Original Article

Lung functions in children with Type 1 diabetes mellitus: A cross sectional study

A R Somashekhar, S A Nagarajan, Saketh, H B Mallikarjuna, B M Sunil Kumar
From Department of Paediatrics, MS Ramaiah Medical College, Bengaluru, Karnataka, India
Correspondence to: Dr. A R Somashekhar, Department of Paediatrics, MS Ramaiah Medical College, Bengaluru - 560 078, Karnataka, India. E-mail: s_arshekar2002@yahoo.com
Received – 25 July 2014 Initial Review – 22 August 2014 Published Online – 17 September 2014

Abstract

Background: Diabetes mellitus (DM) is a metabolic disorder precipitating micro and macro vascular complications and peripheral vascular diseases. Normal lung mechanism and gas exchange are influenced by integrity of pulmonary connective tissues and microvasculature. Abnormality in either of these two structural components of lung leads to variations in lung functions. **Objective:** This study was conducted to document lung function patterns by spirometry in patients with Type 1 DM. **Materials and Methods:** This cross-sectional study was conducted in Bangalore, India. Patients in the age group of 1-18 years diagnosed with Type 1 DM between December 2009, and January 2011 were included. Data regarding respiratory symptoms, age, height and weight of each patient with Type 1 DM was collected. The children were trained to use spirometers. Multiple readings of forced expiratory volume in one second and forced vital capacity were obtained until consistent, and the best reading was recorded and analyzed for any association. **Results:** A total of 51 children with Type 1 DM were studied, of whom 24 children were males, with a mean age of 14.06 ± 3.25 years, the minimum age being 5 years and a maximum being 18 years. 25 children (49%) with Type 1 DM were found to have pulmonary dysfunction, of which 19 children (76%) had restrictive lung pattern, and six children (24%) had obstructive pattern. **Conclusion:** Spirometry evaluation showed that restrictive lung pattern was very common in children with Type 1 DM, and there is scope for further study.

Key words: *Obstructive pulmonary pattern, Pulmonary function tests, Restrictive pulmonary pattern, Type 1 diabetes mellitus*

Diabetes mellitus (DM), both Type 1 and 2 is a systemic disease that involves multi-organ systems in the body precipitating micro, and macro vascular complications and peripheral vascular diseases [1]. Less has been known about the after effects of DM on lungs. Normal lung mechanism and gas exchange are influenced by integrity of pulmonary connective tissues and microvasculature. Abnormality in either of these two structural components of lung leads to variations in the lung functions [1,2]. Histopathological evidence in human beings and experimental data suggest that the respiratory system is affected in Type 1 DM as part of the systemic nature of the disease [3]. Although, abnormalities of pulmonary functions are described in subjects with Type 1 DM, the results have been conflicting and inconclusive [4,5]. The most consistent functional abnormality reported in the literature is reduced lung volume, decreased elastic recoil and impaired gas transfer [3]. Spirometry is used to detect abnormalities and classify the ventilatory function into obstructive or restrictive pulmonary patterns. However, the results of spirometry in children with Type 1 DM have been quiet inconsistent, some showing no effects, whereas others are showing a restrictive pattern and a few with obstructive features [6]. There is a need to study the association of Type 1 DM with pulmonary function abnormalities in pediatric age group in India and hence this cross sectional study was undertaken to investigate pulmonary function in children with Type 1 DM.

MATERIALS AND METHODS

This was a cross-sectional study, conducted over a period of 14 months after obtaining the approval from institutional ethical review board and ICH-GCP 2008 Seoul amendment and ICMR 2006 guidelines were followed during the study procedure. A specially designed case record form was used to collect the data. Children in the age group 1-18 years with Type 1 DM diagnosed according to American Diabetes Association (ADA) were included in the study [7]. According to ADA criteria, patients with age of onset below 18 years and requiring insulin for glycemic control were clinically diagnosed to have Type 1 DM. Children with Type 1 DM attending to outpatient department were included in the study after getting informed written consent from the patients or their guardians. Children with previous and present cardio respiratory diseases, known asthmatics or patients with symptoms of asthma and smokers were excluded from the study. Patient's gender, age, height in centimeters and weight in kilograms, and body mass index (BMI), presence or absence of respiratory symptoms and family history of Type 1 DM were collected. Details including history with special importance to any recent history of respiratory symptom such as cold, cough, wheezing, exercise induced breathlessness, allergic manifestation such as triggering factor, causal factors, medications (along with BMI and thorough systemic examination) were recorded. Thorough general and systemic examination was also performed.

Patients who had a cough received bronchodilators within 72 h were excluded. Procedure was explained, and spirometry was performed by pulmonary function technician who was a certified trainer in lung function tests. Results were interpreted by the investigator. Spirometer used was TM Diagnostic spirometer C Model 2001/manufactured by Ndd medizintechnik AG, 8005 Zurich. Calibration was carried out periodically by the technician. Predictive values were derived from advanced spirometry with normograms established for Asian children and specifically derived for age/sex and ethnic groups. The best of three attempts was taken. Following parameters were recorded: Forced vital capacity (FVC) in liters, forced expiratory volume in one second (FEV1) in liters, and FEV1/FVC ratio was calculated. The absolute FEV1 and FVC were compared with the predicted FEV1 and FVC, and the subjects were categorized into normal, obstructive and restrictive pulmonary patterns depending on FEV1/FVC ratio based on Enright Algorithm (Table 1) [8]. Patient showing <80% of expected FEV1 and peak expiratory flow rate was considered significant followed by bronchodilator challenge in the form of inhaler through spacer was given, improvement of more than 12% from the baseline were taken as obstruction with good reversibility and if the results showed FVC <80% of expected then it was taken as restrictive.

Data were entered in MS Excel and imported to SPSS version 20 for further analysis. Descriptive statistics is comprising of mean standard deviation (SD) and percentage (Proportions) for continuous and dis-contiguous data respectively. Independent t test was used to compare mean (SD) of the variables such as height, weight, FVC, FEV1 and FEV1/FVC ratio between males and females. Statistical significance was considered at $p < 0.05$.

RESULTS

Totally 90 children with Type 1 DM were screened for inclusion in our study, but only 51 children were studied and remaining excluded due to various reasons (Fig. 1). The mean age was 14.06 ± 3.25 years with a minimum age of 5 years and a maximum age of 18 years. The mean height of the children was 144.57 ± 16.35 cm and mean weight was 36.19 ± 12.13 kg. Of the 51 children, 24 (47.05%) were male. There was no significant difference in height, weight

Table 1: Enright Algorithm

Pulmonary function	FVC (% of lower limit of normal)	FEV1/FVC	FEV1 (% of predicted value)
Normal	>80		
Abnormal	<80		
Obstructive lung pattern	<80	<70%	
Restrictive lung pattern			
Mild	<80	>70	>80
Moderate	<80	>70	50-80
Severe	<80	>70	30-50
Very severe	<80	>70	<30

FVC: Forced vital capacity, FEV1: Forced expiratory volume in one second

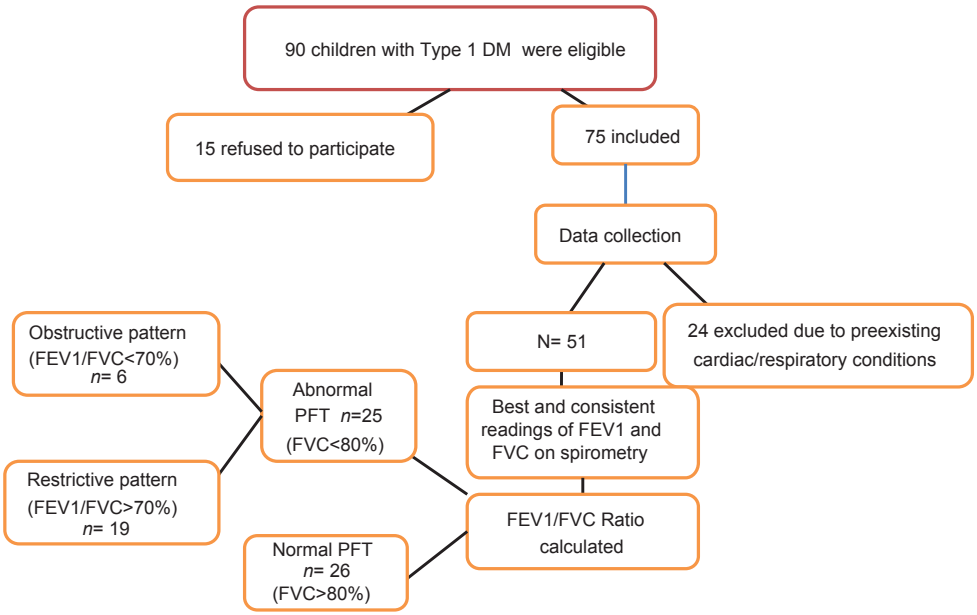

Figure 1: Flow chart of the study

and lung functions between genders (Table 2). Among 51 children, 25 (49%) had abnormal pulmonary functions on spirometry. 19 (76%) of these children had restrictive lung pattern while 6 children (24%) had obstructive lung pattern. The rest of the 26 (51%) children were found to have normal pulmonary function on spirometry (Table 3).

In the patients with restrictive lung pattern, 57.89% were found to have a moderate restrictive pattern, and there was no significant correlation of FEV1/FVC ratio with the height for age or Type 1 DM ($p > 0.05$) (Table 4).

DISCUSSION

In the present study, we found that restrictive lung pattern was common among children with Type 1 DM even with no respiratory symptoms (as patients with pre-existing respiratory conditions were excluded from the study). Interstitial lung disease, an important cause of restrictive lung pattern is very rare among pediatric age group [1]. DM as a multi system disease involves the lungs in the course of complex phenomena it generates. The restrictive lung pattern shown by Type 1 DM children in this study may due to be the damage caused by DM. It may be the initial stage of damage as most of the children did not present with respiratory symptoms [3]. The obstructive lung pattern may be explained by the possibility of environmental factors interfering in the development of disorders like asthma mediated by Th1 and Th2 cells, in the same individual, due to the absence of immunomodulatory mechanisms mediated by interleukin-10 and regulatory cells [4]. Only the lung function tests using spirometry, a non-invasive tool has shown the warning signals of restrictive lung disease. Hence, we recommend the use of spirometry at regular intervals in children with Type 1 DM to take early necessary steps in preventing pulmonary damage due to DM.

Recent studies in animals as well as in human diabetes demonstrated biochemical changes at the pulmonary level such as the suppression of anyline p-hydroxilase, reduction in the activity of glutathione-peroxidase, development of NO dependent endothelial dysfunction, microsomal disorders, increased heparan sulphate at the level of vascular basement membrane, increased levels of advanced glycation end-products and derangement of bronchial mucus production by amyline [2]. Structural modifications of the lung parenchyma were also observed in diabetes such as narrowing of the alveolar space, flattening of alveolar epithelium and expansion of interstitium [1]. Besides basement membranes of the alveolar epithelium, bronchial epithelium and pulmonary capillaries are also involved [1,2]. The consequences of local

Table 2: Comparison of parameters between genders

Variable	N	Mean±SD	Standard error of mean	p value*
Height (in cm)				
Male	24	145.5±18.57	3.73	0.70
Female	27	143.7±14.73	2.83	
Weight (in kg)				
Male	24	35.5±12.88	2.69	0.71
Female	27	33.8±11.66	2.29	
FVC (best) (litres)				
Male	24	2.0±0.92	0.19	0.65
Female	27	1.9±0.69	0.13	
FEV1 (best) (liters)				
Male	24	1.8±0.77	0.18	0.49
Female	27	1.6±0.53	0.12	
FEV1 (%)				
Male	24	76.4±22.69	5.35	0.63
Female	27	73.1±18.81	4.43	
FEV1/FVC ratio				
Male	24	83.5±29.84	6.09	0.46
Female	27	77.9±22.99	4.42	

FVC: Forced vital capacity, FEV1: Forced expiratory volume in one second, SD: Standard deviation

Table 3: Morbidity pattern

Diagnosis	Frequency (%)
Normal	26 (51.0)
Obstructive	6 (11.8)
Restrictive = mild	6 (11.8)
Restrictive = moderate	11 (21.6)
Restrictive = severe	1 (2.0)
Restrictive = very severe	1 (2.0)
Total	51 (100.0)

oxidative stress increased vascular permeability and modifications in mucus secretion lead to the reduction of pulmonary volumes, pulmonary diffusion capacity, elastic recoil, bronchial reactivity and bronchodilatation [2,9-11].

This was a cross-sectional study, and hence, we could not see the changes happened in lung function pattern, the time taken for any changes to occur, the role of gender, BMI, duration of DM and glycemic control in preventing or reversing the damage of lungs. Although, 51 of Type 1 DM is quite good number, more number of patients from multiple centers with long term follow-up will be required to draw a better conclusion.

CONCLUSION

Majority of children with Type 1 DM had restrictive lung functions and were asymptomatic in this study. Only lung function tests using spirometry has shown the warning signals of restrictive lung disease in these asymptomatic children. Therefore, we recommend the use of spirometry at regular intervals in children with Type 1 DM to take early necessary steps in preventing pulmonary damage due to DM.

ACKNOWLEDGMENT

We would like to thank Dr. Nanda Kumar, MBBS, MD, Associate Professor, Department of Community Medicine, M S Ramaiah Medical College, Bengaluru, Karnataka, India and Dr. Lohith, MBBS, MD, Assistant Professor, Department of Medicine, Sree Siddhartha Medical College, Tumkur for their contributions toward the article.

AUTHOR'S CONTRIBUTORS

- Special Thanks to Dr. Nanda Kumar, Statistician. Department of Advanced Studies, M. S. Ramaiah Hospitals.

Table 4: Distribution of Type 1 diabetes patient based on lung functions

Parameters	N	Minimum	Maximum	Mean	Standard deviation
Height (in cm)	51	93.00	175.00	144.57	16.35
Weight (in kg)	49	9.00	69.00	36.19	12.13
FVC (best) (litres)	51	0.19	3.89	1.94	0.80
FEV1 (best) (litres)	36	0.17	3.63	1.68	0.65
FEV1 (%)	36	26.00	113.00	74.72	20.61
FEV1/FVC ratio	51	28.00	200.00	80.55	26.31

FVC: Forced vital capacity, FEV1: Forced expiratory volume in one second

- Special Thanks to Dr. Lohit. K for helping in preparing the manuscript.

REFERENCES

1. Goldman MD. Lung dysfunction in diabetes. Diabetes Care. 2003;26(6):1915-8.
2. Celik P. Pulmonary function parameters in patients with diabetes mellitus. Turk J Endocrinol Metab. 1999;1:5-10.
3. van den Borst B, Gosker HR, Zeegers MP, Schols AM. Pulmonary function in diabetes: A metaanalysis. Chest. 2010;138(2):393-406.
4. Alves C, Diniz AB, Souza MB, Ponte EV, Araújo MI. Controversies in the association between type 1 diabetes and asthma. Arq Bras Endocrinol Metabol. 2007;51:930-7.
5. Stene LC, Nafstad P. Relation between occurrence of type 1 diabetes and asthma. Lancet. 2001;357(9256):607-8.
6. Black MH, Anderson A, Bell RA, Dabelea D, Pihoker C, Saydah S, et al. Prevalence of asthma and its association with glycemic control among youth with diabetes. Pediatrics. 2011;128(4):e839-47.
7. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2010;33(Suppl 1):S62-9.
8. Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, et al. Interpretative strategies for lung function tests. Eur Respir J. 2005;26(5):948-68.
9. Davis WA, Knuiman M, Kendall P, Grange V, Davis TM, Fremantle Diabetes Study. Glycemic exposure is associated with reduced pulmonary function in type 2 diabetes: The Fremantle Diabetes Study. Diabetes Care. 2004;27(3):752-7.
10. Irfan M, Jabbar A, Haque AS, Awan S, Hussain SF. Pulmonary functions in patients with diabetes mellitus. Lung India. 2011;28(2):89-92.
11. Innocenti F, Fabbri A, Anichini R, Tuci S, Pettinà G, Vannucci F, et al. Indications of reduced pulmonary function in type 1 (insulin-dependent) diabetes mellitus. Diabetes Res Clin Pract. 1994;25(3):161-8.

Funding: None; Conflict of Interest: None Stated

How to cite this article: Somashekhar AR, Sowmya AN, Saketh, Mallikarjuna HB, Sunil Kumar BM. Lung functions in children with Type 1 diabetes mellitus: A cross sectional study. Indian J Child Health. 2014;1(2):49-53.