

## Correlates of Abnormal Pulmonary Function Tests in Persons with Type 2 Diabetes Mellitus

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### Abstract

**Background:** This study was conceived to determine the ventilatory pattern of patients with diabetes as well as the effect of body mass index, age, glycosylated haemoglobin, duration of diabetes and blood glucose levels on their pulmonary functions.

**Method:** Two hundred persons with type 2 DM who consented and met inclusion criteria were recruited. The pulmonary function test was carried out using the Spirotrac intuitive version V spirometer made by Vitalograph. This was done according to standard guidelines. Statistic tests employed include Students' test, correlation coefficient analysis and binary logistic regression.

**Result:** Mean age of the Study participants was  $59.6 \pm 11.30$  years, with more than half 114(57%) of the Diabetics having abnormal ventilatory pattern with 76(38%) having restrictive defect. We noted significant associations between Age ( $r = -28, p = 0.000$ ), duration of DM ( $r = -15, p = 0.034$ ) and lung function. A possible predictor of abnormal pulmonary function test was the presence of hypertension (Odds ratio=0.39,  $p = 0.009$ ).

**Conclusion:** We have reported that Restrictive lung function defect is common among patients with diabetes mellitus and non-modifiable clinical parameters are associated with lung function abnormalities in this group of patients.

**The significant findings of this study:** Restrictive lung function defect is the predominant abnormality of pulmonary function in persons with type 2 DM.

**This Study adds:** Hypertension in the presence of type 2 DM is a potential risk factor for the development of abnormal lung function in this group of patients.

**Keywords:** Diabetes mellitus; Lung function; Hypertension

### Introduction

Diabetes Mellitus (DM) is a metabolic disorder characterized by persistent hyperglycemia, abnormal metabolism of carbohydrate, protein and lipid resulting from impaired insulin secretion, altered tissue sensitivity to insulin or co-existence of both mechanisms. Chronically, it results in macro and microangiopathy which affects negatively the function and structures of internal organs. According to WHO (World Health Organization) 346 million people worldwide currently have diabetes with more than 80% of diabetes deaths occurring in low and middle income countries. It is projected that this will double between 2005 and 2030 [1,2].

The lung affection in DM has been poorly characterized while it is known that persons with DM are at increased risk of pulmonary infections, bronchiectasis and abscess, several outcomes has been described regarding the pulmonary functions [3-6]. Abnormal phagocytic actions induced by hyperglycaemia and the impact of non-enzymatic glycation of the lung rich in collagen and elastin may lead to stiffening of the thorax and lung parenchyma are some of the reasons given for lung involvement in diabetic process.

In Nigeria some authors have documented ventilatory abnormalities in patients with DM however the findings noted has not been consistent and the studies involved rather small number of diabetic patients considering the burden of the disease [7-9].

This study was thus conducted determine the pattern of pulmonary function abnormalities among patients with diabetes mellitus (DM) at the outpatient clinic of Lagos State University Teaching hospital (LASUTH) Diabetes Clinic. In addition to describing the effect of the glycaemic control, duration of DM and Body Mass Index (BMI) on the pulmonary function

This is also expected to document the effect of glycaemic control,

duration of DM and body mass index on pulmonary functions of the patients as well as determine the possible predictors of abnormal lung function test in persons with DM.

### Materials and Methods

This cross-sectional study was carried out at the outpatient Diabetic Clinic of LASUTH. Ethical approval was obtained from the research and ethics committee of the hospital. Informed Written consent was obtained from the participants.

Two hundred consecutive consenting previously diagnosed patients with DM without significant tobacco use, exposure to dusty occupation, no previous diagnosis of Asthma, chronic obstructive pulmonary disease (COPD), and heart failure were recruited to participate. The Diabetes mellitus had been diagnosed based on fasting plasma glucose (FPG)  $\geq 126$  mg/dl (7.0 mmol/l) or a random plasma glucose  $\geq 200$  mg/dl (11.1 mmol /l). Those having the age of onset of diabetes of less than 30 years were characterized as having type 1 DM while those managed on oral hypoglycaemic agents (OHAS) with or without insulin in combination; or were initially on OHAS but presently on insulin and whose age of onset of DM was greater than 30 years of age were said to have type 2DM.

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**Received** November 24, 2014; **Accepted** December 24, 2014; **Published** December 29, 2014

**Citation:** Adeyeye OO, Ogbera OA, Dada AO, Bamisile RT, Brodie Mens A (2014) Correlates of Abnormal Pulmonary Function Tests in Persons with Type 2 Diabetes Mellitus. J Pulm Respir Med 5: 231. doi:10.4172/2161-105X.1000231

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Interviewer administered questionnaire was used to obtain information about socio-demographic data, smoking status, occupational exposure and relevant clinical information on their diabetes mellitus status. Those with history of current cigarette smoking or those with cigarette smoking or marijuana use for more than 6 month were excluded in the study.

Anthropometric data such as weight (kg) was measured using a weighing scale, standing height was also measured in meters, The body mass index (BMI) was calculated in all subjects. Waist circumference was determined by applying a tape measure to the midpoint between the inferior margin of the last rib and the crest of the ilium.

Pulmonary function test was done by a trained spirometrist under the supervision of a consultant physician and specialist registrar in respiratory medicine, using a portable spirometer spirotac intuitive version V made by Vitalograph UK. This was calibrated daily with 1litre syringe. The Forced expiratory volume in one second (FEV1), forced vital capacity (FVC), Peak Expiratory flow rates (PEFR) and ratio of FEV1/FVC were measured.

The results are given as measured values in Litres and as percent's of predicted values using the American thoracic standardization of spirometry, (1994) customized in the spirotac intuitive spirometer version iv made by Vitalograph UK. The values were those derived from Africans. All measurements were made in an upright sitting position without nose clips. The subject held the disposable mouth piece attached to the spirometer and placed this around the mouth avoiding the tongue and the mouth tightly round the opening of the mouth piece to prevent leakage of air. The subject was instructed to inspire maximally and then expire forcefully at once through the mouth piece into the spirometer. The best of the three acceptable measurements was taken. All measurements were taking between 8am and 1pm on the clinic days.

The outcomes of the test were classified as Normal if FEV1/FVC was greater than 70%, Obstructive ventilatory defect if FEV1/FVC less than 70%, Restrictive ventilatory defect if the ratio of FEV1/FVC greater than 70% and the ratio of obtained FVC/predicted FVC less than 80% and Mixed ventilatory defect if FEV1/FVC was less than 70% and the ratio of obtained FVC to predicted FVC was less than 80%.

Parameter	Male N=67(33.5%)	Female N=133(66.5%)	t	p
Mean age ± SD (years)	61.15 ± 12.75	58.81 ± 10.49	1.377	0.2
Mean duration of DM ± SD (years)	9.00 ± 8.29	7.11 ± 6.47	1.773	.08
Systolic blood pressure(mm Hg)	137.54 ± 21.40	134.78 ± 21.04	0.869	0.4
Diastolic blood pressure(mmHg)	79.25 ± 12.14	78.74 ± 13.24	0.264	0.8
BMI(kg/M <sup>2</sup> )	26.48 ± 5.45	29.72 ± 8.4	-2.896	.004*
Fasting blood sugar (mg/dl)	145.22 ± 77.32	159.51 ± 114.96	.917	.36
Two hour post prandial (mg/dl)	215.03 ± 114.53	218.68 ± 108.59	-.827	0.22
Glycosylated heamoglobin	8.03 ± 2.0	8.25 ± 2.17	-.638	0.54

**Table 1:** Demographic, anthropometric and clinical parameters of the participants by Gender.  
BMI: Body Mass Index, FBS: Fasting Blood Sugar, 2HPP: Two Hour Post Prandial, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure.

Parameter	Predicted L/min	Obtained L/min	p
Mean FEV1 ± SD L	2.33 ± 0.53	1.61 ± 0.62	0.000*
Mean FVC ± SD L	2.75 ± 0.62	2.03 ± 0.76	0.000*
Mean PEFR ± SD L/sec	400.41 ± 81	222.10 ± 98	0.000*

**Table 2:** Comparison of the Spirometric indices of the diabetic patients with the predicted values.  
\*Significant

The blood pressure was measured with the patient seated and the back of the arm supported at the heart level. The measurement was done with a mercury sphygmomanometer and expressed in mm Hg. The systolic blood pressures correspond to the first korotkoff sound while the diastolic was determined by the 5th korotkoff s sound.

The weight was measured by use of Avery scale in kilogram (Avery Berkel, 2003, UK). Patients were weighed without shoes. The height was measured in meters using a wall mounted stadiometer. The biochemical parameters such as fasting blood sugar, two hours postprandial blood sugar, Lipid profile and glycosylated haemoglobin were obtained from patients clinical records. Only those tests done in the hospital laboratory and carried out within two weeks of assessment were considered.

The body mass index was determined by dividing weight in kg by height in meters squared. (BMI= weight in KG/ Height in M<sup>2</sup>)

The data was analysed using SPSS version 19. All quantitative data were expressed as mean ± SD. The qualitative data were expressed in frequency, ratio or graphically with pie chart. Continuous variables were compared using the student T test while qualitative data were compared using the chi square.

Correlation analysis was done for data of interest and binary logistic regression was carried out to determine the possible predictors of abnormal lung function test in DM.

P values of ≤0.05 were taken as statistically significant.

## Results

A total of 200 patients with DM were studied. The age range of the patients was 19-90 years, with a mean of 59.6 ± 11.30 years. There were 67 males (33.5%) and 133 (66.5%) females. The majority of the subjects had type 2 DM and this was noted in 197 (98%) of the study subjects. The age range of the diabetics was between 19-90 years with a mean age of 59.58 ± 11.28 years. The mean duration of diabetes was 30 ± 7.78 years with a Mean age of onset of 51.80 ± 10.90 years. The majority of the patient developed diabetes after 30 years 184 (97%) while only 6 (3%) developed diabetes at age less than thirty.

Table 1 showed other socio demographic, anthropometric and clinical parameters of the participants by gender. there were no statistically significant difference in the mean age, duration of diabetes, mean systolic blood pressure , mean diastolic blood pressure as well as the glycaemic control of DM in both sexes as reflected by the fasting blood sugar, two hour post prandial as well as glycosylated hemoglobin. However the females had higher BMI when compared with the males. p<0.05

When compared, the mean observed and predicted values for all ventilatory indices studied (FEV1, FVC and PEFR) were significantly lower than the predicted in all cases. P=0.000. This is shown in Table 2. The age of the patients correlates negatively with the lung function and this association was stronger with FEV1 and FVC lung function parameters however there was no significant association between BMI and the PEFR and FEV1 however but there was a positive statistical association between FVC and BMI. These results are shown in Table 3.

The most significant predictor of abnormal lung function was hypertension. (Odds ratio=0.39, P=.009) Other potential predictors considered are shown in Table 4. It was however noted though surprising that the Age of the patients appear to be protective with an odd ratio of 1.02 and CI {0.99-1.06 } p 0.09.

Ventilatory abnormality was common among the diabetic patients studied. Only 86 (43.0%) of the patients had normal ventilatory pattern

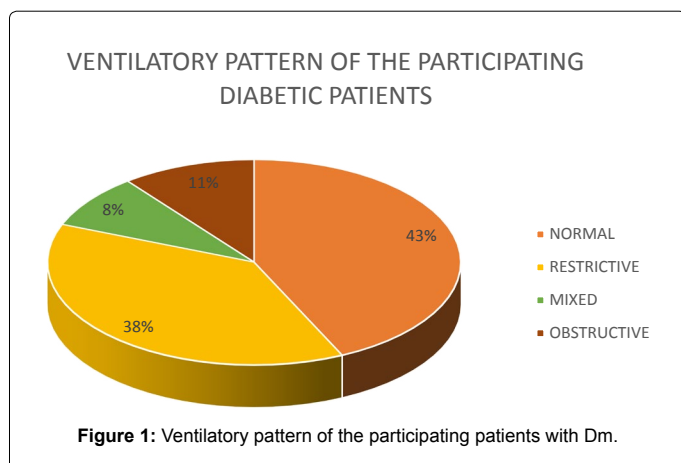
Parameter	Age		Body mass index		Fasting blood sugar		Glycosylated HB		Duration of DM	
	R	p	R	p	r	p	r	p	R	p
FEV1	-1	.000*	-0.017	0.8	-.107	0.134	-.053	0.457	-.169	.017*
FVC	-1	.000*	-2.00	.005*	-.116	.103	.076	.286	-1.35	.058
PEFR	-1	.000*	-.026	.7	-0.41	.563	-0.67	.344	-.151	.034*

**Table 3:** The correlation Matrix showing relationship between age BMI, FBS, Glycosylated Hb and lung function.

Parameter	Odds Ratio	95% CI	p
Age	1.02	0.99-1.06	0.09
Sex	0.78	0.34-1.80	0.57
FHx of asthma	3.37	0.78-14.63	0.1
Second hand smoke	0.83	0.3 -2.29	0.7
History of smoking	0.83	0.36 -2.11	0.7
Body Mass Index	0.7	0.46-1.09	0.12
Hypertension	0.39	0.2-0.79	0.009
Educational status	0.84	0.60-1.1	0.19
Long term Glycaemic control	0.923	0.704-1.21	0.56

**Table 4:** Possible Predictors for Abnormal Lung Function in Persons with Diabetes Mellitus.

FHx: Family History of Asthma



while it was abnormal in the majority 114 (57%). The patterns seen are shown in Figure 1.

## Discussion

Diabetes is a disease with profound multi-organ damage and several studies locally and internationally had attempted to evaluate relationship between diabetes and lung functions [3,5,9,10]. This present study showed that DM patients have significantly lower pulmonary functions compared to the predicted and these findings are comparable to those documented elsewhere [3,5,9,10]. In this study we found a high prevalence of abnormal ventilatory function among our patients which was largely a restrictive defect similar to the pattern widely reported in literature [9,10].

Several reasons has been given for the development of restrictive diseases in DM, some of which included the fact that there exist the potential for microvascular damage and non-enzymatic glycation in persons with diabetes due to the existence of a large vascular network in the lung and its richness in collagen and elastin thus making the lung, a potential organ for damage in DM. This position is further strenghtened by the post mortem histologic study which showed thickening of both the alveolar epithelial and pulmonary basal laminae in patients with

diabetes. This was thought to be suggestive of microangiopathy which is believed leads to restrictive defects [3,4,8-11].

In this study, the high prevalence of obesity in our study population with DM may also contribute to the high prevalence of restrictive lung defect in persons with DM in our series compared to an earlier study in Lagos where only 17% of their patients with DM had Restrictive lung disease [9].

In our study, similar to several other studies longer duration of diabetes was associated with lower pulmonary functions [3,9,11].

Increase in age and longer duration of diabetes has a potential for longer exposure of the lung in diabetics to longer inflammatory processes and end glycation products which are part of the diabetes process and their consequences. In this scenario, possible acceleration of the physiological decline effect of ageing on the pulmonary functions may occur. However in our study the age of the patient did not appear to predict lung damage and this finding may require further evaluation with a larger study.

The potential effect of the BMI cannot be underestimated. In our study similar to those previously done in Nigeria we noted that BMI correlated negatively and significantly with pulmonary function test [10,11]. The effect of BMI on pulmonary function tests has been widely studied and this is found to be consistently lowered in those with higher BMI [3,9,12]. Possible reasons for this scenario include obesity associated chest wall compliance, metabolic syndrome and chronic inflammation [12]. Expectedly we have shown that ageing is related to lung function parameters. Our results showed that age correlated negatively and significantly with the PEFR, FEV1, and the FVC. Similarly the duration of diabetes mellitus correlated negatively with the PEFR as well as the FEV1. These findings suggest that an older age as well as longer duration of diabetes is important determinants of abnormal pulmonary functions in diabetes.

Glycaemic control was not noted to be associated with the pulmonary function test parameters. Thus similar to previous studies long term glycaemic control as determined by glycosylated haemoglobin levels was not a significant determinant of lung function in Diabetes. This is understandable as it only evaluated glycaemic control over the preceding 2-3 months which may not be long enough period to make a reasonable impact on the lung function.

An important and significant finding of this study is the fact that hypertension was the most significant predictor of abnormal lung function among persons with DM. While these findings had been previously documented elsewhere it has not been evaluated amongst Nigerians with Diabetes mellitus [13-15]. This may have a great implication for overall wellness in patients with DM. This may suggest that adequate blood pressure control in DM may in addition to protecting other organs from damage improve lung health in Diabetic patients. This assumption however will require further studies for evaluation.

## Conclusion

Restrictive lung function defect is common among patients with diabetes in Nigeria while clinical parameters namely ageing, high body mass index and long duration of diabetes mellitus all significantly affect the lung functions. It is therefore important to increase awareness of potential damage to the lungs in our patients with diabetes and encourage ideal BMI for this group of persons. Hypertension negatively predict abnormal lung function in our diabetics, thus potentially the lung appears to be at risk of damage from hypertension.it will therefore

be beneficial to the lung in addition to other known target organ for damage in hypertension to have well controlled hypertension in all patients with Diabetes mellitus. It will also be potentially useful to offer periodic lung function as part of diabetes annual checks for early detection of lung abnormalities.

In this study we were however limited by our inability to measure the diffusing capacity for carbon monoxide as well as total lung capacity in our subjects.

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