more than 10 years' duration(Table:1). The minimum duration was 2.5 yrs. and maximum duration was 16 yrs.

With respect to HbA1c%, 20 patients (36.4%) had values more than 9 which indicates the poor glycaemic control. The majority of the patients 32(58.2%) had values between 7 to 9, and the remaining 3 patients (5.5%) had values less than 7 which was suggestive of good glycaemic control. The mean HbA1c value of the group was 8.8 +/- 1.37 (Table: 2).

The difference between the mean predicted and measured spirometric values were shown in Table:3. There was significant difference between the mean predicted FVC (3.4033) and measured FVC values (2.2215). The difference between the measured and predicted values for FEV1 (2.6484 &1.7249), PEFR (6.4253 & 3.6638), and FEF 25-75(3.2362 & 1.7504) were also statistically significant. There

was no statistical significant difference between the predicted and measured FEV1/FVC ratio.

The difference between the measured and predicted spirometric values is more in males than females in case of FEV1(2.9957 – 1.9633 & 2.2316 – 1.4388), FVC (4.0313 – 2.5377 & 2.6496 – 1.842), and PEFR (7.2223 – 4.2067 & 5.4688 – 3.0124). For FEV1/FVC ratio, the difference is not significant (Table:4).

The FEF25-75 value reduction (3.432 – 2.0417 & 3.0012 – 1.4008) was more pronounced in females compared with males.

The relationship between HbA1c% and spirometric values were shown in Table 5. The mean of measured spirometric values decreases as the HbA1c increases. This was seen for all parameters except FEV1/FVC in which there was no significant change observed. Even though there was reducing trend of the spirometric values as HbA1c increases this was not statistically significant.

Table 6 shows the occurrence of various spirometric patterns among the patients. 16 patients had normal spirometry, 33 patients had probable restrictive pattern. Obstructive pattern was seen in 6 patients among which 5 had moderate obstruction and 1 had severe obstruction.

Out of 30 male patients, 7 had normal spirometry, 20 had restrictive pattern, 2 had moderate obstructive pattern, 1 patient had severe obstructive pattern. Out of the total 25 female patients, 9 had normal spirometry, 13 had restrictive pattern, and 3 had moderate obstructive pattern. The incidence of restrictive pattern was more common among the male patients compared with female patients but this was not statistically significant (Table:7).

Table 10 shows the distribution of spirometric patterns in relation to duration of diabetes. With duration less than 5 yrs., among the 10 patients, 3 had normal spirometry, 6 had restrictive pattern and 1 patient had moderate obstructive pattern. With duration between 5 and 10 years, among the total 36 patients, 9 had normal spirometry, 22 had restrictive pattern, 4 had moderate obstructive pattern and 1 had severe obstructive pattern. With duration more than 10 yrs., among the total 9 patients, 4 had normal spirometry, 5 had restrictive pattern. Maximum number of restrictive pattern occurs with the duration between 5 to 10 yrs. but this difference was not statistically significant.

The relationship of HbA1c% and spirometric pattern were shown in Table:8. 3 patients had HbA1c less than 7, among them 2 had normal spirometry and 1 patient had restrictive pattern.

With HbA1c between 7 to 9 there were 32 patients, among them 12 had normal spirometry, 16 had restrictive pattern and 4 had moderate obstruction.

With HbA1c more than 9 there were 20 patients, among them 2 had normal spirometry, 16 had restrictive pattern, 1 had moderate obstruction, and 1 had severe obstruction. This difference was not statistically significant.

DISCUSSION: This study was done in type 2 diabetes mellitus patients to assess the ventilatory pulmonary function based on the predicted and measured spirometric values. The previous studies focused on the relationship between pulmonary function tests and type 1 diabetes mellitus. Very few studies were done with type 2 diabetes patients. In this point of view, we planned to study the comparison of spirometric values with HbA1c levels in type 2 diabetes.

Depending on the patient distribution in our outpatient department, we have taken a total of 55 patients, (male 30, female 25). The age group ranged from 30 to 60 yrs. The distribution of patients in different age group were not equal (15 patients in 30 to 40 yrs., 20 patients in 41 to 50 yrs., 20 patients in 51 to 60 yrs.).

The analysis of measured and predicted spirometric values show that there was a reducing trend of FVC, FEV1, PEFR, FEF25-75, which was more significant with FVC values. This may indicate that there was a restrictive pattern of spirometry along with some obstructive component and this was statistically significant.

When compared with gender distribution there was a reduction in spirometric values, which was more in males for all values except for FEF25-75 which was more reduced in females. The incidence of restrictive pattern was more in males compared to females but this difference was not significant.

There was a negative correlation between duration of diabetes and spirometric values (FEV1, FVC, PEFR, FEF 25-75) except for FEV1/EVC ratio which has a positive correlation. This may indicate that as the age increases, spirometric values were decreasing except for FEV1/FVC which was increased. This may be due to reduction in FVC is more when compared with FEV1 so the FEV1/FVC ratio remains unaltered (Table:9).

Out of the total 55 patients, 42 patients were on oral hypoglycaemic drugs and the remaining 13 patients because of poor glycaemic control they were given insulin therapy in addition to oral drugs. Of the 13 patients on both oral drugs and insulin, 9 patients had restrictive spirometric pattern. This shows that poor glycaemic status correlates with reduction in lung function.

Our studies show that increase in HbA1c % values is associated with reduced spirometric values. The incidence of restrictive pattern was more in patients with HbA1c % greater than 9. This may probably due to the poor control of diabetes which was associated with reduction in lung function. The observations from our study had a similar pattern with the previous study done by P. Lang et al which showed that FEV1 and FVC values reduced in diabetic patients and the reduction is more in patients treated with insulin compared with patients treated only on oral hypoglycaemic drugs.[7]

Obianuju B Ozoh et al had studied spirometric values in Nigerian population with type 2 diabetes and observed a predominant restrictive pattern of lung function abnormality which was also found in our study.[8]

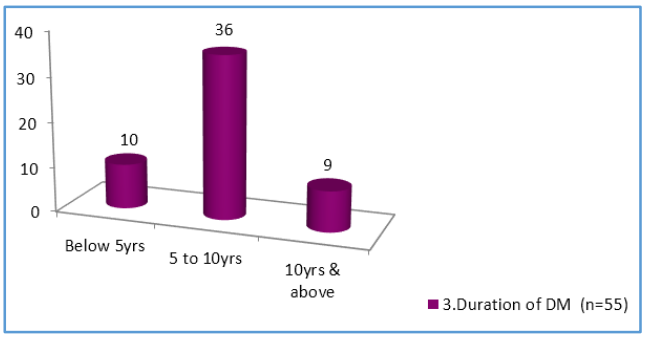
Mahadeva Murthy et al showed that poor diabetic control which was assessed from HbA1c, fasting and postprandial glucose levels was associated with reduction in

lung function and it was more significant with FVC values. This finding also correlates with our study.[9]

We also found that the spirometric values were low in type 2 diabetic patients with a predominant restrictive pattern. The reduction was more pronounced with increase in age, male sex, increased duration of diabetes (Table:10).

Particulars	(n=55)	Percentage -100%
Below 5 yrs.	10	18.2
5 to 10 yrs.	36	65.5
10 yrs. & above	9	16.4

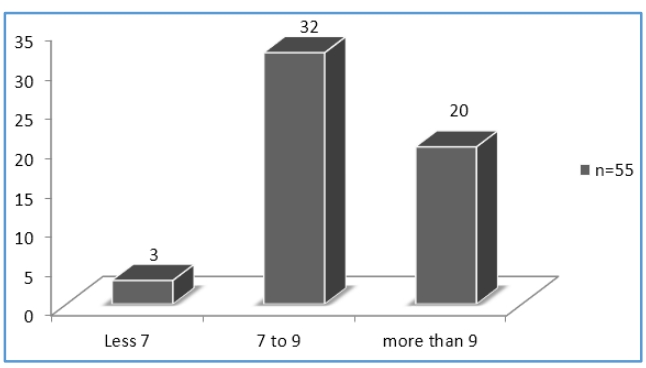
Table 1: Duration of Diabetes



Duration of diabetes

HbA1c%	(n=55)	Percentage -100%
Less 7	3	5.5
7 to 9	32	58.2
More than 9	20	36.4

Table 2: HbA1c%

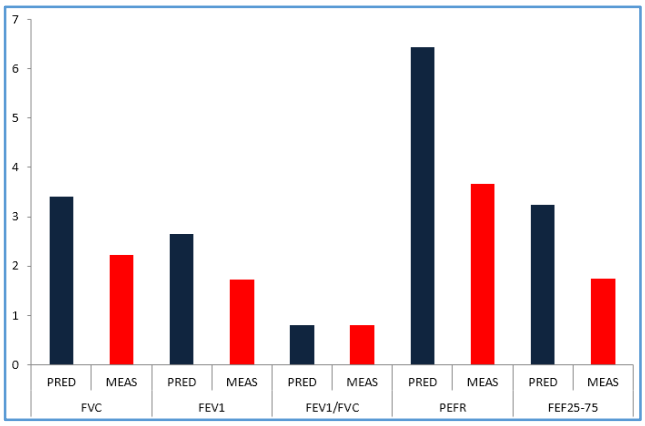


HbA1c% distribution

Variable	Mean	S.D	Mean	S.D	T	Df	Statistical inference
Pair 1							
FVC-p (n=55)	3.4033	0.87139	1.1818	1.00325	8.736	54	.000<0.05
FVC-m (n=55)	2.2215	0.90881					Significant
Pair 2							
FEV1-p (n=55)	2.6484	0.60432	0.9235	0.67216	10.189	54	.000<0.05
FEV1-m (n=55)	1.7249	0.66216					Significant
Pair 3							
FEV1/FVC-P (n=55)	0.7955	0.02348	-0.0002	0.11093	-0.012	54	.990>0.05
FEV1/FVC-M (n=55)	0.7956	0.11218					Not Significant
Pair 4							
PEFR-p (n=55)	6.4253	1.72796	2.7615	1.88402	10.87	54	.000<0.05
PEFR-m (n=55)	3.6638	1.93694					Significant
Pair 5							
FEF 25-75–p (n=55)	3.2362	0.83084	1.4858	1.45744	7.561	54	.000<0.05
FEF 25-75–m (n=55)	1.7504	1.2024					Significant

Table 3: Paired –t-test (comparing the measured and predicted parameters)

P = predicted, m = measured.



Comparison between predicted and measured values

PRED = predicted, MEAS = measured.

The measured values of FEV1, FVC, PEFR, and FEF 25-75, were all less than that of predicted values. This is statistically significant.

Sex	Mean	S.D	Statistical inference
FVC-p			
Male (n=30)	4.0313	0.59742	T=9.601 Df=53
Female (n=25)	2.6496	0.43866	Significant
FVC-m			
Male (n=30)	2.5377	0.82451	T=3.034 Df=53
Female (n=25)	1.842	0.87289	Significant
FEV1-p			
Male (n=30)	2.9957	0.49878	T=5.990 Df=53
Female (n=25)	2.2316	0.43519	Significant
FEV1-m			
Male (n=30)	1.9633	0.66367	T=3.159 Df=53
Female (n=25)	1.4388	0.54587	Significant
FEV1/FVC-P			
Male (n=30)	0.7937	0.02297	T=-.615 Df=53
Female (n=25)	0.7976	0.02437	Not Significant
FEV1/FVC-M			
Male (n=30)	0.7783	0.10366	T=-1.260 Df=53 .213>0.05
Female (n=25)	0.8164	0.12045	Not Significant
PEFR-p			
Male (n=30)	7.2223	1.6763	T=4.316 Df=53
Female (n=25)	5.4688	1.25524	Significant
PEFR-m			
Male (n=30)	4.2067	2.28261	T=2.372 Df=53
Female (n=25)	3.0124	1.15553	Significant
FEF 25-75 -p			
Male (n=30)	3.432	0.84644	T=1.965 Df=53
Female (n=25)	3.0012	0.76288	Not Significant
FEF25-75 -m			
Male (n=30)	2.0417	1.46125	T=2.024 Df=53
Female (n=25)	1.4008	0.66298	Significant

Table: 4 Unpaired-t - test, comparison between males and females

P = predicted, m = measured.

	Mean	S.D	SS	Df	MS	Statistical inference
FVC-m						
Between Groups			0.29	2	0.145	F=.170
Less 7 (n=3)	2.4933	1.24617				.844>0.05
7 to 9 (n=32)	2.2316	1.02881				Not Significant
9 to 11 (n=20)	2.1645	0.66463				
Within Groups			44.311	52	0.852	
FEV1-m						
Between Groups			0.13	2	0.065	F=.144
Less 7 (n=3)	1.9267	0.83584				.866>0.05
7 to 9 (n=32)	1.7172	0.74396				Not Significant
9 to 11 (n=20)	1.707	0.51254				
Within Groups			23.546	52	0.453	
FEV1/FVC-M						
Between Groups			0.001	2	0	F=.024
Less 7 (n=3)	0.79	0.09849				.976>0.05
7 to 9 (n=32)	0.7934	0.11942				Not Significant
9 to 11 (n=20)	0.8	0.10697				
Within Groups			0.679	52	0.013	
PEFR-m						
Between Groups			9.102	2	4.551	F=1.223
Less 7 (n=3)	5.23	3.9944				.303>0.05
7 to 9 (n=32)	3.6994	2.0741				Not Significant
9 to 11 (n=20)	3.372	1.21879				
Within Groups			193.492	52	3.721	

FEF25-75 -m						
Between Groups			1.796	2	0.898	F=.612
Less 7 (n=3)	1.1433	0.53426				.546>0.05
7 to 9 (n=32)	1.8722	1.47026				Not Significant
9 to 11 (n=20)	1.6465	0.67642				
Within Groups			76.276	52	1.467	
Female	9(56.3%)	13(39.4%)	3(60%)	0	25(45.5%)	Not Significant

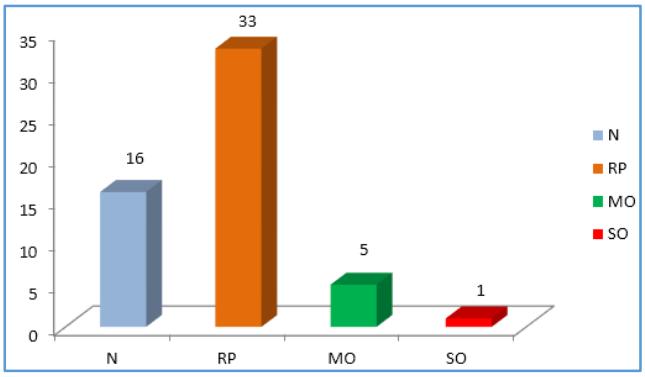
Table 5: One way ANOVA- between Hba1c% and spirometric parameters

Distribution of Spirometric Patterns:

10. Impression		Percentage
	(n=55)	-100%
N	16	29.1
RP	33	60
MO	5	9.1
SO	1	1.8

Table 6: Based on final impression of spirometry

N= Normal, RP= Restriction probable, MO= Moderate obstruction, SO= Severe obstruction.

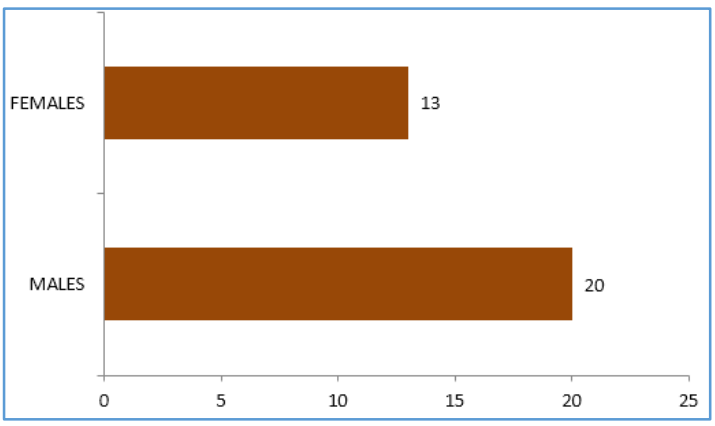


Incidence of spirometric pattern
Restrictive pattern is predominant

Sex	N	RP	MO	SO	Total	Statistical inference
	(n=16)	(n=33)	(n=5)	(n=1)	(n=55)	
Male	7(43.8%)	20(60.6%)	2(40%)	1(100%)	30(54.5%)	
Female	9(56.3%)	13(39.4%)	3(60%)	0	25(45.5%)	Not Significant

Table 7: Comparison of spirometric patterns between males and females

N= Normal, RP= Restriction probable, MO= Moderate obstruction, SO= Severe obstruction.

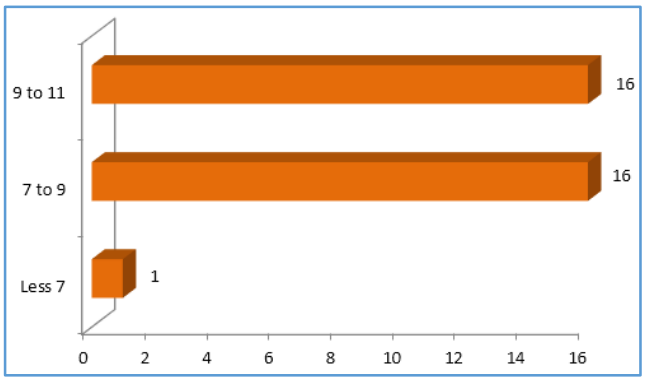


Total = 33, males =20, females = 13
Incidence of Restrictive pattern between males and females

HbA1c	N	RP	MO	SO	Total	Statistical inference
	(n=16)	(n=33)	(n=5)	(n=1)	(n=55)	
Less 7	2(12.5%)	1(3%)	0	0	3(5.5%)	
7 to 9	12(75%)	16(48.5%)	4(80%)	0	32(58.2%)	
More than 9	2(12.5%)	16(48.5%)	1(20%)	1(100%)	20(36.4%)	Not Significant

Table 8: Comparison of spirometric patterns with HbA1c %

N= Normal, RP= Restriction probable, MO= Moderate obstruction, SO= Severe obstruction.



Incidence of restrictive pattern with HbA1c % levels

Duration of DM	Correlation value
FVC-m	-0.166
FEV1-m	-0.131
FEV1/FVC-M	0.12
PEFR-m	-0.079
FEF25-75 -m	-0.021
N	55

Table 9: Duration of Diabetes with spirometric parameters

Duration of DM	N (n=16)	RP (n=33)	MO (n=5)	SO (n=1)	Total (n=55)	Statistical inference
Below 5 yrs.	3(18.8%)	6(18.2%)	1(20%)	0	10(18.2%)	
5 to 10 yrs.	9(56.3%)	22(66.7%)	4(80%)	1(100%)	36(65.5%)	
10 yrs. & above	4(25%)	5(15.2%)	0	0	9(16.4%)	Not Significant

Table 10: Comparison of spirometric patterns with duration of diabetes

N= Normal, RP= Restriction probable, MO= Moderate obstruction, SO= Severe obstruction.

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