Ventiliatory function in Nigerians with type 2 diabetes

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Abstract

Reduced ventilatory function in type 2 diabetes has been reported in other parts of the world. This study aimed to assess the ventilatory function in Nigerians with type 2 diabetes and its relationship to the duration of symptoms of diabetes, glycaemic control, age, and body mass index (BMI). One hundred and one (101) patients with type 2 diabetes were matched to 104 control subjects with normal glucose tolerance. Historical and clinical data were documented and venous blood sampled for HbA_{1c} in the diabetes group. Peak expiratory flow rate (PEFR), forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC) and the ratio of the FEV_1 to the FVC as a percentage (FEV_1/FVC%) were measured for both groups. Study subjects and controls were similarly matched. Mean PEFR (L/s), FEV_1 (L), and FVC (L) were 5.6±2.24, 2.36±0.74, and 2.94±0.90, respectively, in the diabetes group and 6.31±1.62, 2.58±0.62, and 3.19±0.79, respectively, in the control group (p=0.006, 0.02, and 0.03, respectively). The FEV_1/FVC% was 81.90±24.17 in the diabetes group and 81.26±5.99 in controls (p= 0.86). Compared with predicted values for Nigerians, 11 (11%) of diabetes subjects had restrictive lung disease and 6 (6%) had obstructive lung disease while 1 (1%) of controls had restrictive lung disease and 5 (5%) had obstructive lung disease (χ^2=9.46, p=0.009). In multivariate analysis, age was inversely related to the PEFR (p=0.04). BMI was inversely related to PEFR, FEV_1, and FVC (p= 0.01, 0.001, 0.002, respectively). Duration of diabetes was also inversely related to FEV_1 (p= 0.02). HbA_{1c} was not significant for any ventilatory index. It was concluded that Nigerians with type 2 diabetes have significantly lower ventilatory function (with a restrictive pattern), compared with matched controls. Symptom duration, age, and BMI are independent determinants of ventilatory function.

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Introduction

Lung function is an independent risk factor for cardiovascular, pulmonary, and all-cause mortality in diabetes.[1] This is evident even in the absence of any overt limitation of activities due to reduced lung function; however, lung impairment may become debilitating with age and conditions of increased stress such as chronic hypoxia and volume overload and this effect may contribute to impact on mortality. This indicates that despite the presence of other strong diabetes-related causes of death, airflow limitation is an important predictor of mortality. This makes lung function and factors affecting it an important aspect of diabetes care.

Ventilatory function testing non-invasively quantifies physiological reserve in a large microvascular bed, and unlike myocardial and skeletal muscle function, pulmonary indices can be measured despite limitations in physical fitness and can, therefore, provide a useful measure of progression of diabetic microangiopathy. Histopathological changes in the lungs of subjects with diabetes, such as basal lamina thickening and fibrosis, support the effects of diabetes on lung function.[2] Therefore the lungs have been proposed as a target organ for diabetic microangiopathy in type 1 and type 2 diabetes.[3,4]

The impact of ethnicity and environment on lung function has been well documented,[5,6] and may contribute to a variation in ventilatory function in Nigerians with type 2 diabetes. This provides the premise for our study which was designed to compare the ventilatory function of Nigerians with type 2 diabetes to those without, and also to explore the factors that determine these indices.

Materials and methods

This was a cross-sectional case-control study conducted at the outpatient clinic of the Endocrinology Unit of the Lagos University Teaching Hospital (LUTH). Ethical approval for the study was obtained from the LUTH Health Research and Ethics Committee. Informed consent was obtained from all participants.

Consecutively consenting subjects with type 2 diabetes (study group) who satisfied the inclusion criteria were recruited. Healthy volunteers were recruited as controls.

The study group included those with type 2 diabetes attending the clinic for at least 1 month, between the ages of 30 and 60 years, who had never smoked and without any current respiratory complaints or a history of respiratory disease or occupational exposure that

could compromise lung function. Exclusion was based on physical examination only. Subjects with cardiovascular disease that could compromise lung function, such as heart failure, and those with physical disability capable of affecting lung function, such as kyphoscoliosis, pectus carinatum, and pectus excavatum, were excluded. The control group comprised healthy volunteers without diabetes, who had never smoked, and with similar exclusion criteria as for the study group.

The protocol followed involved documentation of historical details, physical examination, and anthropometric measurements. Venepuncture and spirometry were also performed. In brief, height and weight were measured by standard methods and the body mass index (BMI) calculated.[7,8] Waist circumference, and blood pressure were also measured by standard methods.[7]

The oral glucose tolerance test (OGTT) was obtained for the control group only to exclude diabetes in addition to impaired fasting glycaemia (IFG) and impaired glucose tolerance (IGT). Fasting blood glucose of ≥126 mg/dL) was used to define diabetes while fasting blood glucose of ≥110 mg/dL and <126 mg/dl was used to define IFG. IGT was defined as a 2 hour blood glucose post 75 g of glucose of ≥140 mg/dL and <200mg/dL.[9] Only control subjects with a normal fasting blood glucose of <110 mg/dl and 2 hour post oral glucose of <140mg/dL) were recruited into the study.

Peak expiratory flow rate (PEFR), forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), and the ratio of the forced expiratory volume in 1 second to the forced vital capacity in percentage (FEV_1/FVC%) were measured using the SBG® spirometer (SDI Diagnostics Inc, USA) which utilises a turbine sensor and is, therefore, not affected by temperature, pressure, or gas density and does not require calibration. The procedure was demonstrated to all subjects individually. A minimum of three and maximum of eight maximal performances were recorded until the results were reproducible, based on the 2005 European Respiratory Society (ERS)/American Thoracic Society (ATS) guidelines.[10] Recorded value was the maximum obtained. Using the predicted equation by Patrick and Femi-Pearse for adult Nigerians aged 17–60 years,[11] predicted values for FEV_1 and FVC were calculated for each patient and used to assess normalcy of ventilatory function and the pattern of ventilatory defect. An obstructive ventilatory defect was described when the FEV_1 was markedly reduced compared to the FVC, such that the FEV_1/FVC% was reduced to less than 70%. In a restrictive ventilatory defect, both the FEV_1 and FVC are markedly reduced such that the FEV_1/FVC% is about 70% or above.

Data analysis

The results were analysed using Epi Info version 3.5 2008 statistical software. Mean and standard deviation were computed for all continuous variables and comparison was done using Student's t-test. Frequencies were generated for categorical variables and compared with the chi square test. Multiple linear regression analysis was utilized for the determinants of ventilatory function; $p<0.05$ was accepted as significant.

Results

A total of 205 subjects were studied. The diabetes group comprised 101 subjects, while the control subjects comprised 104 subjects without diabetes.

Demographic and anthropometric data for the diabetes subjects and controls are summarised in Table 1 and show no significant difference in age distribution, gender, height, BMI, and blood pressure ($p>0.05$ in all cases). The waist circumference of the diabetes group was just significantly higher than that of controls ($p=0.04$)

For the diabetes subjects, the mean HbA_{1c} was 7.8±2.1 and 41.6% of them had HbA_{1c} levels less than 7%, indicating good glycemic control. The duration of diabetes ranged from 1 month to 18 years.

Table 1 Summary of demographic and anthropometric values for the type 2 diabetes subjects and control subjects

Parameter	Diabetes n=101		Control n=104		*p* value
	Range	Mean ± SD	Range	Mean ± SD	S<0.05
Age (years)	30–59	46.12±7.82	30–60	45.14±7.95	0.38
Gender		F=53.5%		F=52.9%	0.95
Height (m)	1.46–1.98	1.66±0.88	1.45–1.93	1.67±0.08	0.41
BMI (kg/m²)	19.94–39.63	28.29±4.54	18.78–40	27.21±4.75	0.10
WC (cm)	75.5–119	94.49±10.17	75–121	91.48±10.27	0.04
SBP (mmHg)	100–210	136.05±23.11	90–200	131.47±20.56	0.14
DBP(mmHg)	60–140	89.61±15.76	60–130	87.91±12.77	0.40

Note: BMI = body mass index; WC = waist circumference; SBP = systolic blood pressure; DPB = diastolic blood pressure.

Ventilatory indices

Table 2 is a comparison of the ventilatory indices in the study group and control group and it shows that the PEFR, FEV_1, and FVC were significantly lower in the diabetes subjects compared with the control subjects ($p=0.006$, 0.02, and 0.03, respectively); but the FEV_1/FVC% was not significantly different in the two groups ($p=0.86$).

Table 3 is a comparison of the ventilatory indices by

Table 2 Mean ventilatory indices in type 2 diabetes and controls

Ventilatory indices	Diabetes subjects Mean +SD (n=101)	Control subject Mean +SD (n=104)	T statistics	*p* value S< 0.05
PEFR L/s	5.56±2.24	6.31±1.62	2.76	0.006
FEV_1 L	2.36±0.74	2.58±0.62	2.34	0.02
FVC L	2.94±0.90	3.19±0.79	2.16	0.03
FEV_1/FVC%	81.70±24.17	81.26±5.99	0.18	0.86

Note: PEFR = peak expiratory flow rate; FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity. FEV_1/FVC% = forced vital capacity in percentage.

Table 3 Mean ventilatory indices in type 2 diabetes group and controls by gender category

	Diabetes subjects Mean±SD	Control subjects Mean±SD	T statistics	*p* value
Females	**n=54**	**n=55**		
PEFR (L/sec)	4.56±1.53	5.35±1.4	2.82	0.006
FEV_1 (Litres)	1.92±0.56	2.22±0.41	3.26	0.002
FVC(Litres)	2.40±0.67	2.74±0.51	2.96	0.004
FEV_1/FVC%	79.56±7.61	81.35±6.48	1.32	0.19
Males	**n=47**	**n=49**		
PEFR (L/s)	6.70±2.39	7.38±1.10	1.81	0.07
FEV_1 (L)	2.87±0.58	2.99±0.56 1.	1.03	0.31
FVC(L)	3.55±0.73	3.70±0.73	1.01	0.31
FEV_1/FVC%	84.16±34.52	81.16±5.45	0.60	0.55

Table 4 Number of subjects with abnormal ventilatory function in the diabetes group and control group

	Type 2 diabetes	Controls
Number of subjects with abnormal ventilatory function	17(17%)	6(6%)
Number of subjects with restrictive ventilatory defect	11(11%)	1(1%)
Number of subjects with obstructive ventilatory defect	6(6%)	5(5%)

Table 5 Mean values (±SD) or anthropometric data, historical data, and HbA_{1c} levels of diabetes subjects with normal and abnormal ventilatory function

	Normal ventilatory function n=84 (84%)	Abnormal ventilatory function n=17 (17%)	T statistics	*p* value
HbA_{1c} (%)	4.85±2.2	3.77±1.9	0.8	0.42
Age (years)	45.19±7.7	50.65±6.7	2.7	0.008
BMI (kg/m²)	28.03±4.5	29.56±4.6	1.27	0.2
Waist circumference (cm)	93.77±10.3	98.06±8.9	1.60	0.11
Diabetes duration (years)	5.05±5.2	6.55±5.0	1.1	0.28

gender category showing that the PEFR, FEV_1, and FVC were significantly lower in only the female subjects with diabetes compared with female control subjects.

Compared with predicted values, 84 (83%) of type 2 diabetes subjects had normal ventilatory function compared with 98 (94%) of control subjects with normal ventilatory function (χ^2= 5.23, p=0.02). Eleven (11%) of the subjects with type 2 diabetes had restrictive lung disease and 6(6%) had obstructive lung disease, while 1(1%) of controls had restrictive lung disease and 5(5%) had obstructive lung disease (χ^2=9.46, p=0.009). This is shown in Table 4.

Determinants of ventilatory indices

Multiple linear regression analysis was utilised for the determinants of ventilatory indices in the diabetes subjects. The model included the following variables: HbA_{1c} (%), duration of symptoms of diabetes (years), age (years), BMI (kg/m²), waist circumference (cm), systolic blood pressure (mmHg), and diastolic blood pressure (mmHg).

BMI was significantly and inversely related to the PEFR, FEV_1, and FVC (p=0.01, 0.002, 0.002, respectively). Duration of diabetes was significantly and inversely related to the FEV_1 only (p=0.02), while age was significantly and inversely related to the PEFR only (p=0.04).

Table 5 shows a comparison of the mean ±SD of the age, BMI, duration of diabetes, waist circumference, and HbA_{1c} between diabetes subjects with normal ventilatory function and those with abnormal ventilatory function. The mean age ±SD is the only variable significantly higher in those diabetes subjects with abnormal ventilatory function compared with those with normal ventilatory function (p=0.008).

Discussion

Diabetes is a multisystemic disease and microangiopathy affects almost every organ. The effect of diabetes on the ventilatory function is the focus of this study.

The main finding is that ventilatory function is significantly reduced in diabetes subjects compared with

controls without diabetes. Ventilatory dysfunction in diabetes subjects is predominantly restrictive as shown by the preserved ratio of FEV_1/FVC% and the number of diabetes subjects with restrictive defect compared with controls. Our study confirms the findings in large population studies in Australia, Denmark, and the United States, including those in which the measured values were compared with predicted values.[3, 12, 13] Another study in the Asian population in Saudi Arabia also had similar findings when they compared to controls.[14] The proportion of diabetes subjects with obstructive lung disease was similar to the proportion in controls, suggesting that this defect is not necessarily due to diabetes. Our finding of predominantly restrictive lung defect in type 2 diabetes is supported by studies of lung function in diabetes in which carbon monoxide diffusing capacity (DLCO) was also measured and found to be significantly lower than that of controls.[15–17] Also, the histopathological finding in the lungs of subjects with diabetes, which consists of fibrosis and basal lamina thickening, that are suggestive of microangiopathy, will lead to a restrictive lung defect.[2] The explanation for the finding of reduced ventilatory function in only the female subjects with type 2 diabetes when categorised by gender is not clear at this time.

In addition, we evaluated some possible determinants of ventilatory defect in diabetes and found age, BMI, and the duration of diabetes to be the significant determinants with an inverse relationship to the ventilatory indices.

The duration of diabetes was a significant determinant of FEV_1 and a trend was seen for the FVC. This agrees with the findings in earlier population-based studies in Australia, Denmark, and India.[3,12,17]. The underlying mechanism of reduced ventilatory function in diabetes may be related to inflammation. This inflammation hypothesis also underscores the putative mechanism of development of diabetes and as such progressive decrease in lung function may be mediated via progression in inflammation, the severity of which would increase with longer duration of diabetes. Prospective studies have found that lower baseline ventilatory function is a risk factor for developing type 2 diabetes.[18–20] The National Health and Nutrition Examination Survey (NHANES) found that subjects who developed diabetes after 8 years of follow up had lower baseline ventilatory function and that restrictive lung defect and not obstructive defect was associated with a greater risk of diabetes.

The BMI had a significant inverse relationship to the PEFR, FEV_1, and FVC. The Fremantle Diabetes Study (FDS), a population-based study in southern Australia also found that BMI, coronary artery disease, and age were significant determinants of ventilatory function.[3] The effect of BMI in reducing lung function has been well documented.[21–24] Factors responsible for this include reduced chest wall compliance and increased airway resistance. Another more important effect of BMI on lung function is related to the metabolic syndrome in which low-grade inflammation plays a central role in the development of diabetes as well as reduced lung function.[23] Waist circumference also showed a trend as a determinant of reduced FVC. The higher waist circumference of the diabetes subjects in this study despite a similar BMI reflects abnormal fat distribution in diabetes subjects. Truncal obesity on its own contributes to insulin resistance and increases the risk for type 2 diabetes.[21] Abdominal adiposity independent of the BMI has been shown to have an inverse relationship with FEV_1 and FVC supporting the finding in this study.[24] This is thought to be due to limited ability of the diaphragm to displace abdominal fat as well as the role of waist circumference in the metabolic syndrome.

Age was found to be a significant determinant of PEFR in this study as well as in the FDS. The age of the diabetes subject with ventilatory defects was also significantly higher than the age of the diabetes subjects with normal ventilatory function, reflecting the expected age-related decline in lung function.[25,26] This finding, however, suggests that diabetes may accelerate this decline.

HbA_{1c} was not a significant determinant of ventilatory function in multivariate analysis and this finding is supported by previous studies.[3,17] This is reasonable because the HbA_{1c} reflects only the glycaemic control in the previous 2 to 3 months, a duration which may not be long enough to impart an effect on lung function. However long-term glycaemic control, which is determined as the mean updated HbA_{1c} over many years and referred to as glycaemic exposure has been found to be a major determinant of lung function.[4]

Conclusion

The profile of reduced ventilatory function in Nigerians with type 2 diabetes is similar to that of other populations, with a predominant restrictive pattern. The effect of diabetes on ventilatory function increases with advancing age, longer duration of symptoms of diabetes, and higher BMI. Since BMI is the only modifiable factor among these, achieving and maintaining a normal BMI, therefore, is paramount in diabetes care. This is to help preserve an already declined ventilatory function, which is a major determinant of mortality.

Limitations in this study include the fact that lung volumes, especially the total lung capacity and the DLCO, were not measured to determine clearly that restrictive ventilatory defect is present in type 2 diabetes.

References

1. Ferguson GT, Enright PL, Buist AS, Higgins MW. Office spirometry for lung health assessment in adults: a consensus statement from the national lung health education program. *Chest* 2000; 117: 1146–61.
2. Matsubara T, Hara F. The pulmonary function and histopathological studies of the lung in diabetes mellitus. *Nippon Ika Daigaku Zasshi* 1991; 58: 528–36.
3. Davis TME, Knuiman M, Kendall P, Vu H, Davis WA. Reduced pulmonary function and its associations with type 2 diabetes: the Fremantle Diabetes Study. *Diabetes Res Clin Pract* 2000; 50: 153–9.
4. Davis WA, Knuiman M, Kendell P, Grange V, Davis TME. Glycemic exposure is associated with reduced pulmonary function in type 2 diabetes: The Fremantle Diabetes Study. *Diabetes Care* 2004; 27: 752–7.

5. Elebute EA, Femi-Pearse D. Peak flow rate in Nigerians. *Thorax* 1971; 26: 597.
6. Ambromowitz S, Leiner GC, Lewis AW. Vital capacity in the Negro. *Am Rev Respir Dis* 1965, 92: 287–92.
7. Tolonen H, Kuulasma K, Laatikain T, Wolf H and the European Health Risk Monitoring Project. Recommendation for indicators, international collaboration, protocol and manual operations for chronic disease risk factor surveys. October 2002. URL: http.// www ktl.fi/publications/ehrm/products/title.htm.
8. Garabed E. Adolf Quetelet (1796–1874): The average man and indices of obesity. *Nephrol Dial Transplant* 2008; 23 (Suppl 1): 47–51.
9. Standards of Medical Care in Diabetes: Position statement. *Diabetes Care* 2009; 32: 513–61.
10. Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. *Eur Respr J* 2005; 26: 319–38.
11. Patrick JM, Femi-Pearse D. Reference values for FEV1 and FVC in Nigerian men and women: a graphical summary. *Niger Med J* 1976; 6: 380–5.
12. Lange P, Parner J, Schnohr P, Jensen G: Copenhagen city heart study: longitudinal analysis of ventilatory capacity in diabetic and non-diabetic subjects. *Eur Respir J* 2002; 20: 1406–12.
13. Hsin-Chieh Y, Naresh MP, Nae-Yuh W, et al. Cross sectional and prospective study of lung function in adults with type 2 diabetes. *Diabetes Care* 2008; 31: 741–6.
14. Meo SA, Al-Drees AM, Arif M, Al-Rubean K. Lung function in type 2 Saudi diabetic patients. *Saudi Med J* 2006; 27: 338–43.
15. Schuyler M, Niewoehner D, Inkley S, Kohn R. Abnormal lung elasticity in juvenile diabetes mellitus. *Am J Resp Disease* 1976; 113: 37–41.
16. Sandler M, Burn A, Stewart R. Cross-sectional study of pulmonary function in patients with insulin dependent diabetes mellitus. *Am Rev Respir Dis* 1987; 135: 223-228.
17. Sinhs S, Guleria R, Pandey RM, Tiwari S. Pulmonary functions in patients with type 2 diabetes mellitus and correlation with anthropometry and microvascular complications. *Indian J Med Res* 2004, 119: 66–71.
18. Engstrom G, Hedbland B, Nilsson P, et al. Lung function, insulin resistance and incidence of cardiovascular disease: a longitudinal study. *J Intern Med* 2003; 253 (Suppl 5): 574–81.
19. Lazarus R, Sparrow D, Weiss ST. Baseline ventilatory function predicts the development of higher levels of fasting insulin and fasting insulin resistance index: The normative aging study. *Eur Respir J* 1998; 12: 641–5.
20. Ford SE, Mannino DM. Prospective association between lung function and the incidecnce of diabetes: findings from the national health and nutrition examination survey epidemiologic follow up study. *Diabetes Care* 2004; 27: 12.
21. Canory D, Luben R, Welch A, et al. Abdominal obesity and respiratory function in men and women in the EPIC-Norfolk study United Kingdom. *Am J Epidemiol* 2004; 159 (Suppl 12): 1140–9.
22. Ochs-Balcom HM, Grant BJ, et al. Pulmonary function and abdominal obesity in the general population. *Chest* 2006; 129 (suppl 4): 853–62.
23. Wen-Yuan L, Chien-An Y, Hao-Chien W, Kuo-Chin H. Impaired lung function is associated with obesity and metabolic syndrome in adults. *Obesity* 2006; 14: 1654–61.
24. Li AM, Chan. The effect of obesity on pulmonary function. *Arch Dis Child* 2003; 88: 361–3.
25. Ele PU. Reference values for FEV1 and FVC in male adolescents and young adults of Ibo origin. *East Afr Med J* 1992; 69: 105–9.
26. Schoenberg JB, Beck GJ, Boubuys. Growth and decay of pulmonary function in healthy blacks and whites. *Resp Physical* 1978; 33: 367–93.