Lung function in type 2 Saudi diabetic patients

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ABSTRACT

Objectives: To study the effects of type 2 diabetes mellitus on lung function and to determine its severity in relation to duration of disease.

Methods: We conducted this study in the Department of Physiology, College of Medicine, King Khalid University Hospital and Diabetic Centre, King Abdul-Aziz University Hospital, Riyadh, Saudi Arabia during the year 2002 - 2004. A group of 32 apparently healthy volunteer male type 2 diabetic patients were randomly selected with an age range from 24-73 years. We matched the diabetic patients with another group of 40 control healthy male subjects in terms of age, height, weight, and socioeconomic status. Both groups met with exclusion criteria as per standard. Spirometry was performed on an Electronic Spirometer (Schiller AT-2 Plus, Switzerland) and results were compared using the 2-tailed student t-test.

Results: Diabetic patients showed a significant reduction in the forced vital capacity (FVC), forced expiratory volume in one second (FEV1) and peak expiratory flow (PEF) relative to their matched controls. However, there were no significant difference in the forced expiratory ratio (FEV1/FVC%) and middle half of the FVC (FEF 25-75%) between the groups.

Conclusions: Lung function in type 2 diabetic patients is impaired by a decrease in FVC, FEV1 and PEF, as compared to their matched controls. Stratification of results by years of disease showed a dose-response effect on lung function.

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Type 2 diabetes mellitus is a serious, progressive condition associated with number of chronic complications that are mainly a consequence of macro-vascular and micro-vascular damage.[1] Type 2 diabetes mellitus is the most prevalent form of the disease and likely to account for over 90% of the total diabetic cases.[2] It is often asymptomatic in its early stages and can remain undiagnosed for many years.[3] Diabetes mellitus, although worldwide in distribution, used to be more seen commonly in the developed European countries, United States and Middle-East countries.[4] The prevalence rate is higher in the Saudi Arabia compared to other Arab countries for example United Arab Emirates, Kuwait, Yemen, Qatar, Oman, Bahrain, Jordan, and Libya.[5] The most probable reason of this high incidence in Saudi Arabia is the economical development over the last 20 years; this has resulted in the adaptation of western life style with respect to nutritional habits and physical activity, which results in a high incidence of diabetes mellitus.[6] Diabetes mellitus is associated with long term damage, dysfunction and failure of various organs[7] and its complications are mostly due to macro-vascular and micro-vascular damage; include cardiovascular disease, nephropathy, diabetic retinopathy, neuropathy, and lung damage.[8] The histopathologic evidence of the involvement of lungs in subjects with diabetes mellitus showed thickened alveolar walls, alveolar capillary walls

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and the pulmonary arteriolar walls, these histological changes in the lungs are become a cause of pulmonary dysfunction.[9,10] It has been also demonstrated that both the pulmonary and renal complications of diabetes share a similar microangiopathic background.[11] These complications have a significant impact on the quality of life of affected individuals[12-13] and impose a heavy burden on health care provider's world wide.[1]

Despite availability of effective interventions, diabetes is often accompanied by long term disabling complications which are primary causes of clinical, social and economic burdens of the disease.[14] However, a great attention was centered for the complications of diabetes include cardiovascular disease, nephropathy, diabetic retinopathy, neuropathy, though, the pulmonary complications of diabetes mellitus has been poorly characterized. Although, some authors have reported normal pulmonary function[15] others found abnormalities in lung volumes, pulmonary mechanics, and diffusing capacity.[16,17] Additionally, the pulmonary functions has not been studied extensively and were not explained by promising factors which greatly influence the lung functions such as age, height, weight, smoking and socioeconomic status especially in type 2 diabetic patients. Moreover, the point deserved to be discussed is that the physicians should know the size of the problem of pulmonary complications as a consequence the novel techniques used in the treatment of diabetes such as inhaled insulin. In view of the facts, the present study was designed to determine the effects of type 2 diabetes mellitus on lung function and our additional intention was to find out the association between duration of the disease and lung function impairment.

Methods. This study was conducted in the Department of Physiology, College of Medicine King Khalid University Hospital and Diabetic Centre, King Abdul-Aziz University Hospital (KAUH), Riyadh, Saudi Arabia during the year 2002-2004. The authors reviewed 165 medical files of diabetic patients. After reviewing the files, patients were called at the Diabetic Center, KAUH for interviewed. A detailed history was taken to determine whether they would be included in the study or not on the basis of the exclusion criteria. They were questioned with regard to smoking cigarettes, other tobacco products, chewing tobacco or betel nut products. After the initial interviews, 32 apparently healthy male type 2 diabetic patients with a mean age of 52.56 ± 1.97 years (mean ± SEM), range 24-73 years with a mean duration of disease 10.06 ± 1.14 years (mean ± SEM), range 1-21 years, were selected and 133 were excluded. Controls were selected in a similar manner to that of the diabetics, from approximately 106 interviewed, 40 apparently healthy male control subjects were selected with a mean age of 48.58 ± 2.26 years (mean ± SEM), range 22-74 years. Diabetic patients were individually matched for age, height, and weight with controls. It was attempted that the matching between both groups was ± 3 years for age, ± 4 cm for height, ± 6 kg for weight. Out of all these pairs, none had more than one difference in anthropometry. A very few pairs did not fall within the age matching, but it was within the height and weight matching. Overall, there were no significant differences in the anthropometric means, in the combined or stratified data. Age and height were given more emphasis for matching as these 2 relate better to lung function than weight.[18] Controls were of a similar community with socio-economic group relative to diabetics; both were assessed by a detailed history. All the subjects were non-smokers, who had never smoked. All subjects completed a questionnaire, which included introduction, consent form; and the anthropometric data was obtained by one of the member of the investigating team. The Ethics Committee, College of Medicine, King Khalid University Hospital, King Saud University approved the study.

Exclusion criteria. Subjects with gross abnormalities of the vertebral column or thoracic cage, restricted joint mobility, known cases of gross anemia, pulmonary tuberculosis, bronchial asthma, chronic bronchitis, bronchiectasis, emphysema, neuromuscular disease, malignancy, and those who had undergone abdominal or chest surgery were excluded from participating in the study. In addition, subjects with current or previous history of drug or tobacco (smoked or chewed) were also excluded. Furthermore, patients with known complications of diabetes mellitus such as diabetic neuropathy, nephropathy, and retinopathy were also excluded from the study.

Spirometry. Spirometry was performed on an electronic spirometer (Schiller AT-2 Plus Switzerland). All pulmonary function tests were carried out at a fixed time of the day (10.00–14.00 hours) to minimize diurnal variation.[19] The apparatus was calibrated daily and operated within the ambient temperature range of 20-25^{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 a special reference to the official statement of the American Thoracic Society of Standardization of Spirometry.[20] After taking a detailed history and anthropometric data, the subjects were informed about the whole maneuver. The subjects were encouraged to practice this maneuver before doing the pulmonary test. The test was performed with the subject in the standing position by using a nose clip. The test was repeated

3 times after adequate rest and results were printed with built-in printer available in the spirometer. The parameters were force vital capacity (FVC), force expiratory volume in one second (FEV1), force expiratory ratio (FEV1/FVC), force expiratory flow (FEF25-75%) and peak expiratory flow (PEF).

Statistical analysis. Statistical analysis was conducted using a student t-test for independent group (2-tailed), on initial analysis, all matched pairs of subjects, and then in 3 groups divided by their duration of disease. The level of significance was taken as $p<0.05$.

Results. The results are presented as an overall group and stratified according to duration of disease in the type 2 diabetic patients (<5, 5-10 and >10 years). In **Tables 1-4**, the formal statistical comparison of the 'matching' variables (age, height and weight) was thought to be appropriated, as these variables are insignificant for the 2 groups hence, statistical confirmation of this fact is not discussed to avoid the repetition.

Overall group results. Lung function data for type 2 diabetic patients and their matched controls are shown in **Table 1**. Type 2 diabetic patients had statistically significant reductions in FVC, FEV1 and PEF. The means for FEV1/FVC%, and FEF 25-75% were not significantly different. The mean duration of the disease for the type 2 diabetics was 10.06 ± 1.14 years (mean ± SEM.), range 1-21 years.

Duration of disease <5 years. **Table 2** summarizes the comparison of the lung function parameters between type 2 diabetic patients and their matched control group. There was no significant difference between the means of any lung function data between the groups. The mean duration of disease for diabetic patients was 3.22 ± 0.36 years (mean ± SEM), range 1-4 years.

Duration of disease 5-10 years. There were no significant difference between the means of FVC, FEV1, FEV1/FVC%, FEF25-75% and PEF, for type 2 diabetic patients on the basis of duration of disease compared with their matched controls (**Table 3**). The mean duration of disease in type 2 diabetics was 7.50 ± 0.63 (mean ± SEM), range 5-10 years.

Duration of disease >10 years. Type 2 diabetic patients with >10 years of diseases, showed a significant reduction in FVC, FEV1, FEF25-75% and PEF relative to their matched controls (**Table 4**). Similarly, the percentage change in the diabetic patient's data relative to controls was also decreased for FVC, FEV1, FEF25-75% and PEF. However, there was no significant difference for FEV1/FVC% relative to controls. The mean duration of disease in this group was 16.76 ± 1.06 years (mean ± SEM), range 11-21 years.

Discussion. Diabetes mellitus is incurable life-long disease, it involve the multiple systems with wide ranging and devastating complications which end up in severe disability and death.[4] In spite of effective interventions centered for the complication of diabetes mellitus includes cardiovascular disease, nephropathy, diabetic retinopathy, neuropathy, however, the pulmonary functions has not been studied extensively and were not explained by promising factors, which greatly influence the lung functions such as age, height, weight, smoking and socioeconomic status especially in type 2 diabetic patients. Therefore, the present study was designed

Table 1 - Anthropometric and lung function data for the total type 2 diabetic patients compared with their matched controls.

Parameters	Diabetic patients (mean ± SEM) (n=32).	Control subjects (mean ± SEM) (n=40)	Percentage change (%)	P value
Age (years)	52.56 ± 1.97	48.58 ± 2.26	-8.19	NS
Height (cm)	167.84 ± 1.18	170.05 ± 1.30	+1.29	NS
Weight (kg)	78.88 ± 2.37	81.47 ± 1.80	+3.17	NS
FVC (litres)	3.14 ± 0.18	3.70 ± 0.10	+15.13	0.012
FEV_1 (litres)	2.66 ± 0.14	3.07 ± 0.08	+13.35	0.016
FEV_1/FVC%	85.63 ± 1.71	83.40 ± 0.83	-2.67	NS
$FEF_{25-75\%}$ (litres/s)	3.29 ± 0.25	3.66 ± 0.16	+10.10	NS
PEF (litres/sec)	5.77 ± 0.46	6.91 ± 0.28	+16.49	0.001

FVC - Forced vital capacity, FEV_1 - forced expiratory volume in one second, FEF - forced expiratory flow, NS=non-significant

Table 2 - Anthropometric and lung function data for type 2 diabetic patients with duration of disease less than 5 years, compared with their matched controls.

Parameters	Diabetic patients (mean ± SEM) (n=9).	Control subjects (mean ± SEM) (n=40).	Percentage change (%)	P value
Age (years)	51.11 ± 3.91	48.58 ± 2.26	-5.20	NS
Height (cm)	170.11 ± 2.41	170.05 ± 1.30	-0.03	NS
Weight (kg)	77.22 ± 5.85	81.47 ± 1.80	+5.21	NS
FVC (litres)	3.30 ± 0.32	3.70 ± 0.10	+10.81	NS
FEV_1 (litres)	2.83 ± 0.28	3.07 ± 0.08	+7.81	NS
FEV_1/FVC%	86.30 ± 1.73	83.40 ± 0.83	-3.47	NS
$FEF_{25-75\%}$ (litres/s)	3.38 ± 0.40	3.66 ± 0.16	+7.65	NS
PEF (litres/sec)	5.63 ± 0.70	6.91 ± 0.28	+18.52	NS

FVC - Forced vital capacity, FEV_1 - forced expiratory volume in one second, FEF - forced expiratory flow, PEF - peak expiratory flow, NS - non-significant

Table 3 - Anthropometric and lung function data for type 2 diabetic patients with duration of disease 5-10 years compared with their matched controls.

Parameters	Diabetic patients (mean ± SEM) (n=10)	Control subjects (mean ± SEM) (n=40)	Percentage change (%)	P value
Age (years)	48.40 ± 3.77	48.58 ± 2.26	+0.37	NS
Height (cm)	165.90 ± 2.57	170.05 ± 1.30	+2.44	NS
Weight (kg)	81.60 ± 2.89	81.47 ± 1.80	-0.15	NS
FVC (litres)	3.36 ± 0.37	3.70 ± 0.10	+9.18	NS
FEV_1 (litres)	2.84 ± 0.20	3.07 ± 0.08	+7.49	NS
FEV_1/FVC%	87.71 ± 3.66	83.40 ± 0.83	-5.16	NS
$FEF_{25-75\%}$ (litres/s)	3.81 ± 0.41	3.66 ± 0.16	-4.0	NS
PEF (litres/sec)	6.98 ± 0.63	6.91 ± 0.28	-1.01	NS

FVC - Forced vital capacity, FEV_1 - forced expiratory volume in one second, FEF - forced expiratory flow, PEF - peak expiratory flow, NS - non-significant

Table 4 - Anthropometric and lung function data for type 2 diabetic patients with duration of disease greater than 10 years compared with their matched controls.

Parameters	Diabetic patients (mean ± SEM) (n=13)	Control subjects (mean ± SEM) (n=40)	Percentage change (%)	P value
Age (years)	56.77 ± 2.61	48.58 ± 2.26	-16.85	NS
Height (cm)	167.77 ± 1.36	170.05 ± 1.30	+1.34	NS
Weight (kg)	77.92 ± 3.81	81.47 ± 1.80	+4.35	NS
FVC (litres)	2.86 ± 0.27	3.70 ± 0.10	+22.70	0.002
FEV_1 (litres)	2.39 ± 0.24	3.07 ± 0.08	+22.14	0.002
FEV_1/FVC%	83.56 ± 2.97	83.40 ± 0.83	-0.19	NS
$FEF_{25-75\%}$ (litres/s)	2.83 ± 0.45	3.66 ± 0.16	+22.67	0.037
PEF (litres/sec)	4.94 ± 0.86	6.91 ± 0.28	+28.50	0.007

FVC - Forced vital capacity, FEV_1 - forced expiratory volume in one second, FEF - forced expiratory flow, PEF - peak expiratory flow, NS - non-significant

to determine the effects of type 2 diabetes mellitus on lung function and our additional intention was to find out the association between duration of disease and lung function impairment. The present study shows a strong association with a dose-effect response of duration of disease and decreased pulmonary function impairment in diabetic patients. This association is explained by age, height and weight. Type 2 diabetics with longer than 10 years showed a significant reduction in FVC, FEV1, FEF25-75% and PEF, relative to their matched controls. Asanuma[21] Lange et al,[17] Boulbou et al,[8] reported that FVC and FEV1 were reduced in diabetic subjects compared to control subjects. Similarly, Cazzato et al,[22] conducted a cross-sectional study to assess the pulmonary function in diabetic children and reported that the FVC, FEV1 were found to be significantly lower in diabetics than controls. Our results for FVC and FEV1confirms the results observed by Asanuma,[12] Lange et al,[17] Boulbou et al,[8] and Cazzato et al.[22] On contrary, Benbassat et al[23] showed that the FVC, FEV1, FEF and FEF25-75% were within the predicted values. In Addition, comparison by diabetes type showed non significant differences in FEV1, FEF, FEF25-75%. The most probable reason for the contradiction is that Benbassat et al,[23] studied pulmonary function among a group of diabetic patients by considering their predicted values but they did not compare their results with the matched control group. Matsubara and Hara[10] studied the pulmonary function and microscopic change of the lungs of diabetic patients compared with those of non-diabetic patients and reported that the FVC, total lung capacity (TLC), residual volume (RV), and maximal expiratory flow rate (MEFR) were significantly decreased in the diabetic group than in the control group. Rosenecker et al,[24] reported that in patients with diabetes mellitus FVC and FEV1 declined significantly over 5-year study period, whereas patients without diabetes did not show a significant decline during the study period. Barret and Frette[25] conducted a study in type 2 diabetic patients and reported that FVC and FEV1 were not associated with newly diagnosed type 2 diabetic patients after adjusted for age, height, and cigarette smoking. However, FVC and FEV1 were reduced in men with type 2 diabetes mellitus of 10 or more year's duration. Our results also demonstrated that, lung functions parameters are decreased in type 2 diabetic patients with >10 years of disease compared with their matched controls. Lawlore et al,[26] demonstrated that FVC and FEV1 are inversely associated with insulin resistant and type 2 diabetes mellitus. In addition, Davis et al,[27] determine the association between type 2 diabetes mellitus and reduced lung function; they reported that the FVC, FEV1, vital capacity (VC), and PEF were reduced. Furthermore, the duration of disease was significantly associated with FEV1 and PEF. Similarly, Davis et al,[28] conducted a recent study in type 2 diabetic patients and demonstrated that VC, FVC, FEV1, and PEF mean percentage-predicted values were decreased in type 2 diabetic patients. They also suggested that the reduced lung volumes and airflow limitation are likely to be chronic complications of type 2 diabetes. Our results are in agreement with the results observed by Lawlore et al,[26] Davis et al,[27] and Davis et al.[28]

While discussing the patho-physiological aspects of decline in the values of lung function parameters, FVC is decreased in pulmonary obstruction, emphysema, pleural effusion, pneumothorax, pulmonary edema[29] and in subjects with weakness of respiratory muscles which is most probably because of reduced chest wall and lung compliance.[30] Similarly, the FEV1 is low in obstructive lung diseases and in reduced lung volume.[31] Airway obstruction slows the delivery of the vital capacity so that FEV1 is reduced and the restrictive disorders reduce the vital capacity but do not slow its delivery, so that, the FEV1 is similarly reduced but the FEV1/FVC ratio is normal or increased.[32] However, low FEF25-75% represents the involvement of peripheral bronchioles.[33] Furthermore, the PEF reflects not only the lung volume and the state of the airways, but it also shows the expiratory muscle force[34] and persistently low PEF represent collapsing of large airways.[35] As diabetes mellitus is a serious, progressive condition associated with number of chronic complications that are mainly a consequence of macro-vascular and micro-vascular damage.[1] Additionally, the histopathologic evidence of the involvement of lungs in subjects with diabetes mellitus showed thickened alveolar, capillary and pulmonary arteriolar walls and with the passage of time, these changes in the lungs become a cause of pulmonary dysfunction[9-10] and lung function impairment.

In conclusion, keeping in view, the patho-physiological aspects and drop of FVC, FEV1, FEF25-75% and PEF parameters, our result suggests that type 2 diabetes mellitus adversely affect the lung function. This impairment shows a restrictive pattern of airways disease and is associated with dose-effect response of period of exposure to disease. The findings are of importance in that they demonstrate the need for prevention of lung damage. It is advisable, therefore, that diabetic patients must undergo periodic spirometry test to assess the severity of lung function impairment. Spirometry will identify more susceptible diabetic patients so they can take additional preventive measures to prevent the lung damage in initial stage, which often, over time,

contributes to morbidity and mortality in diabetic patients. Additionally, the aforementioned facts has suggestion for the physicians that they should contemplate on lung in a same way as that of other complications of diabetes mellitus and they know the size of the problem of pulmonary complications as a consequence of the novel techniques used in the treatment of diabetes such as insulin inhaler.

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