Lung functions in poorly controlled type 1 Saudi diabetic children and adolescents

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ABSTRACT

الأهداف: التحقق من وظائف الرئة لدى السعوديين المصابين بداء السكري من النمط الأول وذلك في فئتي الأطفال والبالغين.

الطريقة: أُجريت هذه الدراسة في قسم الأطفال، وحدة أمراض الرئة ومركز السكري التابع للجامعة، كلية الطب، جامعة الملك سعود، الرياض، المملكة العربية السعودية، واستمرت خلال الفترة من ديسمبر 2008م إلى يوليو 2010م. شملت الدراسة 52 متطوعاً من الأطفال (26 ذكراً، و26 أنثى) المصابين بالسكري من النمط الأول، والذين تتراوح أعمارهم ما بين 14-8 عاماً (متوسط العمر: 1.42±12.05 عاماً). وقد وصل متوسط فترة المرض إلى 0.47±5.25 عاماً، فيما كان متوسط مستوى الهيوغلوبين السكري 0.31±11.27%. لقد قمنا بقياس وفحص وظائف الرئة بواسطة مقياس وظائف الرئة الالكتروني (Electronic Spirometer).

النتائج: لقد أظهرت وظائف الرئة لدى الأطفال المصابين بالسكري انخفاضاً واضحاً في متوسط قيم مقاييس وظائف الرئة الحقيقية والمتمثلة في كل من: السعة الحيوية القهرية، وأكبر زفير يمكن إخراجه، وأقصى قيمة لمتوسط سريان الزفير وذلك عند مقارنة هذه القيم بالقيم المتوقعة. بالمقابل لم يكن هناك انخفاضاً واضحاً في القيم الحقيقية لحجم الزفير القهري خلال 1 ثانية، ولا حتى في قيم السعة الحيوية القهرية بالنسبة لحجم الزفير القهري خلال 1 ثانية.

خاتمة: أثبتت هذه الدراسة مدى تدني قيم مقاييس وظائف الرئة الحقيقية لدى الأطفال والبالغين المصابين بالسكري من النمط الأول والمتمثلة في السعة الحيوية القهرية، وأكبر زفير يمكن إخراجه، وأقصى قيمة لمتوسط سريان الزفير وذلك عند مقارنة هذه القيم بالقيم المتوقعة لوظائف الرئة.

Objectives: To determine the lung function among Saudi type 1 diabetes mellitus (T1DM) children and adolescents.

Methods: This study was conducted in the Department of Pediatrics, Division of Pediatric Pulmonology and University Diabetes Centre, College of Medicine, King Saud University, Riyadh, Kingdom of Saudi Arabia from December 2008 to July 2010. A group of 52 (26 male and 26 female) volunteer T1DM children were recruited with an age range from 8-14 years (mean 12.05 ± 1.42 years), mean duration of disease of 5.25 ± 0.47 years, and mean glycosylated hemoglobin of 11.27 ± 0.31%. Spirometry was performed on an Electronic Spirometer (Compact Vitalograph, Stockwell, London, UK).

Results: Pulmonary function in children with diabetes showed significant lower mean values of actual lung function parameters forced vital capacity (FVC), peak expiratory flow (PEF), and maximum mid expiratory flow rate (MMEF) compared to their predicted values. However, there was no significant reduction in the actual forced expiratory volume in the first second (FEV1), and FEV1/FVC% compared to their predicted values.

Conclusion: The actual lung function data among Saudi T1DM children and adolescents showed significantly lower values of FVC, PEF, and MMEF compared to the predicted lung function data.

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Diabetes mellitus (DM) is a major rapidly growing public health care problem in all age groups.[1] The prevalence of diabetes is increasing globally, but presently the incidence is rising rapidly in the Arab world especially in Saudi Arabia, United Arab Emirates, Kuwait, Qatar, Oman, Bahrain, Jordan, and Libya. The most probable reason for the high incidence of type 2 diabetes in Saudi Arabia is the intake of high caloric diet and less physical activity, which results in a high incidence of obesity, and DM.[2] The rise in the incidence of diabetes has broken the age limit boundaries, and currently seen in all age groups including primary school-age children. Chronic hyperglycemia of DM involves multiple systems, associated with continuing damage, dysfunction, and failure of various organs.[3] Complications of diabetes are mainly a consequence of macro- and micro vascular damage.[4] Diabetes mellitus impairs the various physiological functions of different organs, including the lungs. The mechanism, by which impaired glycemic control may lead to a reduction in lung function is uncertain, although, it has been reported that increased systemic inflammation associated with hyperglycemia[4] may result in pulmonary inflammation[5] and hence, it can cause airway damage.[6] Moreover, secondary reduction in the antioxidant defense of the lungs, and increased susceptibility to environmental oxidative insult results in the subsequent loss of lung functions.[7] It has been suggested that pulmonary complications in DM are due to the thickening of the walls of the alveoli, alveolar capillaries and pulmonary arterioles, and these changes cause pulmonary dysfunction.[8-9] Great attention was centered towards the complications of diabetes including coronary artery disease, diabetic nephropathy, retinopathy, and neuropathy, however, the pulmonary complications of DM have been poorly characterized, specially in primary school-age children. Therefore, the present study was designed to determine the lung functions in type 1 (T1)DM Saudi children and adolescents, and to find out the difference between the actual and predicted lung function values.

Methods. This cross-sectional study was conducted in the Department of Pediatrics and University Diabetes Centre, College of Medicine, King Saud University, Riyadh, Kingdom of Saudi Arabia (KSA) from December 2008 to July 2010. Seventy apparently healthy children and adolescents with T1DM were recruited from the follow-up clinics of the University Diabetes Centre of King Saud University, Riyadh, KSA. Eighteen children with diabetes were excluded: 4 due to respiratory tract infection, and 14 as they were unable to perform the reproducible tests. Finally, a group of 52 (26 male and 26 female) apparently healthy volunteer children with T1DM were included in the study. The age range was 8-14 years (mean 12.05 ± 1.42 years), with a mean duration of the disease of 5.25 ± 0.47 years, and a mean glycosylated hemoglobin (HbA1C) of 11.27 ± 0.31%. All recruited children or their parents completed a questionnaire, which included a demographic data, and a consent form. The Ethical Board of College of Medicine Research Centre, King Saud University approved this study that was conducted according to the principles of Helsinki Declaration.

Children with gross clinical abnormalities of the vertebral column, thoracic cage, neuromuscular diseases, known cases of gross anemia, asthma, cardiopulmonary diseases, malignancy, cigarette smokers, and children who had undergone abdominal, or chest surgery were excluded from the study. Furthermore, children with known complications of diabetes such as diabetic neuropathy, nephropathy, retinopathy, and children who were exposed to, or living in close vicinity of an industry, which may produce dust or fumes, such as cement,[10] flour[11] and oil[12] were also excluded from the study. We adopted a well-standardized controlled exclusion criteria to minimize the possible factors, which may affect lung function test parameters.

Spirometry. Spirometry was performed in an electronic spirometer (Schiller AT-2 Plus, Switzerland). All pulmonary function tests were carried out at a fixed time of the day (10:00-12:00) to minimize any diurnal variation. The apparatus was calibrated daily and operated within the ambient temperature range of 20-24^{0}C. 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] After obtaining a detailed history and anthropometric data, the children were informed of the whole maneuver. The children were 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, and results were printed with a built-in printer integrated in the spirometer. The lung function parameters were measured including forced vital capacity (FVC), forced expiratory volume in first second (FEV1), forced expiratory ratio (FEV1/FVC), peak expiratory flow (PEF), and maximum mid expiratory flow rate (MMEF).

Data were entered in MS Excel, and analyzed using the Statistical Package for Social Sciences (SPSS Inc, Chicago, IL, USA) PC+ version 17, and MedCalc version 10.1.3.0 software programs. Descriptive statistics (mean, standard deviation, and proportion) were used to

quantify continuous and categorical variables. Student's t-test for paired samples was used to compare the mean values of continuous variables (actual and predicted lung function values). Bland and Altman plot was used to assess the agreement between actual and predicted values of the lung function. A $p<0.05$ was considered statistically significant.

Results. In this study, 52 (26 male and 26 female) volunteer T1DM children were recruited, and the anthropometric parameters including age, gender, height, and weight were obtained. **Table 1** summarizes the comparison of the actual versus predicted lung function data among children with diabetes. There was a significant difference between the means of actual versus predicted lung function data. The actual lung function parameters, FVC, PEF, and MMEF were significantly lower when compared to their predicted values. However, there is no significant difference in the actual FEV1, and FEV1/FVC% compared to the predicted values. Bland and Altman plot also indicates lower actual values of FVC, PEF, and MMEF when compared with the predicted values (**Figures 1-3**).

Discussion. Diabetes mellitus is rapidly growing worldwide, and is a leading health care problem of all age group people.[1] It impairs various physiological functions of different organs including the lungs.[14,15] Regardless of effective interventions centered for the complication of DM, the pulmonary complications of DM especially in children have been poorly characterized. Moreover, physicians should pay attention to the extent and impact

Table 1 - Comparison of actual versus predicted lung function data among Saudi type 1 diabetic children and adolescents.

Parameter	Diabetic children (n=52)		t-value	*P*-value	95% CI's for the difference of mean	
	Predicted values (mean ± standard deviation)	Actual values (mean ± standard deviation)			Predicted	Actual
FVC (liters)	3.25 ± 0.48	2.20 ± 0.69	15.4	0.0001	(0.91)	(1.20)
FEV_1 (liters)	3.069 ± 0.41	2.32 ± 2.62	2.0	0.05	(-0.001)	(1.5)
FEV_1/FVC%	91.18 ± 1.66	90.78 ± 7.86	0.38	0.71	(-1.7)	(2.5)
PEF (liters/sec)	6.53 ± 0.96	3.87 ± 1.15	17.2	0.0001	(2.3)	(2.9)
MMEF	3.84 ± 0.39	2.39 ± 0.87	12.6	0.0001	(1.2)	(1.7)

CI - confidence interval, MMEF - mid expiratory flow rate, FVC - forced vital capacity, PEF - peak expiratory flow, FEV - forced expiratory volume.

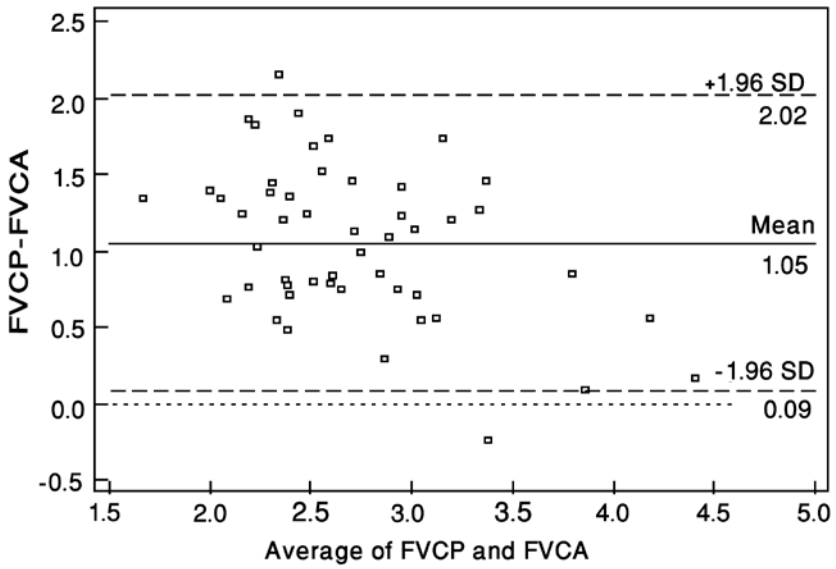

Figure 1 - Agreement of predicted versus actual lung function data forced vital capacity (FVC) among Saudi type 1 diabetic children and adolescent. □ - indicates a paired numerical value of difference between predicted and actual FVC values against its average values. FVCP - forced vital capacity predicted, FVCA - forced vital capacity actual

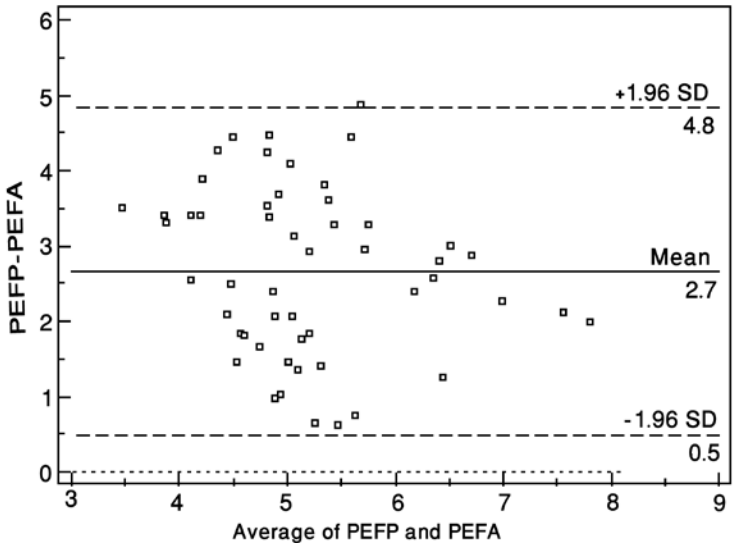

Figure 2 - Agreement of predicted versus actual lung function data peak expiratory flow (PEF) among Saudi type 1 diabetic children and adolescents. ☐ - indicates a paired numerical value of difference between predicted and actual PEF values against its average values. PEFP - peak expiratory flow predicted, PEFA - peak expiratory flow actual

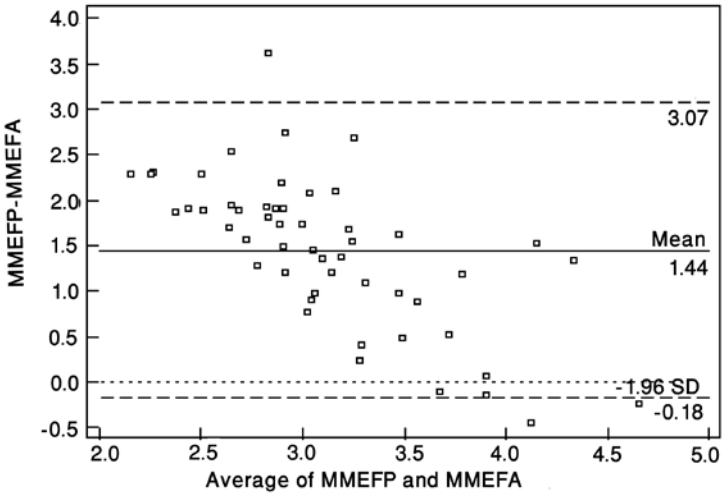

Figure 3 - Agreement of predicted versus actual lung function data maximum mid expiratory flow (MMEF) among Saudi type 1 diabetic children and adolescents. ☐ - indicates paired numerical value of difference between predicted and actual MMEF values against its average values.

of pulmonary complications of diabetes among children. Therefore, the present study was designed to determine the lung function among Saudi T1DM children and adolescents. In this study, we found a significant reduction in the means of actual lung function data. Children and adolescents with T1DM in this study had a poor glycemic control demonstrated by high HbA1C. The American Diabetes Association recommended that optimum HbA1C for children 6-12 years of age should be less than 8%, and less than 7.5% for 12-16 years old. Compared to this benchmark, our patients had clearly very high HbA1C indications of poor glycemic control. It has been shown from the Diabetes Control and Complication Trial that poor glycemic control in adolescents is associated with increased relative risk of development of long term complications of diabetes.[16] The actual lung function parameters FVC (p=0.0001), PEF (p=0.0001), and MMEF (p=0.0001) were significantly lower when compared to their predicted values. However, there was no significant reduction in the actual lung function values for FEV1 and FEV1/FVC% compared to their predicted values.

A number of reports have suggested that glucose intolerance or diabetes is associated with impaired lung

function.[14,15,17-19] Recently, few published studies have shown that decreased lung function is associated with metabolic syndromes (MS),[17,20-22] Oda and Kawai[23] reported that lower vital capacity is associated to diabetes and may involve factors other than MS, or insulin resistance. Kim et al[24] found that the decreased FVC in Korean adult male subjects is associated with MS irrespective of obesity. The above-cited studies have demonstrated that poor diabetes control, or increased HbA1c is associated with abnormal lung function. In the present study, we found that the mean HbA1c was 11.25±0.31% which indicates poor metabolic control. Moreover, the actual lung function data for FVC, PEF, and MMEF were significantly decreased compared to their predicted lung function data. This decreased lung function in our patients may be explained by poor metabolic control. These findings agree with McKeever et al,[25] who reported that an increase in markers of impaired glycemic control would be associated with a reduction in FEV1. It has also been demonstrated that in adults without a diagnosis of diabetes, impaired glucose regulation as indicated by higher levels of HbA1C is associated with impaired lung function.[25] Our results are in agreement with the results of McKeever et al[25] and Laakso[26] that the actual lung function parameters were decreased in diabetic children with increased HbA1c level when compared to their predicted values. Cazzato et al[27] conducted a cross-sectional study to assess the pulmonary function in children with T1DM, and reported that the FVC, and FEV1 were significantly lower than the controls. This study suggests that the lungs is functionally involved in children with T1DM early in the course of the disease. However, Benbassat et al[28] reported that the FVC, FEV1, forced expiratory flow (FEF), and mid expiratory phase (MEF) were within the predicted values compared to their actual values. However, in the present study, we found that the actual lung function data in diabetic children showed a significant reduction in FVC, PEF, and MMEF compared to their predicted lung function data. The most probable reason for the contradiction is that, Benbassat et al[28] studied pulmonary functions in a group of patients with diabetes, who may have optimum metabolic control. This is in contrast to our patients who have poor metabolic control as illustrated by their high HbA1C.

Innocenti et al[29] described the abnormalities of pulmonary function tests in T1DM, and reported that diabetic patients had a reduced FVC and FEV1 compared to their matched control. These findings agree with the study of Primhak et al[30] who performed spirometry on 88 children with T1DM and 216 healthy controls. They reported that children with T1DM had significantly lower percentage predicted FVC than the reference norms. Similarly in the present study, we found that the actual lung function data of FVC, PEF, and MMEF were significantly decreased among the diabetic children.

Makkar et al[31] demonstrated that the ventilatory pulmonary function parameters FVC, FEV1, peak expiratory flow rate (PEFR), MEF 75%, and MEF 25% were significantly reduced in T1DM patients. They also reported that patients with HbA1c more than 10% showed significant reduction in FVC, FEV1, PEFR, and MEF 75%. In the present study, the mean HbA1c was high, and the actual lung function data for FVC, PEF, and MMEF were significantly decreased among the diabetic children.

Davis et al[32] determined the association between DM and reduced lung function. They reported that the FVC, FEV1, and PEF when expressed as a percentage of those predicted for age, gender and height, and the means of spirometric measures were reduced. These findings are in agreement with our study that the actual lung function data in children with T1DM was decreased compared to their predicted lung function data for age, gender, height, and weight.

The present study had some limitations, including the small sample size of participating diabetic children. As we had selected the diabetic children randomly, and their mean HBA1c was 11.27, this resulted in narrowing the sample spectrum, and reduced the study generalizability. Furthermore, we did not perform the diffusion of lung capacity due to the inavailability of the equipment at the time of study.

We conclude that the actual lung function data FVC, PEF, and MMEF among children with T1DM who have poor metabolic control were significantly decreased compared to their predicted lung function data for age, gender, height, and weight. These findings emphasize the importance of optimum glycemic control in children with T1DM in order to prevent long-term complications of diabetes, including pulmonary manifestations. Therefore, we propose that children with diabetes may benefit from periodic lung function test to predict early pulmonary changes, and prevent further damage to the lungs. Further large sample sized studies will be conducted to further confirm the findings.

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