

## Assessment of Maximum Voluntary Ventilation (MVV) in Female Hypothyroids and Its Relationships with Serum TSH and FT4 Levels

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### Abstract

**Background:** Hypothyroidism is a common hormonal disorder affecting various organs including lungs and pulmonary dysfunction in hypothyroid patients has been noted.

**Objective:** To observe maximum voluntary ventilation (MVV) in hypothyroid female patients. **Materials and method:** This cross-sectional study was carried out in the Department of Physiology, BSMMU, Dhaka, Bangladesh, from 1st July 2008 to 30th June 2009 on 60 hypothyroid female patients of 30-50 years old. Based on treatment, hypothyroid patients were divided into B1 (untreated patients on their 1st day of diagnosis) and B2 (patients treated for at least 12-18 months). For comparison, 30 age and BMI matched apparently healthy subjects (Group A) were also studied. The study group was selected from the Out Patient Department of Endocrinology, BSMMU, Dhaka, Bangladesh, and the control group was selected by personal contact. Serum TSH and serum FT4 levels were measured by Microparticle Enzyme Immunoassay (MEIA) principle in AxSYM system. Maximum voluntary ventilation (MVV), which is a lung function parameter, was measured by a digital MicroDL spirometer. Data were analyzed by one way ANOVA test, independent sample t-test and Pearson's correlation coefficient test. **Results:** The mean percentage of predicted values of lung function parameter of MVV in control subjects and treated hypothyroids were within normal ranges. However, this value was significantly lower in untreated hypothyroid subjects in comparison to those of control and treated hypothyroid subjects. In addition, MVV showed negative correlation with serum TSH level and positive correlation with serum FT4 level and these relationships were statistically significant in control group and treated hypothyroid subjects. **Conclusion:** This study reveals that MVV may be lower in untreated hypothyroid female patients compared to control and treated hypothyroids and the deterioration may be positively correlated with serum FT4 level and negatively correlated with serum TSH level. Treatment of hypothyroids may reverse these changes.

**Keywords:** Maximum Voluntary Ventilation; Pulmonary Dysfunction; Hypothyroidism.

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## Introduction

Hypothyroidism is a common endocrine disorder resulting from deficiency of thyroid hormone. The major thyroid hormones are thyroxine and triiodothyronine, commonly called T4 and T3 respectively which maintain the level of metabolism in the tissues that is optimal for their normal function. Thyroid hormones stimulate the O<sub>2</sub> consumption and heat production of most of the cells in the body which are necessary for normal growth and maturation. Thyroid hormones increase the basal metabolic rate (BMR) and regulate protein, fat, carbohydrate and vitamin metabolism. The increased rate of metabolism increases the utilization of O<sub>2</sub> and formation of CO. All these effects activate all the mechanisms that increase the rate and depth of respiration.<sup>1</sup>

Hypothyroidism commonly manifests as a slowing in physical and mental activity but may be asymptomatic. Symptoms may not appear until the thyroid gland has stopped functioning and systemic effects are due to reduction in metabolic activity and deposition of glycosaminoglycans in interstitial tissues.<sup>1</sup>

Like other target organs, the lungs are also affected in hypothyroidism. Mucopolysaccharide deposition in the lungs may cause fibrosis and thickening of the alveolar wall which may lead to decreased diffusing capacity of the lung and cause loss of elastic tissue and increase the work of breathing. These changes may cause reduction in many ventilatory lung functions which is mainly restrictive in pattern.<sup>2</sup> Several researchers reported that pulmonary function may decrease in hypothyroid female and after thyroid hormone replacement these values may increase significantly in this group of patients.<sup>3-7</sup> Incidence of such pulmonary dysfunction is greater in female than in males (ratio is 5-10:1).<sup>8</sup>

Bangladesh is an iodine deficient area and thyroid related diseases are common in our country. Internationally 2.2 billion people worldwide are at risk for iodine deficiency disorder. The latest national survey showed that about 17% of our

population is suffering from thyroid disorder and the number of thyroid patients in our country is increasing day by day.<sup>9</sup> It is surprising that there is no age limitation for presentation of hypothyroidism. Along with this it is also remarkable that many of the patients are diagnosed after development of one or more complications. Many studies on pulmonary functions in hypothyroidism have been done in other countries. To the best of our knowledge no such data is available in Bangladesh. Therefore, the present study was conducted to observe some aspects of lung functions in hypothyroid female patients to evaluate their correlation with TSH and FT4 levels.

This study may help to create awareness among the physicians and also the hypothyroid patients in Bangladesh regarding the damaging effect of hypothyroidism on lung functions. This may help in earlier diagnosis and proper management of pulmonary complications in this group of patients.

## Material and method

This cross sectional study was carried out in the Department of Physiology, BSMMU, Dhaka, from 1st July 2008 to 30th June 2009 on 60 hypothyroid female patients of 30-50 yrs of age (Group B). For comparison, 30 age, BMI and socioeconomic status matched apparently healthy female subjects (Group A) were also studied. The protocol of this study was approved by Departmental Ethical Committee. Patients with serum TSH level >5.01 mIU/L and serum FT4 level <9.14pmol/L were selected as hypothyroid. Based on receiving treatment, hypothyroid patients were divided into Group B1 (30 untreated patients on their 1st day of diagnosis) and Group B2 (30 patients treated for at least 12-18 months). The patients were selected from the Out Patient Department (OPD) of Endocrinology of BSMMU, Dhaka, Bangladesh. Subjects with history of any type of smoking, chronic obstructive pulmonary disease, heart disease, diabetes mellitus, hypertension, or chronic renal failure were excluded from the

study. After selection of the subjects the purpose and procedure of the study were explained to each subject with a cordial attitude giving emphasis on the benefits they would obtain from this study. They were encouraged for their voluntary participation and were also allowed to withdraw themselves as soon as they need. All the subjects were requested to attend at Department of Physiology, BSMMU within 9 am (after taking breakfast at 7 am) on the day of examination. Before examination an informed written consent was taken from each subject. A detailed personal, medical, family, socio economic, occupational and drug history were taken and a thorough physical examination was done which were documented in a prefixed questionnaire. Height and weight of the subject were measured for calculation of BMI. Then after taking all the aseptic precautions, 5 ml of venous blood was collected at 9 am from the subject for estimation of serum glucose, serum creatinine, TSH and FT4 level. Then the subject was taken to the Respiratory Laboratory. Spirometric examination was explained to the subject and MVV was measured by a digital MicroDL Spiro meter manufactured by Clement Clarke International Ltd., Edinburgh Way, Harlow, Essex CM202TT test England. Data were analyzed by Oneway ANOVA test, independent sample t-test and Pearson's correlation coefficient test, as applicable.

## Results

The demographic variables of the study subjects are presented in Table I. All the groups were matched for age and BMI.

**Table I: Age and BMI in different groups (N=90)**

Groups	n	Age (years)	BMI (kg/m <sup>2</sup> )
A	30	37.27 ±6.20 (30-48 )	24.52±4.31 (16.38-34.69)
B <sub>1</sub>	30	38.00± 6.64 (30-50)	24.68±4.77 (17.31-35.52)
B <sub>2</sub>	30	37.83 ±5.93 (30-50)	25.91±4.57 (17.84-35.08)

## Statistical analysis

Groups	p value	p value
A vs B <sub>1</sub> vs B <sub>2</sub> <sup>a</sup>	0.902 <sup>ns</sup>	0.437 <sup>ns</sup>
A vs B <sub>1</sub> <sup>b</sup>	0.660 <sup>ns</sup>	0.893 <sup>ns</sup>
A vs B <sub>2</sub> <sup>b</sup>	0.724 <sup>ns</sup>	0.231 <sup>ns</sup>
B <sub>1</sub> vs B <sub>2</sub> <sup>b</sup>	0.807 <sup>ns</sup>	0.312 <sup>ns</sup>

Data were expressed as mean ± SD. Figures in parentheses indicate ranges.

a = one way ANOVA, b = independent sample t - test.

BMI = Body Mass Index.

Group A: Apparently healthy Euthyroids (control group)

Group B: Hypothyroid (study group)

B1: Untreated

B2: Treated

ns = non significant ( p > 0.05)

n = number of subjects

Serum TSH level was significantly (p<0.001) higher and serum FT4 level was significantly lower in group B1 than those of group B2 and A. But statistically no significant differences of these values were observed between group B2 and A which has been shown in Table II.

**Table II: Serum TSH and FT<sub>4</sub> level in different groups (N=90)**

Groups	n	TSH level (mIU/L)	FT <sub>4</sub> level (pmol/ L)
A	30	2.19 ±1.04 (0.5-4.1)	15.09± 4.14 (10-23)
B <sub>1</sub>	30	38.16±30.51 (8.2-90)	5.12±1.89 (1.5-8.7)
B <sub>2</sub>	30	2.05±1.02 (0.47- 4.0)	15.01±3.82 (9.5- 22)

**Statistical analysis**

Groups	p value	
A vs B <sub>1</sub> vs B <sub>2</sub> <sup>a</sup>	0.000***	0.000***
A vs B <sub>1</sub> <sup>b</sup>	0.000***	0.000***
A vs B <sub>2</sub> <sup>b</sup>	0.608 <sup>ns</sup>	0.9647 <sup>ns</sup>
B <sub>1</sub> vs B <sub>2</sub> <sup>b</sup>	0.000***	0.000***

Data were expressed as mean ± SD. Figures in parentheses indicate ranges.

a = one way ANOVA, b = independent sample t - test.

TSH = Thyroid stimulating hormone, FT4= Thyroxine (free form).

Group A: Apparently healthy Euthyroids (control group)

Group B: Hypothyroid (study group)

B1 : Untreated

B2 : Treated

\*\*\* = p<0.001

ns = non significant ( p > 0.05)

n = number of subjects

The mean percentage of predicted value of MVV was significantly (p<0.001) lower in group B1 than those of A and B2. But statistically no significant differences of these values were observed between group A and B2 which has shown in Table III.

**Table III: Maximum Voluntary Ventilation (MVV) in different groups (N=90)**

Groups	n	Predicted value (liters/min)	Measured value (liters/min)	Percentage of predicted value (%)
A	30	83.27 ± 7.05 (67-97)	79.13 ± 13.32 (51-101)	94.97± 17.21 (59-131)
B <sub>1</sub>	30	88.47± 10.92 (67-108)	73.53± 12.26 (53-99)	77.47 ± 9.95 (60-93)
B <sub>2</sub>	30	86.53 ± 10.58 (61-105)	78.37± 12.78 (52-98)	90.37± 15.67 (56-120)

**Statistical analysis**

Groups	p value
A vs B <sub>1</sub> vs B <sub>2</sub> <sup>a</sup>	0.000 ***
A vs B <sub>1</sub> <sup>b</sup>	0.000 ***
A vs B <sub>2</sub> <sup>b</sup>	0.284 <sup>ns</sup>
B <sub>1</sub> vs B <sub>2</sub> <sup>b</sup>	0.000***

Data were expressed as Mean ± SD. Figures in parentheses indicate ranges.

a = one way ANOVA, b = independent sample t -test .

Group A: Apparently healthy Euthyroids (control group)

Group B: Hypothyroid (study group)

B1 : Untreated

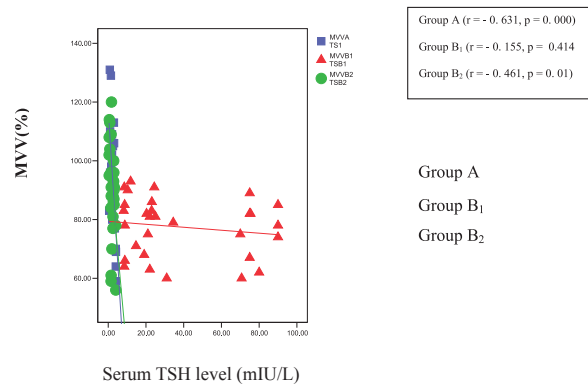
B2 : Treated

\*\*\* = p<0.001

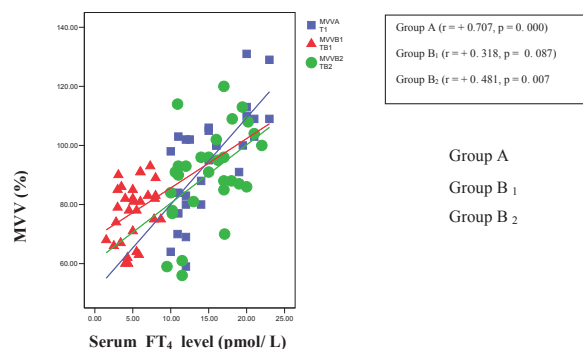
ns = non significant ( p > 0.05)

n = number of subjects

Again, all the parameters were negatively correlated with serum TSH level and positively correlated with serum FT4 level and these relationships were statistically significant only in group A and B2 which are shown in Figure 1 and 2.



**Fig. 1: Correlation of percentage of predicted value of MVV with serum TSH level in different groups (N=90)**



**Fig. 2: Correlation of percentage of predicted value of MVV with serum FT4 level in different groups (N=90)**

## Discussion

In the present study, the lung function parameters in healthy subjects were almost similar to the findings reported by the various investigators from different countries as well in our country.<sup>5,6,10-12</sup> No abnormal pulmonary tests were detected in them.

Serum TSH level was significantly higher and serum FT4 level was significantly lower in untreated hypothyroids than those of control and treated hypothyroids. However, statistically no significant difference in TSH and FT4 level was observed between control and treated hypothyroid patients. The mean percentage of predicted values of MVV was significantly lower in untreated hypothyroids compared to treated patients and healthy control and the observation was similar to other findings.<sup>3,4,6</sup> But no significant difference of these values were observed between treated hypothyroids and control and this findings were in agreement with several investigators from different countries.<sup>4,10,13</sup> The observed changes in MVV was correlated with serum FT4 level. This relationship was statistically significant in treated hypothyroids and control group but non-significant in untreated hypothyroids. These observations were in partial agreement with those of Cakmak et al.<sup>6</sup>

Various mechanisms have been proposed for these observed changes in spirometric lung functions in

hypothyroidism. It was suggested that respiratory muscle such as diaphragmatic weakness in hypothyroidism may be due to decreased phrenic nerve conduction velocity which may lead to prolonged phrenic nerve conduction time. It was also suggested that hypothyroidism is also associated with poor skeletal muscle strength and quality which may decrease the respiratory muscle endurance and may reduce the maximal voluntary ventilation in hypothyroid patients.<sup>13</sup>

In addition to hypothyroidism, reduced surfactant phospholipid, phosphatidylglycerol and phosphatidic acid along with increase in surface active lipids phosphatidylserine and phosphatidylinositol in alveolar epithelium may decrease alveolar septation and reduce lung compliance and surfactant adsorption.<sup>14-17</sup> Moreover, mucopolysaccharide deposition in the lungs may cause fibrosis and thickening of the alveolar wall with loss of elastic tissue and may reduce ventilatory lung functions.<sup>2,18</sup> It was also suggested that in hypothyroidism, there is also alteration in the distribution of type of fibers i.e. decrease in type I and increase in type IID fibers of diaphragm which may significantly reduce the strength of the diaphragm and may decrease the lung function.<sup>18</sup>

In this study, decreased percentage of predicted values of MVV in untreated hypothyroid patients in comparison to the control subjects and treated hypothyroids are most likely due to decreased thyroid hormone level which may cause respiratory muscle weakness and reduction in contractile strength. This low thyroid hormone level may also decrease lung elastic tissue and increase the work of breathing. This is further supported by negative correlation of MVV with serum TSH level and positive correlation of this ventilatory variable with FT4 level.

## Conclusion

This study reveals that hypothyroidism may cause decrease in ventilatory lung functions and the deterioration may be positively correlated with serum FT4 level and negatively correlated with serum TSH level.



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