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# Reduced pulmonary functions and respiratory muscle strength in Type 2 diabetes mellitus and its association with glycemic control

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**Abstract. – OBJECTIVE: Diabetes mellitus is one of the main devastating causes of mortality and morbidity due to its detrimental complications. We aimed to evaluate the pulmonary functions and respiratory muscle strength in relationship with glycemic control and gender in type 2 Diabetes Mellitus (T2DM).**

**MATERIALS AND METHODS: This cross-sectional study was performed at King Saud University and King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia from June 2107 to June 2019. We evaluated pulmonary functions, respiratory muscle strength, body composition and glycemic control in T2DM (n=110) and control group (n=119). Gender differences were also evaluated in T2DM.**

**RESULTS: Subjects with T2DM have significantly decreased forced vital capacity (FVC) (3.6±0.7 *vs.* 3.3±0.9, $p$ = 0.012), forced expiratory volume in first second ($FEV_1$) (3.3±2.2 *vs.* 2.7±0.6, $p$ = 0.019), peak expiratory flow (PEF) (127.4±210.9 *vs.* 49.2±133.6, $p$ = 0.003), FEF25-75 (3.6±1.3 *vs.* 3.1±1.1, $p$-value = 0.025), and maximum inspiratory pressure (MIP) (99.3±26.9 *vs.* 87.4±19.3, $p$=0.001). However, no significant difference between control and diabetes was found in maximum expiratory pressure (MEP) (132.5±34.9 *vs.* 126.2±30.0, $p$ = 0.202). Significant reduction in FVC (male=3.7±0.8 *vs.* female = 3.0±0.7 $p$ = 0.000), $FEV_1$ (3.3±1.9 *vs.* 2.6±0.5 $p$ = 0.000), FEF25-75 (3.6 ± 1.3 *vs.* 2.9 ± 1.0 with $p$-value = 0.000), MIP (96.9±23.1 *vs.* 87.5±27.1 with $p$ = 0.017), and MEP (134.0±32.2 *vs.* 120.1±33.5 with $p$ = .011) were observed in females compared to males in T2DM subjects.**

**CONCLUSIONS: Decline in the pulmonary function and inspiratory muscle strength are associated with poor glycemic control in T2DM. Moreover, there are significant differences between male and female in lung parameters and inspiratory as well as expiratory muscles strength. The exact pathophysiological mechanism to explain this association requires further investigations.**

*Key Words:*
Diabetes mellitus, Spirometry, Respiratory muscle strength, Maximum inspiratory pressure, Maximum expiratory pressure, HbA1c, Gender.

## Introduction

The international diabetic federation stated that approximately 10% of the world population (around 695 million) has diabetes mellitus (DM) and among those, 232 million do not know that they are diabetic[1]. Literature regarding the impact of DM on lung functions parameters and respiratory muscles is controversial. Some researchers have identified that adults with Type 2 Diabetes Mellitus (T2DM) have decreased lung function compared with normal subjects[2]. Furthermore, the severity of diabetes, duration of the disease, and the increase blood glucose levels have inverse relationship with lung functions[3-14]. In contrast, no relationship was observed between DM and spirometry values or diffusing lung capacities[15,16].

The effect of diabetes on the respiratory muscle is not well defined. Some researchers suggested that DM reduced respiratory muscle strength which subsequently affects lung volumes[17]. On the other hand, some researchers found DM has detrimental effect on respiratory muscles but lung volumes and diffusing capacities are not affected[16]. One important factor that should not be neglected, is the effect of gender in DM on lung functions. It is previously observed that the effect

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of DM on lung function parameters is independent of sex difference[3].

The pathophysiological explanations behind these effects are not well understood. This may be due to the effects of T2DM on nerves supplying the respiratory muscles (neuropathy), that may indirectly affect the pulmonary functions[18,19]. Furthermore, it is reported that low levels of carnitine might be associated with low PImax (maximum inspiratory ratio) and PImax% causing this decline[20].

Therefore, in this study we examined the pulmonary function parameters and respiratory muscle strength in subjects with T2DM along with gender differences.

## Materials and Methods

This cross-sectional study was carried out in the Department of Physiology, College of Medicine, King Saud University, Riyadh and King Khalid University Hospital, Riyadh from June 2107 to June 2019. Informed consent was obtained from all the participants. Demographic data were recorded from medical record of the participants.

A total of 229 participants out of a sample of 249 subjects were included in the study. These were further divided into 110 patients with T2DM (71 males & 39 females) along with matched 119 healthy control subjects (75 males & 44 females). American Diabetes Association (ADA) criteria were used for T2DM selection. All the patients were in stable metabolic condition. We excluded subjects with nephrotic syndrome, renal failure, thyroid disorders, acute infections, stroke, diabetic ketoacidosis, non-kenotic hyperosmolar coma patients, using oral contraceptives or steroids, and familial hypercholesterolemia. The control group had no acute infection or metabolic or psychological disorder, and no family history of hypercholesterolemia or DM.

### Pulmonary Function Tests

Spirometry parameters were recorded using an electronic spirometer (Schiller, Switzerland) using the American Thoracic Society criteria. The apparatus was calibrated daily with a 1-liter calibration syringe. For spirometry, three trials were performed after adequate rest and highest lung function values were recorded.

### Measurement of Respiratory Muscle Strength

Measurement of inspiratory and expiratory muscle strength was performed by Micro RPM. The recording of inspiratory muscle strength was performed by emptying the lungs initially followed by applying maximum effort to inspire forcefully through the machine. While the expiratory muscle strength was recorded by filling the lungs up to total lung capacity and then maximum effort expiring forcefully through the machine. The machine records maximum inspiratory and expiratory pressures. The highest value is recorded after three trials.

A Vitalograph Model S bellows spirometer (Vitalograph, Buckingham, U.K.) was used for ventilatory parameters. Each subject provided at least three acceptable tracings, from which forced vital capacity (FVC), forced expiratory volume in 1 second ($FEV_1$), vital capacity (VC), and peak expiratory flow (PEF) were measured. All values were corrected for body temperature, air pressure, and water saturation. Normalization of spirometric data was performed by dividing the square of the subject's height and expressing them as a percentage of those predicted for age, sex, and height based on data from healthy non-smoking Caucasian subjects aged 25–79 years for PEF and 25–84 years for VC, FVC, and $FEV_1$.

### Statistical Analysis

The data were analyzed by Statistical Package for Social Sciences (SPSS version 20.0, IBM, Armonk, NY, USA). Descriptive characteristics and lipid profile of the study patients were calculated as Mean ± SD (Standard Deviation) for continuous variables and percentages for categorical variables. Student's *t*-test was used for comparing different groups. Spearman's correlation coefficients were applied where necessary. Multiple logistic regression models were created to see the predictive value of different variables for respiratory muscle strength. A $p$-value of $< 0.05$ was considered as statistically significant.

## Results

The characteristics between control and T2DM subjects are summarized in Table I. Significant differences are observed between the control and T2DM group in age (39.6±11.9 *vs.* 51.7±10.8 with $p$-value= 0.000), weight (78.4±14.3 *vs.* 83.9±19.4 with $p$-value= 0.021), waist-hip ratio (WHR) (0.9±0.1 *vs.* 0.9±0.1 with $p$-value= 0.000), TG (1.2 ±0.6 *vs.* 2.0±1.4 with $p$-value=0.001), and HOMA-IR (5.3 ±3.031 *vs.* 9.4 ±5.0 with $p$-value= 0.000). However, no significant difference is seen

**Table I.** Comparison of demographics and clinical characteristics between control and T2DM subjects.

| Variables | Males, n=71 | Females, n=39 | *p*-value |
|---|---|---|---|
| Age (years) | 39.6±11.9 | 51.7±10.8 | 0.000 |
| Height (cm) | 167.4±8.2 | 165.6±13.8 | 0.266 |
| Weight (kg) | 78.4±14.3 | 83.9±19.4 | 0.021 |
| WHR | 0.9±0.1 | .9±0.1 | 0.000 |
| BMI (kg/m$^2$) | 27.9±4.8 | 29.2±4.9 | 0.063 |
| Fat mass | 23.9±8.6 | 26.1±10.2 | 0.096 |
| Fat% | 29.9±7.6 | 31.8±9.9 | 0.128 |
| FBS | 4.9± 0.5 | 8.7± 3.2 | 0.000 |
| HbA1C | 4.9±0.5 | 7.5±1.4 | 0.000 |
| Insulin | 24.1±12.1 | 24.3 ±9.0 | 0.910 |
| HOMA-IR | 5.3 ±3.0 | 9.4 ±5.0 | 0.000 |
| TG (mmol/dl) | 1.2 ±0.6 | 2.0±1.4 | 0.001 |
| TC (mmol/dl) | 4.8±0.9 | 4.4±1.0 | 0.073 |
| HDL (mmol/dl) | 1.1±0.2 | 1.0±0.3 | 0.135 |
| LDL (mmol/dl) | 2.9±0.8 | 2.6±0.9 | 0.172 |

Differences were studied by Student's *t*-test. T2DM (Type 2 Diabetes Mellitus), WHR (waist hip ratio), BMI (body mass index), FBS (fasting blood sugar).

in BMI between control and T2DM (27.9±4.8 and 29.2±4.9 with *p*-value=0.063).

The comparison of pulmonary function tests between control and T2DM subjects are summarized in Table II. It shows that the T2DM subjects have significantly decreased FVC (3.6±0.7 *vs.* 3.3±0.9, *p*=0.012), $FEV_1$ (3.3±2.2 *vs.* 2.7±0.6, *p*=0.019, MIP (99.3±26.9 *vs.* 87.4±19.3, *p*=0.001), PEF (127.4±210.9 *vs.* 49.2±133.6, *p*-value= 0.003), and FEF25-75 (3.6 ±1.3 *vs.* 3.1 ±1.1 with *p*-value=0.025). However, no significant difference is found in MEP (132.5±34.9 *vs.* 126.2±30.0, *p*= 0.202).

Table III shows gender differences in pulmonary function test of T2DM subjects. Significant differences between male and females included forced vital capacity (FVC) (3.7±0.8 *vs.* 3.0±0.7 *p*=0.000), forced expiratory volume in first second ($FEV_1$) (3.3±1.9 *vs.* 2.6±0.5, *p*=0.000), maximum expiratory pressure (MEP) (134.0±32.20 *vs.* 120.10±33.50 with *p*=0.011), FEF25-75 (3.6 ± 1.3 *vs.* 2.9 ±1.000 with *p*-value= 0.000), and maximum inspiratory pressure (MIP) (96.9±23.1 *vs.* 87.5±27.10 with *p*=0.017). Figures 1 and 2 shows the correlations between MEP and MIP and HbA1C. Significant correlation was observed between MIP and HbA1C. Table IV, V shows regression model of MIP and MEP as variable dependent.

## Discussion

Diabetes mellitus is one of the main devastating causes of mortality and morbidity worldwide. The relationship of T2DM with lung functions is essential and needs to be explored for understanding of any possible realtionship[21]. The reduction in

**Table II.** Comparison of PFTs between control and T2DM subjects.

| Variables | Control (Mean±SD), n=119 | T2DM (Mean±SD), n=110 | *p*-value |
|---|---|---|---|
| FVC | 3.6±0.7 | 3.345±0.9 | 0.012 |
| $FEV_1$ | 3.3±2.2 | 2.781±0.6 | 0.019 |
| $FEV_1$% | 84.5±11.5 | 84.910±9.1 | 0.792 |
| PEF | 127.4±210.9 | 49.209±133.6 | 0.003 |
| FEF25-75 | 3.6 ±1.3 | 3.194 ±1.11 | 0.025 |
| MEP | 132.5±34.9 | 126.297±30.0 | 0.202 |
| MIP | 99.3±26.9 | 87.425±19.3 | 0.001 |

Differences were studied by Student's *t*-test.

**Table III.** Comparison of PFTs between Male and Female T2DM subjects.

| Variables | Males, n=71 | Females, n=39 | *p*-value |
|---|---|---|---|
| Age | 44.2±12.7 | 47.9±13.3 | 0.064 |
| Height | 170.4±6.3 | 157.3±15.0 | 0.000 |
| Weight | 82.3±16.0 | 77.3±19.4 | 0.057 |
| BMI | 28.2± 5.1 | 29.2±4.4 | 0.164 |
| Fat mass | 24.5±10.1 | 25.8±7.1 | 0.284 |
| Fat% | 28.8±7.0 | 35.7±10.8 | 0.000 |
| WHR | 1.0±0.1 | 1.0±0.1 | 0.013 |
| FBS | 6.9±3.1 | 6.0±1.8 | 0.601 |
| HbA1C | 6.1±1.6 | 6.0±1.8 | 0.601 |
| Insulin | 24.5±12.2 | 23.5±6.2 | 0.418 |
| HOMAIR | 7.6±5.0 | 6.4±2.8 | 0.036 |
| TG | 1.8±1.4 | 1.8±1.2 | 0.996 |
| TC | 4.6±1.0 | 4.5±1.3 | 0.977 |
| HDL | 1.1±0.4 | 1.0±0.2 | 0.076 |
| LDL | 2.7±0.9 | 2.9±0.9 | 0.219 |
| FVC | 3.7±0.8 | 3.0±0.7 | 0.000 |
| $FEV_1$ | 3.3±1.9 | 2.6±0.5 | 0.000 |
| $FEV_1$% | 84.8±10.5 | 84.2±9.1 | 0.728 |
| PEF | 86.6±187.7 | 90.4±162.0 | 0.897 |
| FEF25-75 | 3.6 ± 1.3 | 2.9± 1.0 | 0.000 |
| MEP | 134.0±32.2 | 120.1±33.5 | 0.011 |
| MIP | 96.9±23.1 | 87.5±27.1 | 0.017 |

Differences were studied by Student's *t*-test.

lung volumes along with airflow limitations are the chronic complications related to T2DM and glycemic control has an important role in the severity of the lung dysfunction. Our results suggested significant impairment in lung function parameters and respiratory muscle strength in T2DM patients compared to control. These findings are in accordance with the results of the previous studies showing impaired pulmonary functions[3,4,10,17,22]. In addition, we observed significant differences between males and females in lung function parameters in T2DM subjects, which is in contrast to the findings observed previously[3]. Furthermore, significant differences in the respiratory muscle strengths between male and female were observed, however, this can be due to the normal gender differences in muscle strength.

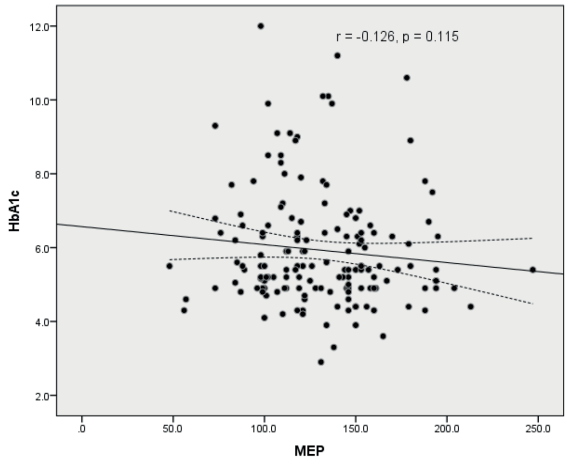


**Figure 1.** Linear regression analysis between HbA1c and MEP.

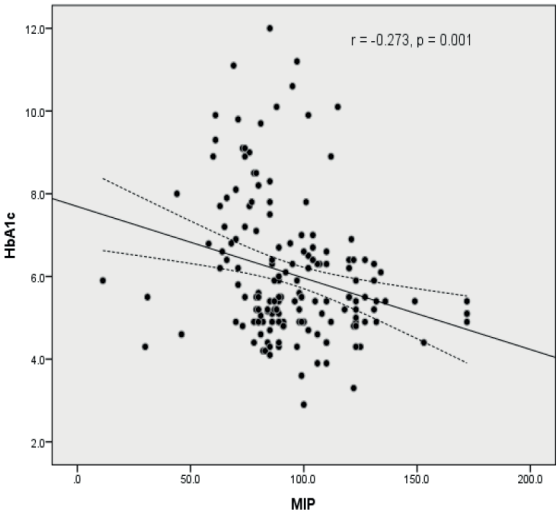


**Figure 2.** Linear regression analysis between HbA1c and MIP.

Several mechanisms are proposed that might cause lung functions impairment, respiratory muscle defect, and gender difference in T2DM. The complications of T2DM and hyperglycemia might lead to alveolar-capillary barrier damage in the lungs[23]. In addition, increased resistance to gas exchange through the respiratory membrane may lead to reduction in the pulmonary volumes[24]. This airflow resistance and alveolar damage may lead to the impairment of pulmonary functions in T2DM as observed in this study. In addition, the duration of hyperglycemia is an important factor in the development of complications. Some studies also identified micro-angiopathy of the alveolar capillaries and pulmonary arterioles[25,26]. Moreover, autonomic neuropathy is a common complication in T2DM and the involvement of respiratory muscles may lead to respiratory complications[18,19].

Impaired lung functions and skeletal muscle weakness are shown to be better predictors of insulin resistance[27,28] and can be studied further to find a relationship between insulin resistance and PFTs. In addition, some studies claimed that reduction in gas exchange is a predictor of death in T2DM, which needs further studies to explore these relationships[29]. The exact pathophysiological mechanism to explain this association requires further investigations.

## Conclusions

Decline in the pulmonary function and inspiratory muscle strength are significantly associated with poor glycemic control in T2DM. Moreover, there are significant differences between male and female in lung parameters and inspiratory as well as expiratory muscles strength. The exact pathophysiological mechanism to explain this association requires further investigations.

### Conflicts of Interest

The authors declare no conflicts of interest.

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