

# Spirometric Evaluation of Pulmonary Expiratory Flow Volume and Flow Rate in Patients with Clinical Hypothyroidism at a Tertiary Care Hospital, West Bengal, India: A Case-control Study

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## ABSTRACT

**Introduction:** Hypothyroidism is defined as a clinical condition caused by insufficient thyroid hormone secretion from the thyroid gland as a result of structural or functional defects in thyroid hormone production. Hypothyroidism can impair respiratory function and cause ventilation problems. Spirometry is used to assess pulmonary function in patients with thyroid disorders because low thyroid hormone levels can cause bronchial hyperactivity and obstructive pulmonary disease.

**Aim:** To find out the changes of spirometric parameters in clinical hypothyroid patients compared to apparently healthy individuals.

**Materials and Methods:** The study was a case-control study conducted in the Department of Physiology of Burdwan Medical College and Hospital on 50 cases and 50 apparently healthy subjects. Inclusion criteria were diagnosed cases of clinical hypothyroidism, Body Mass Index (BMI) under 30 kg/m<sup>2</sup>, and age between 20 to 50 years. Serum TSH and free T4 (FT4) were measured by Quantitative EIA method using RFCL-

manufactured commercial “ELISCAN-TSH”-kit and “ELISCAN-Ft4”-kit. Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV1), FEV1/FVC, Forced Expiratory Flow (FEF) of 25-75%, and Peak Expiratory Flow Rate (PEFR) parameters of pulmonary function test were tested by RMS Helios 401 Spirometer. Pearson’s two-tailed correlation study and student independent-test were done for analysis.

**Results:** The present study showed that spirometric parameters FEV1, FVC, FEV1/FVC, PEFR and FEF25%-75% were significantly decreased in clinical hypothyroidism compared to control. Mean values of parameters of FEV1, FVC, FEV1/FVC, PEFR and FEF25%-75% in clinical hypothyroid cases were 85.30%, 92.42%, 90.70%, 74.86%, and 75.63%, respectively which were significantly ( $p < 0.001$ ) decreased compared to that of healthy individuals.

**Conclusion:** This study concluded that clinical hypothyroidism causes significant changes in respiratory function. Thus, a proper knowledge in respect to this infection would help in management of these patients in time.

**Keywords:** Forced vital capacity, Lung function, Spirometer, Thyroid

## INTRODUCTION

Anatomist Andreas Vesalius gave the anatomic description and illustration of the thyroid gland in 1543 [1]. The gland was named thyroid by the anatomist Thomas Wharton in 1656 [2], Thomas Curling first described hypothyroidism in 1850 [3]. All organ systems are affected by hypothyroidism [4,5]. The clinical manifestation of thyroid hormone deficiency differs from person to person depending on the degree of deficiency, cause, and duration.

Diaphragmatic dysfunction may be experienced by the patients of hypothyroidism that can range from mild forms having decreased tolerance to physical effort to severe forms of diaphragmatic weakness that may mimic diaphragmatic paralysis [6]. In hypothyroid patients, the respiratory rate is reduced, resulting in hypoventilation and mild hypercapnia [7,8]. Hypercapnia stimulates the respiratory centre, which is unable to respond to an increased need for ventilation due to low thyroid hormone levels. Birring SS discovered that patients with low thyroid hormone levels, the cough reflex is more sensitive, and the airways are more responsive [9]. Obstructive sleep apnoea is a common symptom of hypothyroidism.

Studies evaluating the static (vital capacity, tidal volume, inspiratory reserve volume, expiratory reserve volume, inspiratory capacity, total lung capacity) and dynamic parameters of pulmonary function (FVC, FEV1, PEFR, FEF 25-75%) with spirometry are inconsistent

regarding whether thyroid disorders are leading to lung dysfunction. In hypothyroid patients, there is decrease in vital capacity values, while FVC and FEV were inconsistently lowered [10-12]. Several studies have found that patients with clinical hypothyroidism have a significant decrease in the strength of their inspiratory and expiratory muscles [13-15]. Therefore, there may be respiratory dysfunction in clinical hypothyroidism [16]. Very few studies are there regarding this, only one study [17] on spirometric assessment of lung function in eastern zone of India.

On this background the present study was conducted to assess the presence of any respiratory dysfunction in clinical hypothyroid patients. This study was conducted with an intent to enlighten the alteration of function of lung, if any by spirometry in patients of clinical hypothyroidism in a semi-urban population of Burdwan district and neighbouring areas of West Bengal, a part of Eastern India.

## MATERIALS AND METHODS

This case-control study was conducted in the Physiology Department of Burdwan Medical College & Hospital, West Bengal, India for a period of one year from February 2010 to January 2011. Clearance certificate from IEC was obtained (Certificate no-BMC/PG/167(56) Dated 14<sup>th</sup> January. Patients and healthy volunteers both provided informed written consent.

**Inclusion criteria:** Subjects with clinical hypothyroidism, aged between 20 to 50 years with BMI under 30 kg/m<sup>2</sup> were taken as cases. Age and sex matched healthy subjects were selected as control.

**Exclusion criteria:** Smoking history and any other respiratory and systemic disease that affect respiratory system were excluded from our study.

**Sample size calculation:** The formula used for calculating the adequate sample size [18] was  $n = Z^2 P(1-P)/d^2$ . Where n was the sample size, Z was the statistic corresponding to level of confidence, P was expected prevalence, and d was precision (corresponding to effect size), Confidence Interval (CI),  $Z=1.96$ ,  $CI=95\%$ ,  $P=10.95\%$  [19],  $d(\text{absolute precision})=0.05$ . Thus,  $n=150$  (approx.)

### Study Procedure

Fifty clinical hypothyroid patients along with 50 apparently healthy subjects were considered for the study based on the laboratory values of TSH and fT4. Clinical features of hypothyroidism range from no symptoms to life-threatening symptoms [20-22]. Clinical hypothyroidism is defined as an elevated TSH level ( $> 6.16 \mu\text{U/mL}$ ) with a decreased serum fT4 levels ( $<0.8 \text{ ng/dL}$ ) [20,23]. The term hypothyroidism was defined using reference ranges for the relevant biochemical parameters; normal TSH level (0.39-6.16  $\mu\text{U/mL}$ ) and normal serum fT4 levels (0.8-2.0  $\text{ng/dL}$ ) [23]. Apparently healthy individuals were considered as comparative normal group.

**Study parameters:** (i) Estimation of serum TSH: by 'Quantitative EIA method' using RFCL-manufactured commercial "ELISCAN-TSH"- kit [24].

(ii) Estimation of serum free T4: by 'Quantitative EIA method' using RFCL-manufactured commercial "ELISCAN-fT4"- kit [25].

(iii) Assessment of spirometric parameters like FVC, FVC%, FEV1, FEV1%, FEV1/FVC, FEF25-75%, PEFR, PEFR% by RMS Helios 401 Spirometer.

The thyroid function of all the subjects was rechecked in biochemistry laboratory to confirm their TSH and fT4 status. Then, history was recorded for all the study subjects and they were clinically evaluated with a thorough general survey and systemic examination. Respiratory system examination was done meticulously. Demonstration was given about the technique of FVC to all study subjects after taking rest for 10 minutes. Then spirometry was carried out in a room with privacy, in a sitting posture closing the nostrils with a nose clip. An average of three readings was taken. Spirometry necessitates a voluntary manoeuvre in which patient in sitting postures inhales maximally from tidal respiration to total lung capacity then exhales rapidly to the greatest extent possible until no more volume is exhaled at residual volume. The manoeuvre was carried out forcefully in order to generate a FVC.

### STATISTICAL ANALYSIS

It was done using SPSS software version 17 and Microsoft Excel software of MS-office 2007 software package in computer. Pearson's

two tailed correlation study and student independent t-test were done for analysis. The p-values were calculated to deduce the significance level and p-value  $<0.05$  has been considered statistically significant. To assess the relationship between TSH and respiratory parameters and fT4 and respiratory parameters, Pearson's correlation test was used for finding the correlation.

### RESULTS

In this study, 50 clinical hypothyroidism patients with BMI under 30 kg/m<sup>2</sup> were selected. Among all the 50 subjects 78% were females and 22% were males. The mean ages of the clinical hypothyroidism and the control group of subjects were  $38.60 \pm 5.05$  years,  $36.78 \pm 4.62$  years respectively [Table/Fig-1]. There were no significant differences in ages between cases and control. There the mean fT4 and TSH values were significantly ( $p < 0.001$ ) different between the cases and the controls [Table/Fig-2]. [Table/Fig-3] shows the comparison between spirometric values of the clinical hypothyroidism and control groups of patients. It showed that in the control group all the spirometric parameters were significantly ( $p \leq 0.05$ ) higher than that of the clinical hypothyroidism patients.

[Table/Fig-4-6] shows correlation between TSH value and spirometric parameters of clinical hypothyroidism patients. It is clear that only FEF25-75 (L) and PEFR (L) had highly significant ( $p < 0.01$ ) negative correlation with TSH values ( $r = -0.462$ ,  $p = 0.002$  and  $r = -0.396$ ,  $p = 0.009$ , respectively). The other spirometric parameters do

Parameters		Cases	Controls	p-value
Age (years)		38.60±5.05	36.78±4.62	0.063
Gender	Female	39 (78%)	31 (62%)	0.08
	Male	11 (22%)	19 (38%)	
Presence of common symptoms of respiratory illness, like cough, any difficulty in breathing.	Yes	39 (78%)	0 (0%)	0.00001*
	No	11 (22%)	50 (100%)	

**[Table/Fig-1]:** Demographic features of participants.

\*p-value  $<0.05$  considered as statistically significant

Chi-square test, Independent student t-test were used.

	Clinical hypothyroidism (n=50)			Control group (n=50)			p-value
	Mean	Standard deviation	Standard error	Mean	Standard deviation	Standard error	
fT4 (ng/dL)	0.57	0.12	0.02	1.4	0.26	0.04	$<0.0001$
TSH ( $\mu\text{m/L}$ )	50.77	22.84	3.48	2.12	0.62	0.09	$<0.0001$

**[Table/Fig-2]:** Mean TSH and fT4 values of the participants in clinical and control groups.

Independent student t-test, \*p-value  $<0.05$  considered as statistically significant

	Clinical hypothyroidism (n=50)			Comparative group of healthy subjects (n=50)			t-value	p-value	Significance level
	Mean	Standard deviation	Standard error	Mean	Standard deviation	Standard error			
FVC(L)	2.83	0.29	0.04	3.57	0.35	0.05	-11.226	$<0.001$	HS**
FVC%	92.42	1.16	0.18	106.20	2.80	0.40	-31.784	$<0.001$	HS**
FEV1(L)	2.57	0.24	0.04	3.41	0.35	0.05	-13.696	$<0.001$	HS**
FEV1%	85.30	2.09	0.32	98.64	2.53	0.36	-27.851	$<0.001$	HS**
FEV1/FVC %	90.70	2.04	0.31	95.53	2.00	0.28	-11.473	$<0.001$	HS**
FEF 25 -75 (L)	4.68	0.33	0.05	5.98	0.35	0.05	-18.380	$<0.001$	HS**
FEF 25-75%	75.63	5.43	0.83	78.78	3.72	0.53	-3.213	0.002	S*
PEFR(L)	4.63	0.32	0.05	5.94	0.39	0.06	-17.669	$<0.001$	HS**
PEFR%	74.86	5.33	0.81	79.50	3.56	0.50	-4.856	$<0.001$	HS**

**[Table/Fig-3]:** Spirometric means of clinical hypothyroidism and a group of healthy subjects were compared.

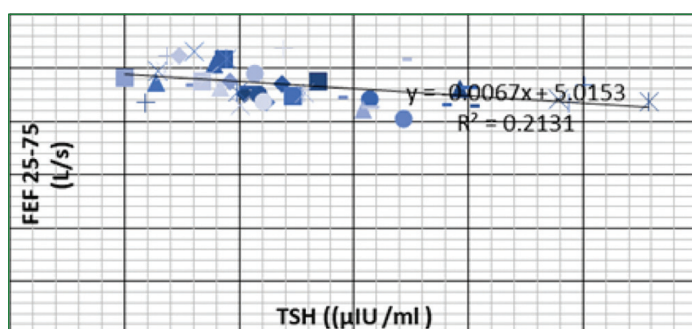
p-value  $<0.05$  considered as statistically significant; Independent Student t-test was used;

HS\*\* Highly Significant, S\* - Significant

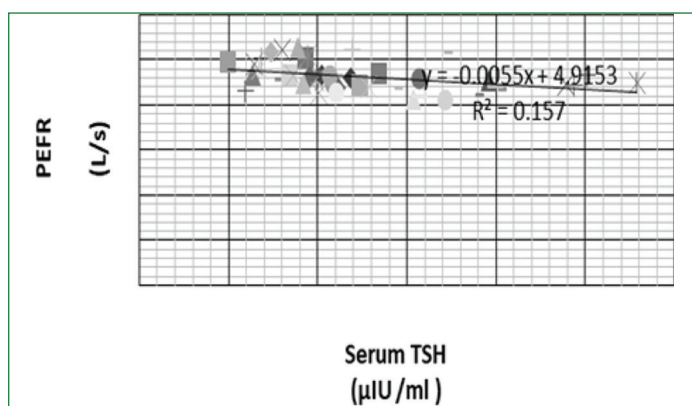
Spirometric Parameters	TSH		
	Pearson Correlation Coefficient(r)	p-value	Significance level
FVC (L)	0.160	0.306	NS
FVC%	0.077	0.626	NS
FEV1 (L)	0.19	0.202	NS
FEV1%	0.188	0.228	NS
FEV1/FVC (%)	0.141	0.366	NS
FEF25-75 (L)	-0.462	0.002	HS**
FEF25-75%	-0.293	0.056	NS
PEFR (L)	-0.396	0.009	HS**
PEFR%	-0.268	0.082	NS

**[Table/Fig-4]:** Correlation between TSH value and spirometric parameters of clinical hypothyroidism patients.

p-value <0.05 considered as statistically significant. Pearson correlation test was used. HS\*\*=Highly significant, S\*=Significant, NS=Not significant



**[Table/Fig-5]:** Correlation between TSH and FEF25-75(L) values in the clinical hypothyroidism patients.



**[Table/Fig-6]:** Correlation between TSH and PEFR (L) values in the clinical hypothyroidism.

not have statistically significant correlation ( $p < 0.05$ ) with TSH value. The [Table/Fig-7-10] shows that statistically significant positive correlation is present between FT4 and FEF25-75 (L) ( $r = 0.457$ ,  $p = 0.002$ ), between FT4 & PEFR (L) ( $r = 0.437$ ,  $p = 0.003$ ). Significant negative correlation persists between FT4 & FEV1/FVC ( $r = -0.367$ ,  $p = 0.015$ ). But no significant association was there between FT4 and other spirometric parameters.

## DISCUSSION

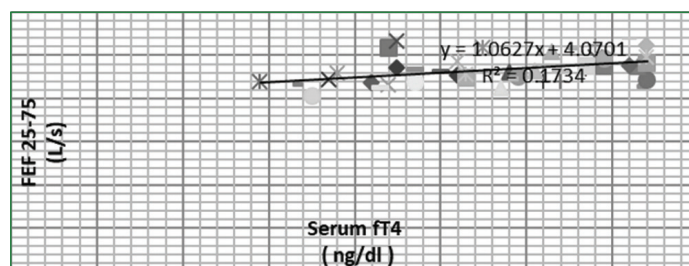
The impairment of pulmonary function in hypothyroidism is caused by both central and peripheral factors. Thyroid hormone deficiency centrally suppresses hypoxic and hypercapnic ventilatory drives. Low thyroid hormone causes peripheral myopathy with decreased respiratory muscle strength. Hypothyroidism causes hypoventilation as ventilatory response to hypoxia and hypercapnia is reduced in hypothyroidism [26]. Hypothyroidism is characterised by diminished expiratory and inspiratory muscle strength [27].

In this study, in the control group all spirometric parameters were higher than that of the in the clinical hypothyroidism patients. Low FVC% in the hypothyroid group indicated a restrictive pattern of

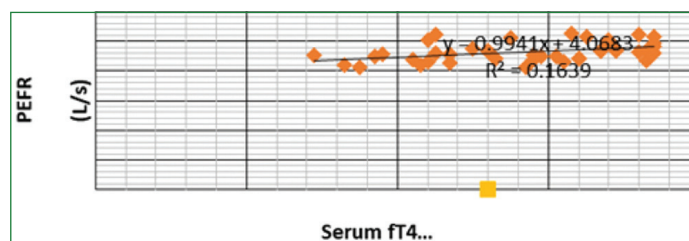
Spirometric Parameters	FT4		
	Pearson Correlation Coefficient(r)	p-value	Significance level
FVC	0.250	0.107	NS
FVC%	0.129	0.409	NS
FEV1 (L)	0.179	0.251	NS
FEV1%	-0.062	0.694	NS
FEV1/FVC (%)	-0.367	0.015	S*
FEF25-75 (L)	0.457	0.002	HS*
FEF25-75%	0.231	0.136	NS
PEFR (L)	0.437	0.003	HS*
PEFR%	0.190	0.222	NS

**[Table/Fig-7]:** Correlation between FT4 value and spirometric parameters of clinical hypothyroidism patients.

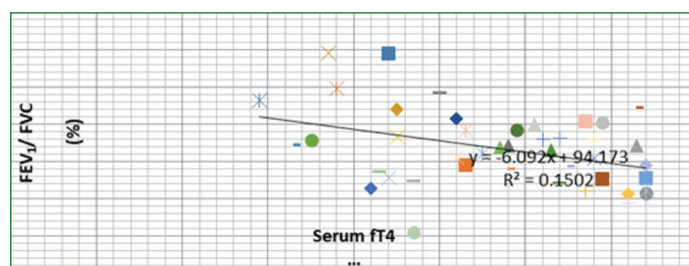
p-value <0.001 considered as statistically significant. Pearson correlation test was used.



**[Table/Fig-8]:** Correlation between ft4 and FEF 25-75 (L) values in the clinical hypothyroidism patients.



**[Table/Fig-9]:** Correlation between ft4 and PEFR(L) values in the clinical hypothyroidism patients.



**[Table/Fig-10]:** Correlation between ft4 and FEV1/FVC values in the clinical hypothyroidism patients.

pulmonary impairment. A study by Cakmak G et al., reported reduced FVC, FVC%, and FEV1 in hypothyroid patients which were similar to the findings with the present study [28]. Maiti SR et al., found a significant reduction in FVC, FEV1, and FEV1/FVC in hypothyroidism [17]. Sharon R et al., also found that both of FVC% and FEV1/FVC were significantly reduced whereas Sadek SH et al., showed that in hypothyroidism patients FVC% was reduced. These studies corroborated with the present study [29,30]. Sadek SH et al., and Valjevac S et al., also found that hypothyroidism was associated with decreased FEV1, FVC and total lung capacity [30,31].

In present study, a significant negative correlation of TSH with FEF25-75(L) and PEFR (L) was found. A positive correlation of FT4 with FEF25-75 (L) and PEFR (L) was also observed in this study. Cakmak G et al., found that FVC% was significantly negatively associated with TSH whereas FVC%, and FEF25-75, FEF25-75%, PEFR, % PEFR were significantly positively correlated with FT3 in clinical hypothyroidism patients [28]. However, in euthyroid subjects

S. No.	Name of author and year	Study Place	Sample size	Parameters to be compared	Conclusion
1.	Duranti R et al., 1992 [26]	Florance, Italy	13 patients of severe hypothyroidism and 7 age- and sex-matched normal subjects were studied,	Maximal Inspiratory Pressure (MIP), minute ventilation (Ve), tidal volume (Vt), mean inspiratory flow (Vt/Ti),	1) In patients with severe hypothyroidism, the ventilatory control system may be altered at the neural level, resulting in decreased chemosensitivity. (2) Impaired respiratory muscle function does not appear to play a significant role in the reduced ventilatory response to carbon dioxide stimulation; and (3) Replacement therapy appears to normalise the response.
2.	Ali ER 2011-2013 [27]	Ain Shams University Hospitals and Misr	30 hyperthyroid, 30 hypothyroid and 30 normal subjects.	FEV1, FEV1%, FVC, FVC%, FEV1/FVC, FEF 25-75%, and PEFR%.	All spirometric parameters were reduced.
3.	Cakmak G et al., 2007[28]	Istanbul, Turkey,	87 clinical hypothyroid patients with 60 healthy subjects	FVC, FVC%, FEV1, FEF25-75	FVC, FVC%, FEV1, FEF25-75 reached significantly ( $p < 0.05$ ) reduced in clinical hypothyroidism patients.
4.	Maiti SR, et al., 2014 [17]	Calcutta Medical College, Kolkata	55 hypothyroid and 55 controls	FEV1, FVC, FEV1/FVC, PEFR, FEF 25%-75%	1. A highly significant decrease in FVC and FEV1 in hypothyroids when compared with FVC and FEV1 in controls, 2. While the FEV1/FVC ratio was actually higher in patients than controls. Again this is also suggestive of a restrictive pathology. 3. Significant positive correlation between FT4 with each of the following: FVC, FEV1 and FEV1/FVC ratio. 4. FVC and FEV1 were significantly negatively correlated with TSH 5. all lung parameter was not associated with FT4
5.	Sharon R et al., 2013 [29]	RIMS, Imphal, Manipur	21 hypothyroid patients and 21 control	FVC, FEV1, FEV1 /FVC, PEFR, FEF 25-75%	1. TSH levels have an inverse relationship with the spirometric parameters. FVC, FEV1, and FEV1/FVC. 2. A positive relationship was discovered between T4 levels and FVC, FEV1, and FEV1/FVC. However, none of these results were statistically significant.
6.	Sadek SH et al., [30]	Assiut University Hospital, Assuit, Egypt, Dec 2015-Dec 2016	42 patients with newly diagnosed hypothyroidism and 12 control subjects.	[FEV1]/FVC, FVC%, FEV1%, FEF25-75 %,	FEV1% was significantly negatively correlated with TSH. While FEV1 and FVC were significantly positively correlated with FT4 respectively.
7.	Valjevac S et al., [31]	Clinical Centre of Sarajevo University, 2011	20 patients with hypothyroidism and 20 euthyroid subjects	Vital capacity, FVC, FEV1, FVC/FEV1	Percentage of VC, FVC and FEV1 were significantly lower in hypothyroidism patients compared to euthyroid subjects
8.	Present study	Burdwan Medical College and Hospital, India. 2010-2011	50 hypothyroid patients and 50 controls	FEV1, FVC, FEV1/FVC ratio, FVC%, FEV1%, FEV1/FVC(%), FEF25-75(L), FEF25-75%, PEFR(L), PEFR%	The present study showed that there was a significant reduction in FVC, FEV1, FEV1/FVC, PEFR% and FEF 25-75(L) in the clinical hypothyroidism patients

[Table/Fig-11]: Comparative evaluation of similar studies from the literature [17,26-31].

they found no significant correlation between thyroid hormones and parameters of lung function. Similar findings were showed by Maiti SR et al., and Valjevac S et al., [17,31]. They reported that TSH and FVC were positively associated in hypothyroidism patients. However, Roel S et al., found no significant correlation between TSH and FT4 and spirometric parameters. Lower thyroid hormone levels and higher TSH levels indicated more severe hypothyroidism, which resulted in a greater decrease in spirometric parameters. [Table/Fig-11] contains a comparison of similar studies from the literature [17,26-31].

### Limitation(s)

FT3 value could not be measured due to lack of facility in our institution and the sample size was less than the estimated size. The study will be better evaluated in future with considering these limitations.

### CONCLUSION(S)

The current study found a statistically significant difference in FVC, FEV1, FEV1/FVC, PEFR% and FEF 25-75 in the clinical hypothyroidism patients compared to apparently healthy controls. Therefore, pulmonary function test must be done in all the patients diagnosed as hypothyroidism. A convenient, cost-effective and non invasive simple spirometry may help in early detection of abnormal lung function in clinical hypothyroidism and thus plays an important role in early initiation of treatment which may prevent serious respiratory problems.

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**PLAGIARISM CHECKING METHODS:** <sup>[Jain H et al.]</sup>

- Plagiarism X-checker: Dec 23, 2023
- Manual Googling: Apr 07, 2023
- iThenticate Software: Apr 11, 2023 (13%)

**ETYMOLOGY:** Author Origin**AUTHOR DECLARATION:**

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. N/A

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