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Lung Function in Sudanese Children and Adolescents with Type 1 Diabetes Mellitus

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Authors' contributions

This work was carried out in collaboration between all authors. Author OMAT designed the study, wrote the protocol and wrote the first draft of the manuscript. Author HAA managed the literature searches, analyses of the study performed the spectroscopy analysis and author AMB managed the experimental process. All authors read and approved the final manuscript.

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ABSTRACT

Background: Diabetes Mellitus Type 1 (DMT1) is a chronic, debilitating and multifactor disease that is emerging as an important health problem in Sudan. The aim of this study was to investigate the lung functions in Sudanese children and adolescents as well as to explore the effects of duration, age, gender and insulin dose on the pulmonary functions.
Methods: This is a hospital-based controled study conducted in the diabetic center of Wad Madani Pediatrics Hospital. A total of 80 males and 80 females with DMT1 and matching healthy controls were included. Spirometry was performed on a microspirometer (compact hand instrument, Switzerland, 2000).
Results: Our data revealed that children with diabetes showed significantly lower mean values of Forced Expiratory Volume in First Second (FEV_1), Forced Vital Capacity (FVC) and Peak Expiratory Flow Rate (PEFR), except the ratio FEV_1/FVC that has shown a significant increase compared with the healthy controls. Male patients with diabetes demonstrated a greater increase in FEV_1, FVC and PEFR than the females, but the ratio FEV_1/FVC was increased in both equally

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and significant correlations between FEV_1, FVC, PEFR and age, gender, duration dose of insulin were found in patients with diabetes.
Conclusion: The actual lung function data among Type 1 diabetic children and adolescents showed significantly lower values of FVC, FEV_1, and PEFR with increased FEV_1 and FVC compared to the predicted lung function data which indicated a restrictive pattern.

Keywords: Pulmonary function tests; type I diabetes mellitus; insulin.

1. INTRODUCTION

Diabetes Mellitus Type 1 (DMT1), or juvenile-onset or insulin-dependent diabetes, is a chronic, debilitating and multifactor disease. About 208,000 Americans under age 20 are estimated to have diagnosed diabetes, approximately 0.25% of that population. DMT1 accounts for 5–10% of the total cases of diabetes [1]. Diabetes mellitus causes various macro- and micro vascular complications such as retinopathy, nephropathy, neuropathy and lung damage. This is mainly a consequence of biochemical and structural changes in basal membrane proteins in different organs that result in non-enzymatic glycosylation of proteins such as collagen, elastin leading to thickening of basement membrane and micro–angiopathy [2,3].

Previous studies assessing the association of reduced lung function in patients with diabetes are contradictory [4-7]. Schernthaner et al. reported normal pulmonary function [8], while other authors found abnormalities in pulmonary functions, mechanics, and diffusing capacity [6,7]. It has been proposed that the lung is a target organ in DM with the thickening of the walls of the alveoli, alveolar capillaries and pulmonary arterioles with a consequent pulmonary dysfunction [9,10]. Pulmonary gas exchange occurs across the respiratory membrane that consists of a basal alveolar membrane, interstitial tissue and capillary endothelium. Therefore any disruption of the integrity of alveolocapillary membrane will affect the alveolar gas exchange [11]. So we can assume that pulmonary dysfunction such as reduced alveolar gas exchange can occur in patients with diabetes.

Yet, there is limited evidence available regarding the role of DMT1 on the pulmonary functions especially in primary school-age children. Moreover, far as we know this the first study in Sudan (Al Gezira State) that aimed to investigate the lung functions in Sudanese children and adolescents as well as to explore the effects of duration, age, gender and insulin dose on the pulmonary functions.

2. METHODOLOGY

2.1 Study Area and Population

This a hospital-based controlled study conducted at the diabetes center of the Wad Madani Pediatrics Hospital (WMPH), which is the largest hospital for treatment of patients with diabetes in Al Gezira State, Sudan. During January to September 2011, one hundred and sixty children and adolescents (80 males and 80 females) with DMT1 were selected from the outpatient clinics of WMPH. Eighty healthy matching volunteers, forty for each gender (controls) were selected from the outpatient clinic.

2.2 Inclusion and Exclusion Criteria

Children or adolescents 5-20 years old, with diabetes for at least one year, were included. The controls were non-diabetics. Exclusion criteria children with gross clinical abnormalities of the vertebral column, thoracic cage, neuromuscular diseases, known cases of anemia, asthma, cardiopulmonary diseases, malignancies, cigarette smokers, as well as children with previous abdominal, or chest surgery were excluded from the study. In addition, any child with known complications of diabetes such as diabetic neuropathy, nephropathy, retinopathy, or exposed to industrial pollutants, or living in close vicinity of an industry producing dust, fumes, flour or oil [12] were also excluded from the study.

Both groups were matched according to age, sex, height, weight and area of residence. Clinical examination was carried out by a specialist pediatrician to exclude signs of acute or chronic medical abnormalities.

2.3 Measurement of Pulmonary Function Tests

A micromedical spirometer (compact hand instrument, Switzerland, 2000) was used. It contains a mouthpiece tube and digital volume transducer which consists of an acrylic tube with a freely rotating vane, the rotation of which is detected by the interruption of an infrared beam

which produces an electrical pulse train at the output of a phototransistor, the number of rotations being proportional to the volume of air passing through the turbine. The rate of rotation is proportional to the flow rate. The apparatus was calibrated daily and operated within the ambient temperature range of 20-24℃. The precise technique in executing various lung function tests for the present study was based on the operation manual of the instrument with special reference to the official statement of the American Thoracic Society and European Respiratory Society of Standardization of Spirometry [13]. All pulmonary function tests were carried out at a fixed time of the day (8:00-10:00) to minimize any diurnal variation.

2.4 The Technique of the Pulmonary Function Tests

First the participants were interviewed to collect the following data: the personal information (age, sex, duration of disease, insulin dose, weight, height, occupation and exposure to any chemical fumes or gases), health conditions, cigarette smoking, any hereditary disease, any respiratory disease, blood pressure, heart rate and disease-free condition. Then the children were informed of the whole maneuver and encouraged to practice this maneuver before doing the pulmonary test. The test was performed with the children in the standing position using a nose clip. The test was repeated 3 times after an adequate rest, the lung function parameters were measured including forced vital capacity (FVC), forced expiratory volume in first second (FEV1), forced expiratory ratio (FEV1/FVC) and peak expiratory flow rate and (PEFR).

2.5 Data Analysis

Data analysis was performed using the SPSS version 19 for windows (SPSS Inc., Chicago, IL, USA). Descriptive statistics (mean, standard deviation, and proportion) were used. Patients with diabetes were compared with those without diabetes for all subjects using the independent *t*-test. A value of $p<0.05$ was considered statistically significant. The relationship (regression) and correlation between variables were made according to Gomez and Gomez (1984).

2.6 Ethical Considerations

The research conforms to the ethical principles of medical research developed by the World Medical Association Declaration of Helsinki. Ethical clearance was given by the Research Committee (Faculty of Medicine/Omdurman Islamic University). Approval was obtained from the General Manger of Wad Madani Pediatrics Hospital as well as written consents from each participant before entry into the study.

3. RESULTS

One hundred and sixty children and adolescents (80 male and 80 female) with DMT1 were selected from the outpatient clinics of WMPH. Healthy matched eighty volunteers forty for each gender (control) were selected from the outpatient clinic. The mean age among the DMT1 cases was 12.16±3.9 years and that of controls was 13.12±4.12 years. While the mean duration of the disease among cases was 3.4± 2.63 years. Moreover, the cases received Mixtard Insulin, that divided into morning and evening doses, the mean of the morning dose was 17.8±7.87 IU and evening dose was 9.2±4.04 IU. Tables 1 and 2 compares the pulmonary function test parameters between males and females patients with DMT1 and controls respectively. While Table 3, illustrated the significant correlation between gender and rate of FEV_1, FVC and PEFR ($p< 0.01$), and insignificant correlation between gender and FEV_1/FVC ($p> 0.01$). Table 4 demonstrated the correlation between the respiratory parameters and duration of diabetic disease and dose of insulin administered.

Table 1. Comparison of pulmonary function test parameters between patients with type I diabetes mellitus and non-diabetic males

Pulmonary function parameters	Group I controls (no=40) Mean ±SD	Group II children with diabetes (no=80) Mean ±SD	*P* value
FEV_1 (liters)	1.27±0.36	1.20±0.39	0.331
FVC(liters)	4.73±21.77	1.22±0.39	0.148
FEV_1/ FVC%	97.73±2.94	99.82±1.19	0.000*
PEFR(liters/sec)	239.82±89.46	210.08±79.54	0.067

(FVC), forced expiratory volume in first second (FEV1), forced expiratory ratio (FEV1/FVC) and peak expiratory flow rate and (PEFR)

Table 2. Comparison of pulmonary function test parameters between patients with type I diabetes mellitus and non-diabetic females

Pulmonary function parameters	Group I controls (no=40) Mean ±SD	Group II diabetic patients (no=80) Mean ±SD	P value
FEV_1(liters)	1.29±0.38	1.08±0.31	0.001*
FVC (liters)	1.31±1.34	1.08±0.31	0.000*
FEV_1/ FVC%	97.92±1.74	99.68±0.94	0.000*
PEFR(liters/sec)	238.32±74.53	170.60±55.67	0.000*

(FVC), forced expiratory volume in first second (FEV1), forced expiratory ratio (FEV1/FVC) and peak expiratory flow rate and (PEFR)

Table 3. Correlation between the respiratory parameters and gender of children with diabetes

Pulmonary function parameters	Gender				P value
	Male	Female	±S E	t - value	
FEV_1(liters)	1.20	1.09	0.04	2.75	0.005*
FVC(liters)	1.20	1.08	0.04	3.00	0.000*
FEV_1/ FVC	100(10)	100(10)	0.01	0.00	Not Significant
PEFR(liters/sec)	210.09	170.60	7.68	5.14	0.000*

(FVC), forced expiratory volume in first second (FEV1), forced expiratory ratio (FEV1/FVC) and peak expiratory flow rate and (PEFR)

Table 4. Correlation between the studied respiratory parameters, duration of the illness and insulin dose

Variables		Duration	Dose
FEV_1 (liters)	r	0.483*	0.493*
p		0.000	0.000
r^2		0.233	0.243
FVC(liters)	r	0.468**	0.486**
P		0.000	0.000
r^2		0.219	0.236
FEV_1/ FVC%	r	0.036 is	0.154 is
P		0.648	0.052
r^2		0.001	0.024
PEFR (liters/sec)	r	0.376**	0.438**
P		0.000	0.000
r^2		0.141	0.192

r: Correlation Coefficient. P: probability (P< 0.01 - P< 0.05), r^2: Coefficient of determination. d f = 159, female = 1, male = 2, i s: in significant.
**:Significant at 0.05 level of probability.*
***: Significant at 0.01 level of probability*

4. DISCUSSION

The present study was designed to investigate the effect of diabetes Type 1, on the pulmonary function parameters in Sudanese children and adolescents and its correlation with gender, duration of the illness, and dose of insulin administered. The main finding is that all the pulmonary parameters (FEV_1, FVC and PEFR) were significantly reduced in patients with diabetes, except the ratio FEV_1/FVC that showed a significant increase compared with the healthy controls. Our results are in agreement with several studies that reported reduction in FVC and FEV_1 in patients with diabetes compared to control subjects [14-16]. Kerrthi et al. postulated that the observed decrease in total lung capacity might be due to an altered collagen matrix in the lung. A significant decrease in lung volumes were found and this was thought to be due to decreased lung compliance caused by restriction of the chest wall expansion as a result of altered collagen metabolism or altered collagen /elastin ratio [17].

On the contrary, Benbassat et al. showed that the FVC and FEV_1 were within the predicted values [18]. While Maccioni and Colebatch reported that DMT1 does not affect pulmonary function. The most probable reason for the contradiction is that Maccioni and Colebatch did not consider the age, height, weight and sex matched control group, and their number of patients with diabetes was small [19].

Moreover, several studies reported an increase in the FEV_1/FVC ratio in Type I patients with diabetes indicative of a restrictive pattern of respiratory dysfunction [14,20]. On the other hand, Mirrakhimov et al. stated that both types of diabetes mellitus should be viewed as strong contributing factors for the development of obstructive lung disease [21,22]. Many

explanations were given to explain the restrictive ventilatory dysfunction in patients with diabetes. These explanations include the involvement of the neuromuscular respiratory muscles due to diabetic neuropathy of the thoracic nerves that contributes to the respiratory dysfunction [23]. Other investigations found that hyperglycemia was associated with poor skeletal muscle strength due to increased protein catabolism, for this reason respiratory muscles endurance also decreased in diabetes mellitus [24]. Other researchers proposed that there was a combined obstructive and restrictive pattern of pulmonary function in diabetics but it was predominately restrictive. Our study strongly suggests restrictive pattern in diabetes mellitus patients [25,26]. El Azeem et al. [27] found a significant decrease in the ratio FEV_1/FVC in diabetics compared to controls.

The duration of diabetes mellitus is an important factor affecting the lung; the current study showed a significant correlation between the respiratory parameters (FEV_1, FVC, PEFR) and the duration of illness, and an insignificant correlation with the ratio FEV_1/FVC. There are studies that have reported no significant correlation between pulmonary function tests and duration of the disease [28,29]. On other hand, some of these studies have reported a strong correlation between pulmonary function tests and duration [14,25,30,31].

Regarding the gender difference, our study revealed that there were more significant reductions in pulmonary function tests (FEV_1, FVC, and PEFR) in female patients with diabetes than in male patients with diabetes, while there was no correlation between FEV_1/FVC and gender. Awad et al. [32] proposed that that female generally do not cope as well with diabetes and have significantly worse metabolic control than males. In addition, the diabetic females are less adherent to the diabetic diet than the diabetic males. Moreover, the pulmonary function measurements exhibited significantly higher values among males than the females in cases of healthy subjects [33,34].

This study investigated the effect of the level of insulin administered on the respiratory parameters in Type I patients with diabetes and the relationship between them. The results showed that the respiratory parameters (FEV_1, FVC, and PEFR) were increased with the increase of insulin dose administered. Also, there was a correlation between the pulmonary parameters (FEV_1, FVC, and PEFR) and the dose of insulin administered. However, there was no correlation between the ratio FEV_1/FVC and the dose of insulin administered. Zimmet et al. [35] found a significant correlation between uncontrolled diabetes mellitus and pulmonary function impairment.

The current study had some limitations, including the small sample size of diabetic children; this resulted in the narrowing of the sample spectrum, and in the reduction of the possibility of generalizing the study. In addition, we did not measure HBA1c and the diffusion of lung capacity due to the unavailability of the equipment at the time of study.

5. CONCLUSION

We conclude that the actual lung function parameters FEV1, FVC and PEFR among children and adolescents with DMT1 were significantly reduced, except the ratio FEV_1/FVC that demonstrated a significant increase compared to their predicted lung function parameters for age, gender, height, and weight. We suggest that children and adolescents with diabetes may benefit from periodic lung function testing to detect early pulmonary changes and prevent further damage to the lungs. Moreover, with larger cohorts should be conducted to further confirm the findings.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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