

## Original Article



# Bronchial Anthracofibrosis and Tracheobronchomalacia

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## Abstract

**Background:** Tracheobronchomalacia (TBM), presenting with the softening of the walls of trachea and bronchi, can cause respiration problems. Despite the importance of TBM, data on its prevalence and related factors are limited. In the current study, the prevalence and predictive factors of this illness were investigated.

**Methods:** This cross-sectional study was conducted on patients who were bronchoscopy candidates in the diagnostic department of pulmonary diseases in Afzalipour hospital in Kerman, Iran, from May 2017 to May 2018. First, all patients diagnosed with TBM were assessed based on their demographic variables, spirometry indices, anthracofibrosis and TBM severity. TBM was defined as a 50% or higher decrease in the diameter of the main tracheal and bronchial walls on expiration. These patients constituted the case group. Other patients for whom the bronchoscopy findings were not in concordance with TBM were selected through convenience sampling as control group to equal the number of patients in the case group. Data were analyzed using SPSS version 23.

**Results:** In this study, 132 (9.38%, 95% CI: 8–11) of the total 1406 cases who underwent bronchoscopy had tracheomalacia. Also, 22 patients (16.66%) had bronchomalacia, at the same time. Based on the multivariable logistic test results, age ( $P = 0.03$ , 95% CI: 1.00–1.04, OR = 1.02) and having anthracofibrosis ( $P < 0.0001$ , 95% CI: 1.26–4.68, OR = 2.43) were identified as predictive factors for tracheomalacia.

**Conclusion:** The findings of the present study suggest that the presence of anthracotic plaques can be considered as a possible predictive factor for TBM.

**Keywords:** Anthracofibrosis, Anthracosis, Bronchoscopy, Iran, Tracheobronchomalacia

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## Introduction

Tracheobronchomalacia (TBM) is an illness presenting with the softening and flaccidity of the walls of trachea and bronchi, indicating the weakness of the walls of these organs.<sup>1</sup> The weakness of the respiratory tract walls can increase the risk of its collapse, which will, in turn, lead to respiration problems. This condition is especially exacerbated in exhalation.<sup>2-6</sup>

TBM is classified into two types of primary and secondary. In the former case, the problem begins from birth and results from malformation or unnatural consistency of tracheal rings.<sup>7,8</sup> The second form is associated with several factors including chronic inflammatory of respiratory tract such as tracheobronchitis, smoking, chronic obstructive pulmonary disease, asthma, and connective tissue disorders in some studies. Furthermore, some mechanical factors, such as external pressures resulting from vascular problems, tumors, trauma, and previous intubation have also been mentioned as secondary causes. However, the factors associated with the development of this disease are not thoroughly known.<sup>9-11</sup>

The weakness of the walls of trachea and bronchi can lead to dynamic obstruction of the respiratory tract. It can also cause severe conditions such as expiratory stridor, severe cough, inhaled bronchodilator and corticosteroid-

resistant wheezing, recurrent lower respiratory tract infections, and respiratory failure.<sup>12</sup> The symptoms of this illness are nonexclusive, and are often misinterpreted as treatment-resistant asthma, leading to an increase in complications of treatment in patients.<sup>10</sup> Eventually, 7% of patients with the severe and diffuse type of this disease might need mechanical ventilation due to respiratory failure.<sup>12</sup> Stridor and hypoxia emerge in severe cases, leading to an 80% mortality rate if left untreated. In this regard, misdiagnosis as asthma and other respiratory diseases might delay the diagnosis, and lead to more deaths in these patients.<sup>13,14</sup>

In order to diagnose this illness, various methods such as simple pulmonary radiography, dynamic pulmonary CT scan, pulmonary function tests, and fluoroscopy for examining the dynamic function of respiratory tracts are suggested. However, the standard diagnostic method is fiberoptic bronchoscopy.<sup>1,6,15,16</sup>

The exact prevalence of this illness is not known, and the number of studies which have reported it has been on the increase lately.<sup>1,11,17</sup> In some studies, conducted in general populations, this disease has been reported in 1% to 10% of bronchoscopies and in more than 20% of autopsies. In the study conducted by Ikeda et al, which focused on pulmonary patients who had undergone bronchoscopy

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for different reasons, the prevalence of tracheomalacia was reported to be 12.7%.<sup>18</sup> Despite the importance of TBM, there has been a limited number of studies on its prevalence and related factors.<sup>19</sup> In the present study, the prevalence and predictive factors of this illness are examined in patients who visited the bronchoscopy department of Afzalipour hospital in Kerman, Iran (Pulmonary Diseases Referral Center) from May 2017 to May 2018.

## Materials and Methods

### Subject and Setting

This cross-sectional study was conducted from May 2017 to May 2018 on patients who were bronchoscopy candidates in the bronchoscopy department of Afzalipour hospital, in Kerman, Iran (Pulmonary Diseases Referral Center). All patients who were candidates for bronchoscopy for diagnosis of their diseases and referred to the bronchoscopy ward in the mentioned time interval were included in this study. Since history of surgeries on upper respiratory tracts and tracheostomy have been mentioned as causes of TBM in previous studies, these patients were excluded from the present study. Moreover, all the patients who could not tolerate bronchoscopy due to cardiovascular or respiratory impairments or did not consent to bronchoscopy were excluded from the study.

### Patients and Sampling Method

TBM was defined as a 50% or higher decrease in the diameter of the main tracheal and bronchial walls on expiration. Based on the severity of collapse, the patients were divided into three groups, namely mild (50%–75% collapse), moderate (76%–90% collapse), and severe (91%–100% collapse).<sup>15</sup> These patients constituted the case group. Other patients for whom the bronchoscopy findings were not in concordance with TBM were selected through convenience sampling as control group to equal the number of patients in the case group. Thus, on the same day when one patient was diagnosed with TBM, we selected another patient without TBM as control for whom the bronchoscopy findings were not in concordance with TBM.

### Bronchoscopy Procedure

All patients were under cardiovascular monitoring while receiving oxygen and Lidocaine 2% for local anesthesia, and underwent bronchoscopy using a fiberoptic bronchoscope (Pentax K700 Series) made in Japan. All bronchoscopies were performed by pulmonologists and the diagnosis of TBM and anthracosis was based on definitions.

### Data Collection and Outcome

A checklist was used for data collection. This form consisted of three parts. For quality checking (reliability), the pulmonologists reviewed the checklist and after corrections, the checklist was approved. The first part included bronchoscopy findings including positive or negative TBM and anthracofibrosis in which black plaques accompanied by deformity in respiratory tracts were simultaneously recorded as anthracofibrosis.<sup>20</sup> The patients' demographic and clinical information such as age, sex, smoking and opium use, history of baking and working in mines, using corticosteroid drugs and history of intubation were recorded in the second part of the checklist. In the third part of the checklist, spirometry findings were recorded. The spirometry pattern, severity of spirometry and reversibility of airway are presented in Table 1. All checklists were completed by the corresponding author after bronchoscopy in the diagnostic department of pulmonary diseases in Afzalipour hospital.

### Statistical Analysis

In this study, the data were described using descriptive statistical measures such as mean  $\pm$  Standard Deviation (SD), frequency, and 95% confidence interval. To compare the demographic and clinical characteristics of patients with spirometry pattern, severity of spirometry, and reversibility, univariate logistic regression models were used. Finally, to determine the predictors of TBM, a multivariate logistic regression model was performed. For running this model, all variables with P-values less than 0.2 were included. A backward LR elimination method was also utilized and in the last step, variables with P values less than 0.05 were considered as predictors. All

**Table 1.** Spirometry Pattern and Severity of Spirometry and Reversibility

Variables	FEV1	FVC	FEV1/FVC
Spirometry pattern	Normal	>80% predicted	>0.7
	Obstructive	<80% of the predicted normal	<0.7
	Restrictive	<80% of the predicted normal	>0.7
Severity of spirometry	Mild	$\geq$ 80%	—
	Moderate	50-80%	—
	Severe and very severe	<50	—
Reversibility	Negative	—	—
	Positive*	>12% and 200 mL	—

FEV1, forced expiratory volume in one second; FVC, forced vital capacity.

\*The measurement of FEV1 measured after applying 2 puffs of salbutamol inhaler (21).

statistical analyses were performed using SPSS version 23 and the significance level was considered 0.05 in all two-tailed tests.

## Results

In this study, 132 (9.38%, 95% CI: 8-11) out of the total 1406 patients who went through bronchoscopy had tracheomalacia. Also, 22 patients (16.66%) suffered from bronchomalacia. Patients with tracheomalacia were divided into three groups: mild (55 patients, 41.66%), moderate (49 patients, 37.12%), and severe (28 patients, 21.21%). The mean age of the participants in the study (the second phase) was  $62.11 \pm 14.1$  years (ranging from 23 to 93). Men comprised more than half of the population (146 patients, 55.3%). While less than half of the patients reported having a history of smoking (112 patients, 42.4%), narcotics users formed 52.3% (138 patients) of the population. Based on the findings, less than a quarter of the patients had worked in mines (30 patients, 11.4%), while more than 30% (91 patients, 34.5%) had a history of baking bread (Table 2).

**Table 2.** Assessment of the Relation between Contextual and Clinical Variables in the Selected Groups

Variables		Total	Tracheomalacia patients (n = 132)	Controls (n = 132)
Age (mean $\pm$ SD)		264	65.8914.5 $\pm$	58.3312.7 $\pm$
Gender	Male	146	64 (4.8)	82 (56.2)
	Female	118	68 (57.6)	50 (42.4)
Smoking	Negative	152	82 (53.9)	70 (46.1)
	Positive	112	50 (44.6)	62 (55.4)
Opium addiction	Negative	126	65 (51.6)	61 (48.4)
	Positive	138	67 (48.6)	71 (51.4)
Corticosteroid use	Negative	193	95 (49.2)	98 (50.8)
	Positive	71	37 (52.1)	34 (47.9)
Mine working	Negative	234	115(49.1)	119 (50.9)
	Positive	30	17(56.7)	13 (43.3)
Baking history	Negative	173	72(41.6)	101 (58.4)
	Positive	91	60 (65.9)	31 (34.1)
Intubation history	Negative	248	126 (50.8)	122 (49.2)
	Positive	16	6 (37.5)	10 (62.5)
Spirometry indices	Normal	49	10 (20.4)	39 (79.6)
	Obstructive	186	99 (53.2)	87 (46.8)
	Restrictive	29	23 (79.3)	6 (20.7)
Severity of spirometry	Mild	55	10 (18.2)	45 (81.8)
	Moderate	87	55 (63.2)	32 (36.8)
	Severe	76	46 (60.5)	30 (39.5)
	Very severe	46	21 (45.7)	25(54.3)
Reversibility	Negative	51	33 (64.7)	18 (35.3)
	Positive	135	66 (48.9)	69 (51.1)
Anthracofibrosis	Negative	186	74 (39.8)	112 (60.2)
	Positive	78	58 (74.4)	20 (25.6)
Bronchomalacia	Negative	242	110 (45.5)	132 (54.5)
	Positive	22	22 (100)	—

Reversibility was only checked in patients with obstructive spirometry pattern.

According to the univariate logistic model results, the study population was different in terms of age ( $P < 0.0001$ ), gender ( $P < 0.02$ ), history of baking bread ( $P < 0.0001$ ), spirometry indices ( $P < 0.0001$ ), and having pulmonary anthracofibrosis, in such a way that older patients compared to younger ones ( $P < 0.0001$ , 95% CI: 1.02–1.06, OR = 1.04), women compared to men ( $P = 0.02$ , 95% CI: 1.06–2.84, OR = 1.74), patients who had a history of baking bread compared to those who did not ( $P < 0.0001$ , 95% CI: 1.60–4.60, OR = 2.71), patients who, based on spirometry indices, had obstructive patterns ( $P < 0.0001$ , 95% CI: 2.09–9.41, OR = 4.43) and restrictive patterns ( $P < 0.0001$ , 95% CI: 4.80–46.54, OR = 14.94) compared to normal patients, patients who, based on the severity of spirometry indices, were in the mild group ( $P < 0.0001$ , 95% CI: 3.02–15.74, OR = 7.73), the moderate group ( $P < 0.0001$ , 95% CI: 3.02–15.74, OR = 6.90) and the severe group ( $P < 0.0001$ , 95% CI: 1.54–9.27, OR = 3.78) compared to normal patients, and patients with anthracofibrosis compared to those who did not have it ( $P < 0.0001$ , 95% CI: 1.26–4.68, OR = 4.38) had a higher probability of developing tracheomalacia (Table 3).

**Table 3.** The Results of the Univariate Logistic Regression Model of for Determining the Predictive Factors of Tracheomalacia

Variables		Crude Odds Ratio (95% Confidence Interval)	P value
Age		1.04 (1.02, 1.06)	0.001
Gender	Male	1	0.02
	Female	1.74 (1.06, 2.84)	
Smoking	Negative	1	0.13
	positive	0.68 (0.42, 1.12)	
Opium addiction	Negative	1	0.62
	positive	0.88 (0.54, 1.43)	
Corticosteroid use	Negative	1	0.67
	positive	1.12 (0.65, 1.93)	
Mine working	Negative	1	0.43
	positive	1.35 (0.62, 2.91)	
Baking history	Negative	1	0.001
	positive	2.71 (1.60, 4.60)	
Intubation history	Negative	1	0.30
	positive	0.58 (0.20, 1.64)	
Spirometry indices	normal	1	0.001
	Obstructive	4.43 (2.09, 9.41)	
	Restrictive	14.95 (4.80,46.54)	
Severity of spirometry	Normal	1	0.001
	Mild	7.73 (3.43, 17.42)	
	Moderate	6.90 (3.02, 15.74)	
	Severe and very severe	3.78 (1.54, 9.27)	
reversibility	Negative	1	0.05
	positive	0.52 (0.26, 1.01)	
Anthracofibrosis	Negative	1	0.001
	positive	4.38 (2.44, 7.89)	

Finally, according to the multivariable logistic regression model, age ( $P = 0.03$ , 95%CI: 1.00–1.04, OR = 1.02) and having anthracofibrosis ( $P < 0.0001$ , 95% CI: 1.26–4.68, OR = 2.43) were identified as predictive factors for tracheomalacia (Table 4). Furthermore, based on the data of Table 5, although more than half of the patients with tracheomalacia were in favorable conditions regarding the reversibility status, there was no significant relation between having tracheomalacia and reversibility of the respiratory tract ( $P = 0.65$ )

## Discussion

In this study, 132 (9.38%, 95% CI: 8–11) out of the total 1406 patients who went through bronchoscopy, had tracheomalacia. Age and spirometry indices were identified as predictors of tracheomalacia. In this study, bronchial anthracofibrosis was also introduced as a predictor for TBM for the first time.

The prevalence of TBM is not exactly known. Due to the expansion of noninvasive diagnostic methods, as well as more frequent patient evaluations for diagnosing TBM, the reports show a higher prevalence of this illness, and based on the population and method of each study, different prevalence rates, from 4% to 23%, have been reported.<sup>4</sup> In a study conducted by Jokinen et al, the prevalence of TBM was reported to be nearly 4.5%.<sup>22</sup> In another study, the prevalence of TBM among patients with respiratory complaints was 13.5%.<sup>18</sup> In a study, in which patients were examined for chronic cough, bronchoscopy revealed a 14.1% prevalence of an over 50 percent collapse in the trachea and main bronchi.<sup>23</sup> In a study conducted by Jokinen et al., the prevalence of TBM in patients with chronic bronchitis was approximately 23%.<sup>24</sup> Based on the different statistics in different studies, we can say that the reason for the disparity may lie in the difference between populations and diagnostic methods used in these studies.

**Table 4.** The Results of the Multivariate Logistic Regression Model of for Determining the Predictive Factors of Tracheomalacia.

Variables	Adjusted Odds Ratio (95% Confidence Interval)	P value
Age	1.02	0.03
Baking history	Negative	1
	Positive	1.72 (0.95, 3.10)
Spirometry indices	Normal	1
	Obstructive	2.56 (1.13, 5.80)
	Restrictive	9.11 (2.77, 29.87)
Anthracofibrosis	Negative	1
	Positive	2.43 (1.26, 4.68)

**Table 5.** Comparison of Airway Irreversibility Based on Tracheomalacia Diagnosis.

	Reversible	Irreversible	P value
With Tracheomalacia	73 (55.3)	59 (44.7)	0.65
Without Tracheomalacia	86 (57.1)	59 (42.9)	

In a study conducted in 2013 by Dal Negro et al,<sup>12</sup> the prevalence of TBM was evaluated by bronchoscopy in 202 patients with asthma and 62 healthy, non-smoking people. The prevalence of TBM was 1.6% and 9.4% in healthy people and in patients with asthma, respectively. The prevalence of TBM had a positive and significant relation with the severity of obstruction. In our study, the prevalence of TBM was 9.38%, which was similar to the asthma patients in the study by Dal Negro et al. This similarity can be a result of the high prevalence of obstructive pattern in the population of our study. Also, in our study, the prevalence of TBM had a significant relation with the obstructive pattern and obstructive severity, as well as the restrictive pattern.

In a study conducted by Majid et al, nearly 17% of the patients diagnosed with TBM had normal pulmonary function test results, and no significant relation existed between TBM and obstructive or restrictive patterns.<sup>25</sup> In a study by Loring et al., no significant relation was observed between the severity of obstruction, which was measured based on the forced expiratory volume in one second (FEV1) ratio, and central respiratory tract collapse.<sup>26</sup>

However, in the above-mentioned studies, only patients with TBM symptoms were examined while in our study, all bronchoscopy candidates, regardless of the reason, were examined for TBM, and those who were diagnosed underwent pulmonary function tests.

This illness is prevalent in patients with common respiratory diseases, such as asthma or chronic obstructive pulmonary disease (COPD).<sup>1,27</sup> Kandaswamy and Balasubramanian, in a study conducted in 2009, analyzed the relation between adult tracheomalacia and COPD. They stated that since the prevalence of COPD is increasing throughout the world, finding a relation between TBM and COPD is extremely critical. Analyzing the relation between TBM and COPD, they claimed that TBM can be considered as a form of COPD.<sup>28,29</sup>

In our study, a significant relation was observed between obstructive and restrictive spirometry patterns and TBM. Also, based on the findings of the study, although more than half of the patients with tracheomalacia were in favorable conditions regarding their reversibility status, no significant relation was found between tracheomalacia and reversibility of the respiratory tract. Anthracofibrosis is defined as a decrease in the diameter of bronchi accompanied by black pigment, which is diagnosed by bronchoscopy.<sup>30</sup> It is stated that the reactions in respiratory tracts caused by this condition can lead to fibrotic changes and the narrowing of bronchi.<sup>31</sup> This condition can also be accompanied by obstruction of bronchi.<sup>32,33</sup>

The causes of anthracofibrosis are not explained thoroughly yet, but being exposed to smoke, fossil fuels, organic particles, and tuberculosis have been mentioned as some possible causes. In fact, anthracofibrosis was previously considered as a symptom of an old or new tuberculosis infection.<sup>33,34</sup> However, nowadays, new evidence proves that intense exposure to biomass fuels

(any material with herbal or animal origin which is burnt in order to produce energy) are the main cause of anthracofibrosis.<sup>20,34</sup> Also, we can say that anthracofibrosis is a kind of COPD which is related to fossil fuels, and that radiologic and bronchoscopic evidence suggests that anthracofibrosis is the reaction of the lung to fossil fuels.<sup>34</sup>

So far, no study has addressed the association between anthracofibrosis and TBM. In any case, in our study, anthracofibrosis was suggested as a predictive factor for TBM.

This study had several limitations. First, we assessed TBM among patients with pulmonary diseases. Due to some ethical considerations, we could not perform bronchoscopy for the general population. Therefore, the results of our study could not be generalized to the whole population. It would have been better if the bronchoscopy findings were assessed along with chest CT-scan findings, but we did not perform this diagnostic evaluation due to radiation exposure which was not necessary for all patients. The second limitation was using convenience sampling for selecting the control group due to its effect on external validity of the study. It was better to use random sampling, but we did not perform this method due to some restrictions.

In conclusion, considering the significance of the relation between baking bread and being female, and TBM, we can state that due to the fact that use of wood in baking bread is extremely common among the women of the area under study, it can cause anthracotic pigments in the respiratory tract and lungs, and by causing inflammation, predispose them to TBM. The findings of the present study suggest that the presence of anthracotic plaques can be considered as a possible predictive factor for TBM.

#### Authors' Contribution

MSF: The header of the study and the whole idea was hers. MHAB: The information gathering, writing and editing. SMHB, AS, MS and RY performed the procedure and fill up the check lists.

#### Conflict of Interest Disclosures

The authors declare that they have no conflict of interest.

#### Ethical Statement

The protocol of the present study was reviewed and approved by the Ethics Committee of Kerman University of Medical Sciences (code of ethics: IR.KMU.AH.REC.1396.2181). Informed consent was taken from all participants before the procedure.

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