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Pulmonary Function in Females with Type 2 Diabetes in AWKA, Anambra State

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Abstract: Reduced lung volumes have been a complication associated with chronic diabetes mellitus but these findings have been made in other parts of the world with few kinds of literature in relation to this subject matter, in Nigeria. A focus on diabetic Nigerian females for the first time will add in filling the information gap on how pulmonary functions are affected in diabetics from this part of the world in comparison to their counterparts from other parts of the world.166 female subjects (83 subjects as control subjects and 83 subjects as study subjects), aged between 30-68 years participated in this study. Lung function test was carried out on the subjects and on analyzing the data obtained, it was seen that there is a decline in pulmonary function in diabetics. This study concludes that diabetic subjects show a decrease in pulmonary function parameters (Peak Expiratory Flow Rate- PEFR, Forced Vital Capacity- FVC, Forced Expiratory Volume in one second- FEV_1 and FVC/FEV_1% ratio). Also, interplay of anthropometric data and not their individual actions result in negative effect on pulmonary function. Proper pulmonary function test and other investigations may reduce the risk of mortality among diabetics

Keywords: Type 2 Diabetes, Peak Expiratory Flow Rate-PEFR, Forced Vital Capacity-FVC, Pulmonary Function, Lung Function Test

1. Introduction

Type 2 diabetes mellitus is considered a major health concern around the world [33] and being a metabolic disease known to affect a number of body tissues and organs, the lung which ventilates the blood may also suffer various injuries in diabetes which may result in a decrease in pulmonary function [29]. To ascertain a decline in pulmonary function in humans, the lung function test is carried out with a focus on the Peak Expiratory Flow Rate (PEFR), Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV_1) and FVC/FEV_1% ratio.

Though reduced lung volumes have been a complication associated with chronic diabetes mellitus [19, 25], these findings have been made in other parts of the world with few pieces of literature in Nigeria, in relation to this subject matter. Considering climate, diet lifestyle and a lot of other factors, data obtained here may vary from data obtained in other parts of the world. From this, one can see that carrying out more studies in Nigeria will buttress the findings made by reference [26]. Also, a focus on diabetic Nigerian females for the first time will add in filling the information gap on how pulmonary functions are affected in diabetics from this part of the world in comparison to their counterparts from other parts of the world.

The aim of the study is to determine pulmonary function in females with type 2 diabetes mellitus in Nigeria in view of contributing to the provision of improved management of diabetes mellitus. The objective of the study was to establish the values of Peak Expiratory Flow Rate (PEFR), Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV_1), FVC/FEV_1% ratio in female diabetic

subjects and to determine the independent relationship between age, body mass index, fasting blood sugar level and pulmonary function in females with type 2 diabetes mellitus.

2. Materials and Methods

2.1. Study Area and Location

This study was carried out in the Out-Patient Department of the Internal Medicine Unit, Chukwuemeka Odumegwu Ojukwu University Teaching Hospital which is a tertiary healthcare facility in Amaku, Awka South local government area of Anambra State, Nigeria. It is located within Awka metropolis which is an urban area with an estimated population of over 600,000.

2.2. Study Population and Data Collection

The study population was obtained using the random sampling method and comprised of adult females between the ages of 30 and 68. The study sample size of 166 was determined according to Araoye [4]. Anthropometric data on the subjects such as age, weight, and height were obtained from the hospital records.

2.3. Exclusion Criteria

The study excluded subjects with the presence of underlying pulmonary conditions e.g. obstructive respiratory disease, tuberculosis, asthma, etc. In addition, subjects exposed to tobacco smoking, alcohol consumption and exposure to pulmonary occupational hazards were completely excluded from the study.

2.4. Inclusion Criteria

Diabetic subjects considered for the study were those with Fasting blood sugar of about 100mg/dl (5.6mmol/L) and above. While, those with Fasting blood sugar of about 70–99 mg/dl (3.9–5.5mmol/L) were considered for the control group [32].

2.5. Instruments

The following instruments were used to carry out the study; peak expiratory flow meter, digital spirometer, sterile cotton wool, methylated spirit and latex gloves.

2.6. Ethical Consideration

Ethical approval was duly obtained from the Ethical Committee of the Chukwuemeka Odumegwu Ojukwu University Teaching Hospital Amaku, Awka in Anambra State. Meanwhile, a signed consent of the subjects was also obtained before their participation in the study.

2.7. Experimental Procedure

Standing upright and according to the European Respiratory Society (ERS)/American Thoracic Society (ATS) guidelines [25], each subject was asked to inhale maximally through the nose and exhale maximally through the mouth into the mouthpiece of the peak expiratory flow meter to obtain peak expiratory flow rate (PEFR) readings. The procedure was repeated using the digital spirometer to obtain readings for FEV_1 and FVC. Three (3) readings were obtained from each subject for each variable and this was used to obtain the average reading for each variable.

2.8. Statistical Analysis

The data obtained were expressed as Mean ± Standard Deviation (SD). Statistical comparison was performed using the Student's t-Test and the Pearson's Product Moment Correlation Coefficient. The Statistical Package for Social Science Program (SPSS) software (version 21.0) was used and a P-value of less than 0.05 ($P < 0.05$) was considered significant while a P-value greater than 0.05 ($p>0.05$) was considered to be statistically non-significant.

3. Results

All data obtained from this study are expressed in mean ± standard deviation and comparisons conducted using the Student's t-test and the Pearson's Product Moment Correlation Coefficient. Statistical analysis was only considered significant at a level of $p<0.05$.

Table 1. *Age, Body Mass Index (BMI) and Fasting blood sugar (FBS) of diabetic females.*

ANTHROPOMETRIC DATA	GROUPS (MEAN±SD)		p-VALUE
	CONTROL	STUDY	
AGE (years)	51.55±8.77	57.38±8.62	0.041
HEIGHT (m)	1.65±0.06	1.66±0.04	0.064
WEIGHT (kg)	59.72±9.20	75.29±9.02	0.018
BMI (kg/m^2)	21.99±3.70	27.54±3.66	0.001
FBS (mm/dl)	80.48±7.07	136.68±17.27	0.017

Table 1 shows a significant elevation in the mean age of female diabetic subjects were compared with control subjects. More so, a significant increase in the BMI and FBS level is also observed in female diabetic subjects compared to control subjects though there is no significant difference between the height of the study and control groups.

Table 2. *Effect of Type 2 Diabetes on Pulmonary function parameters.*

PARAMETERS	GROUPS (MEAN±SD)		p-VALUE
	CONTROL	STUDY	
FEV1 (L)	1.96±0.43	1.51±0.27	0.002
FVC (L)	2.11±0.49	1.60±0.29	0.016
PEFR (L)	0.25±0.41	0.15±0.28	0.001
FEV1/FVC%	93.02±7.14	94.41±4.35	0.89

Table 2 shows a significant reduction in three pulmonary function parameters (PEFR, FEV_1, and FVC) when female diabetic subjects were compared with control subjects. However, no significant difference was observed in the

FEV1/FVC ratio (%) when the data from female diabetic subjects were compared to control.

In Table 3 below, there is a weak negative correlation between Age and PEFR in female control subjects. A weak negative correlation between age and FEV1 and FVC is also observed in female control subjects. This correlation is however not statistically significant at P<0.05. In female diabetic subjects, a weak positive correlation which is statistically significant at P<0.05 is observed between Age and PEFR. A negative correlation which is not statistically significant at P<0.05 is observed between Age and FEV_1 and FVC.

Table 3. *Descriptive statistics and correlation analysis of the relationship between age and pulmonary parameters in female control and diabetic subjects.*

CORRELATION				
SUBJECTS	**Parameter**	**N**	**PPMCC**	**Significance (2-tailed)**
	Age (years)			
	PEFR (L)		-0.058	0.601
CONTROL	FEV_1(L)		0.101	0.364
	FVC (L)		0.111	0.316
	FEV1/FVC%	166	0.038	0.970
	Age (years)			
	PEFR (L)		0.217	0.049
DIABETIC	FEV_1 (L)		-0.216	0.050
	FVC (L)		-0.197	0.074
	FEV1/FVC%		-0.040	0.969

N: Total number of the sample across all groups
PPMCC: Pearson's Product Moment Correlation Coefficient
Level of Significance at P<0.05 (confidence interval)

In Table 4 below, a weak negative correlation which is statistically not significant is observed between FBS and respiratory parameters in female control subjects. In female diabetic subjects, a weak negative correlation which is not statistically significant at P<0.05 is observed between FBS and PEFR, $FEV_1$and FVC are observed.

Table 4. *Descriptive statistics and correlation analysis of the relationship between fasting blood sugar (FBS) and pulmonary parameters in female control and diabetic subjects.*

CORRELATION				
SUBJECTS	**Parameter**	**N**	**PPMCC**	**Significance (2-tailed)**
	FBS (mm/dl)			
	PEFR (L)		-0.198	0.073
CONTROL	FEV_1 (L)		-0.131	0.238
	FVC (L)		-0.092	0.409
	FEV1/FVC%	166	-0.131	0.896
	FBS (mm/dl)			
	PEFR (L)		-0.044	0.691
DIABETIC	FEV_1 (L)		0.137	0.218
	FVC (L)		0.169	0.128
	FEV1/FVC%		-0.136	0.893

N: Total number of the sample across all groups
PPMCC: Pearson's Product Moment Correlation Coefficient
Level of Significance at P<0.05 (confidence interval)

From table 5 below, a weak negative correlation which is not statistically significant at P<0.05 is observed between BMI and respiratory parameters in female control subjects. In female diabetic subjects, a weak negative correlation between BMI and PEFR, and a positive correlation between BMI and FEV_1& FVC which are not statistically significant at P<0.05 is observed.

Table 5. *Descriptive statistics and correlation analysis of the relationship between the BMI and pulmonary parameters in female control and diabetic subjects.*

CORRELATION				
SUBJECTS	**Parameter**	**N**	**PPMCC**	**Significance (2-tailed)**
	BMI (kg/m^2)			
	PEFR (L)		-0.085	0.444
CONTROL	FEV_1(L)		-0.112	0.313
	FVC (L)		-0.052	0.642
	FEV1/FVC%	166	-0.136	0.892
	BMI (kg/m^2)			
DIABETIC	PEFR (L)		0.204	0.064
	FEV_1 (L)			
	FEV1/FVC%		-0.1164	0.908

N: Total number of the sample across all groups
PPMCC: Pearson's Product Moment Correlation Coefficient
Level of Significance at P<0.05 (confidence interval)

4. Discussion

Table 1 shows that the age, body mass index (BMI) and fasting blood sugar (FBS) of diabetic subjects were all significantly elevated when compared with control subjects. The age difference between diabetic and control subjects in this study shows that diabetes affects most of the population in their 50's. This occurs when body tissues develop a resistance against the insulin produced [30]. Results from the present study are in agreement with findings of Anandhalakshmi, *et al*., who reported that pulmonary functions were decreased in diabetics in comparison with age and sex-matched non-diabetic subjects [3].

The FBS level of diabetics is significantly increased when compared with control subjects in this study and this can be said to occur due to the inability of the tissues to respond to the action of insulin (insulin resistance) thereby resulting in hyperglycemia which is characteristic of type 2 diabetes [13, 28].

An individual with a BMI above $30kg/m^2$ is said to be obese, and according to Gigante, *et al.,* as cited by reference, [27], obesity is a predisposing factor for diabetes. In line with this, this study also observed a significantly elevated BMI for diabetic subjects when compared to control subjects. This elevated BMI in diabetics can be ascribed to the increased accumulation of fat in adipose tissues which results from constant conversion of excess calories, causing reduction in the total water content in the body and according to Zerah *et al.,* as cited by reference [27], increased pulmonary blood volume resulting in the congestion of bronchial vasculature in the submucosa of the airway, the thickening of the airway wall and a decrease in the size of the airway. Also, the release of histamine can be increased by the presence of very low-density lipoproteins in these individuals causing elevated

vascular permeability and smooth muscle contractility [27]. While height is also a determinant of BMI, the reduced height in diabetics may be due to the fact that growth has ceased in the long bones at that age, thus preventing further growth of the individual.

From table 2 of the present study there was a significant decrease in FEV_1, FVC and PEFR in diabetic subjects with an increase in the FEV_1/FVC% ratio in diabetic subjects which is consistent with previous studies on the effects of diabetes on pulmonary functions [1, 2, 11, 19, 21, 31, 34]. This observation may be attributed to poor lung compliance and elastic recoil. In addition, myopathic or neuropathic alterations in the bronchial reactivity affect respiratory muscles further which impair the endurance and efficiency of a ventilator pump [24].

In patients with type-1 diabetes, Wanke and co-workers found that maximal sniff esophageal and trans-diaphragmatic pressures and vital capacity (VC) were significantly lower in diabetics when compared with the control group, and the reduction of VC in these patients was attributed to the reduced capacity of the inspiratory muscles [35]. Barrett-Connor and Frette reported that FVC and FEV_1 were inversely related to the duration of diabetes [6]. However, study conducted by Faith and colleagues, fond no correlation between pulmonary function and diabetes duration, or control or with respiratory muscle strength and they suggested that lower pulmonary function parameters in type 2 diabetes were not correlated with duration of diabetes, fasting blood glucose, or %HbA1c levels in the patient group [16].

The exact mechanisms underlining the diabetic pulmonary damage are not fully understood. However, it has been attributed to the hyperglycemia that occurs in diabetes. In one study, Davis *et al*., [11] revealed that lower lung volumes and reduced airflow were related to glycemic control and identified that pulmonary functions parameters (FVC, FEV_1) were significantly reduced in diabetics with poor glycemic control; hence, poor glycemic control is a strong indicator of reduced lung function [12, 22]; though this factor is not included in this study. The hyperglycemia in diabetics is seen to result in non-enzymatic glycosylation of proteins (collagen and elastin) in the lungs and chest wall causing the accumulation of collagen in lung connective tissue [8, 16]. This collagen accumulation in the lung leads to thickening of basement membrane, increased stiffness of the lung parenchyma, prevention of elastic recoil in the lungs which leads to collapse of small airways during expiration and microangiopathy, thus reducing lung volumes and capacities [1, 9, 24, 31]. Toxic effects such as osmolarity and advanced glycation end products like pentosidine resulting from hyperglycemia induce endothelial dysfunction via the decrease in hydroxylysine residues results in the shortening of collagen fibril diameter thus reducing the rate of pyridinium cross-links formation [36].

There is also an induced change in intracellular pathways particularly; protein kinase C, aldose reductase, reactive oxygen intermediate and the advanced glycation end product pathways resulting in the activation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) pathway and vascular inflammation [23]. Oxidative stress has been reported to play a major role in these complications. A number of studies have implicated hyperglycaemia-induced oxidative stress in the aetiology of a variety of functional and structural disorder in the central and peripheral nervous systems [7, 15, 17, 18]. The authors reported that the axonal loss of the phrenic nerve resulting from diabetic polyneuropathy may lead to poor compliance of the diaphragm.

Another possible mechanism involved in pulmonary disorder in diabetes is systemic inflammation. Excessive inflammatory responses in the lung caused by abnormal inflammatory mechanisms could result in impaired lung function, a possible explanation for the diminished lung function years prior to the diagnosis of diabetes [5, 10, 20, 37]. It has been observed that hyperglycemia is closely associated with raised levels of inflammation markers (ferritin, fibrinogen, TNF-alpha and C-reactive protein), suggesting the possible participation of inflammation in impaired lung function [14]. Cells exposed to hyperglycaemic conditions were seen to have undergone histone modifications in *in-vitro* studies. This resulted in the activation of multiple transcription factors [23], increased H3K4 methylation at the NF-κB-p65 promoter, enhanced expression of NF-κB-p65 and increased NF-κB-induced pro-inflammatory gene expression [23]. Concisely, results of the present study unveiled that patients with type-2 diabetes had a restrictive pulmonary defect as mainly indicated by the increase in the FEV_1/FVC %ratio.

5. Conclusion

Diabetic subjects showed a decrease in pulmonary function parameters (Peak Expiratory Flow Rate- PEFR, Forced Vital Capacity- FVC, Forced Expiratory Volume in one second- FEV_1 and FVC/FEV_1% ratio). There was a slight correlation between age and pulmonary function between diabetic and non-diabetic subjects when compared to the correlation between FBS and pulmonary function and the correlation between BMI and pulmonary function that showed no significant correlation. Hence, a synergy of anthropometric data and not their individual actions result in a negative effect on pulmonary function.

6. Implications and Recommendation

The study has shown that there is a slight correlation between age and pulmonary function between diabetic and non-diabetic subjects in Awka, Anambra State. Also, there was no correlation between FBS and pulmonary function and there was no correlation between BMI and pulmonary function. This suggests that independent of one another, there may be no direct correlation between these factors and pulmonary function parameters although when acting together, there may be a significant correlation.

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