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The Association Between Pulmonary Tuberculosis and Bronchial Anthracosis

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Abstract

Background: Anthracosis is a form of pneumoconiosis induced by frequent contact with smoke from biomass, air pollution, charcoal smoke, or dust particles.
Objectives: This study aimed to investigate the association between anthracosis and pulmonary tuberculosis (TB).
Methods: In this cross-sectional study, 401 patients undergoing bronchoscopy were recruited, and their demographic characteristics, clinical features, bronchoscopy and imaging results, pathologic-cytologic reports, and acid-fast bacilli (AFB) smear were recorded and analyzed.
Results: The bronchoscopic results of 220 patients (54.9%) were normal, 93 (23.2%) had anthracosis, and 32 patients (8%) had anthracofibrosis. Positive pulmonary TB was significantly higher in patients with anthracosis or anthracofibrosis compared to those without (17.6% vs 4%; odds ratio (OR) = 5.09; $P < 0.001$). Patients with TB and anthracosis or anthracofibrosis had more prolonged contact with biomass ($P = 0.002$). Logistic regression showed age ($P = 0.003$) and the presence or absence of anthracosis or anthracofibrosis ($P = 0.006$) as associated factors with pulmonary TB.
Conclusions: Anthracosis is associated with other pulmonary diseases, including TB; therefore, if anthracosis or anthracofibrosis is diagnosed, coincidental pulmonary TB should also be evaluated.

Keywords: Anthracosis, Anthracofibrosis, Tuberculosis, Pulmonary

1. Background

Anthracosis is considered mild asymptomatic pneumoconiosis, suggested to be caused by exposure to biomass fuel and bronchial exposure to environmental particles (1). It can present as simple anthracosis with purely superficial black discoloration, complicated anthracosis with retracted mucosa and scattered foci of black spots, or severe bronchial anthracofibrosis (BAF) with severe submucosal edema, bronchial stenosis, and lung collapse (2). The prevalence of this condition varies among different populations from < 1% to more than 22%, and a high prevalence is reported in developing countries, especially Iran (3, 4).

The pathophysiology of anthracosis is unknown. It has been hypothesized that pollutants and particulate matter from firing biomass, especially in people with previously damaged airways and abnormal ciliary function, lead to carbon pigment deposition and anthracosis (5). In some patients, circulating tuberculosis (TB) antigens in lymphatics induce enhanced immune responses and lead to anthracofibrosis (5). Evidence suggests that most patients with this condition are older women without a history of smoking and are mainly asymptomatic; meanwhile, the most common presenting symptoms include dyspnea, cough, wheezing, and hemoptysis (6). Due to the nonspecific clinical symptoms and obstructive pattern of spirometric changes, anthracosis can be misdiagnosed as more common respiratory diseases, such as asthma and chronic obstructive pulmonary disease (COPD) (7, 8), and many cases of anthracosis are found incidentally in bronchoscopy or other imaging modalities such as computed tomography (CT) scan (9, 10). It can also be diagnosed as a coincidental finding associated with pneumonia, malignancy, and active pulmonary TB (11, 12).

The clinical significance of anthracosis is still unknown, and the necessity and choice of treatment are controversial, while bronchodilators and corticosteroids

are the most common suggested therapies (13, 14). Therefore, the main focus of attention is dedicated to the associated diseases, among which pulmonary TB is of great importance (15, 16). Several studies have suggested the association of active pulmonary TB with anthracosis, especially in Iran (17-19). Others have suggested that malignancy and TB were not higher in patients with anthracosis and BAF (20).

2. Objectives

Due to the high prevalence of anthracosis reported in Iran and the controversy on its association with pulmonary TB, as well as the significance of TB in Iran, (21) this study aimed to investigate the association between anthracosis and pulmonary TB for the first time in Fars Province to help better diagnosis of both of these conditions in Iranian population.

3. Methods

This cross-sectional study investigated patients undergoing bronchoscopy at Shahid Faghihi Hospital, Shiraz, Iran, with two retrospective and prospective phases between March 2014 and September 2017. The study protocol was approved by the Ethics Committee of Shiraz University of Medical Sciences (code: IR.sums.med.rec.1395.s120). The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

All patients who were scheduled for bronchoscopy during the study period according to pulmonologists' decision for indications such as persistent lung infiltrates, suspected lung cancer, hemoptysis, and had complete medical records and contact information were recruited into the study; patients who had more than 20% missing data in the hospital medical records or missed the information on the diagnosis of anthracosis/anthracofibrosis or TB smear (acid-fast bacilli (AFB)) were excluded from the study. Diagnosis of anthracosis was made on bronchoscopy by inspecting black discoloration of the bronchial tree, and anthracofibrosis was diagnosed by narrowing, deformity, or occlusion of airways due to black plaques.

Before bronchoscopy, informed consent was obtained from all patients. The patients were contacted by telephone, and oral consent was obtained from them for using their information in this study. The data were collected retrospectively from the medical records from March 2014 until July 2016 and then prospectively until September 2017.

Bronchial washing specimen was obtained for mycobacteriology assessment (AFB smear and culture) in all patients (sent to the Tuberculosis laboratory of Shiraz Health Center), patients with positive TB culture diagnosed as a case of TB, and the researcher reviewed chest CT scans. Demographic data, including sex, age, occupational history, living place, and underlying diseases, as well as medical history, history and duration of smoking, history and duration of contact with biomass smoke, history of direct contact with active TB, clinical symptoms and their duration, and the results of anthracosis and the involvement site, were recorded in the study checklist. Bronchial brushing and biopsy were taken if an endobronchial lesion was observed during flexible bronchoscopy.

3.1. Statistical Analysis

The collected data were analyzed using SPSS version 24 (SPSS Inc, Chicago, Ill, USA). The results were presented as mean ± SD and median for quantitative variables and frequency (percentage) for categorical variables. The Shapiro-Wilk test was used to test if the data were normally distributed. Quantitative variables were compared between the groups with and without anthracosis/BAF using an independent *t* test or Wilcoxon rank-sum test and qualitative variables using chi-square or Fisher exact test. The association of variables with TB was tested by logistic regression and reported by odds ratio (OR) with 95% CI. P values of 0.05 or less were considered statistically significant.

4. Results

Among 401 patients included in the study, 237 patients (59.1%) were male, and 164 patients (40.9%) were female. The mean age of patients was 59.69 ± 17.84 years. Based on the results of bronchoscopy, 220 patients (54.9%) were normal, 93 (23.2%) had anthracosis, and 32 patients (8%) had anthracofibrosis. The demographic characteristics of all patients and the comparison between the groups with and without anthracosis are shown in Table 1.

A comparison of the variables between the groups with and without anthracosis/anthracofibrosis showed a significant difference between the groups in terms of age and sex, and the group with anthracosis/anthracofibrosis was older and had a higher proportion of women compared to the group without anthracosis/anthracofibrosis (both $P < 0.001$; Table 1). Also, official and self-employed jobs reduced the chance of anthracosis/anthracofibrosis (OR = 0.36 and 0.55, respectively), and bread/pastry cooking, farming/stockbreeding, and housekeeping increased

Table 1. Comparison of Demographic and Clinical Characteristics Between the Groups with and Without Anthracosis [a]

Variable and Category	Total	Patients with Anthracosis/ Anthracofibrosis (n = 125)	Patients Without Anthracosis/ Anthracofibrosis (n = 276)	Odds Ratio (95% CI)	P Value
Sex					
Male	237 (59.1)	51 (40.8)	186 (67.4)	3 (4.64 - 1.94)	< 0.001 [b]
Female	164 (40.9)	74 (59.2)	90 (32.6)		
Age (y)	59.69 ± 17.84	70.85 ± 11.71	54.19 ± 17.8	-	< 0.001 [c]
Job category [d]					
Bread and pastry cooking	14 (3.5)	9 (7.2)	5 (1.8)	4.21 (1.38 - 12.82)	0.017
Farmer or stockbreeder	93 (23.2)	47 (37.6)	46 (16.7)	3.01 (1.86 - 4.87)	< 0.001
Self-employed	138 (34.4)	32 (25.6)	106 (38.4)	0.55 (0.34 - 0.88)	0.003
Housewife	143 (35.7)	67 (53.6)	76 (27.5)	3.04 (1.96 - 4.72)	< 0.001
Civil servant	46 (11.5)	7 (5.6)	39 (14.6)	0.36 (0.16 - 0.83)	0.007
Tobacco use		69 (55.2)	150 (54.3)	1.03 (0.68 - 1.58)	0.867
Nonsmoker	179 (44.6)				
Ex-smoker	41 (10.2)				
Current smoker [e]	181 (45.2)				
Duration of exposure (y)	13.82 ± 16.9	14.04 ± 17.69	13.72 ± 16.58	-	0.524
Biomass contact	177 (44.1)	96 (76.8)	81 (29.3)	7.97 (4.88 - 13)	< 0.001
Type of biomass exposure		-	-	-	-
Wood	162 (40.4)				
Charcoal	123 (30.7)				
Animal waste	12 (3)				
Oil	70 (17.5)				
Duration of exposure	8.55 ± 12.11	16.77 ± 12.12	4.86 ± 10.16	-	< 0.001
Habitation				5.33 (3.37 - 8.45)	< 0.001
Urban	232 (57.9)	38 (30.4)	194 (70.3)		
Rural	151 (37.6)	82 (65.6)	69 (25)		
Unknown	18 (4.5)	5 (4)	13 (4.7)		
Clinical signs					
Cough	348 (86.8)	95 (76)	253 (91.7)	0.29 (0.16 - 0.52)	< 0.001
Dyspnea	277 (69.1)	54 (43.2)	223 (80.8)	0.18 (0.11 - 0.29)	< 0.001
Hemoptysis	120 (29.9)	17 (13.6)	103 (37.3)	0.26 (0.15 - 0.47)	< 0.001
Chest pain	103 (25.7)	17 (13.6)	86 (31.2)	0.35 (0.2 - 0.62)	< 0.001
Weight loss	153 (38.2)	30 (24)	123 (44.6)	0.39 (0.24 - 0.63)	< 0.001
Fever	130 (32.4)	25 (20)	105 (38)	0.41 (0.25 - 0.67)	< 0.001
Positive acid-fast bacilli	33 (8.2)	22 (17.6)	11 (4)	5.09 (2.38 - 10.87)	< 0.001

[a] Values are expressed as No. (%) or mean ± SD.
[b] Independent *t* test (or Wilcoxon rank-sum test)
[c] Pearson chi-square (or Fisher exact test)
[d] Some patients had more than a job.
[e] 119 patients smoked cigarettes, 69 smoked hookahs, and 13 smoked both.

the chance of anthracosis/anthracofibrosis (OR = 4.21, 3.01, and 3.24, respectively).

More than half of the patients had a positive history of tobacco use. However, neither the frequency nor the duration of tobacco use was significantly different between the groups with and without anthracosis/anthracofibrosis (P > 0.05), while the frequency of positive history of biomass smoke exposure (OR = 7.97; 95% CI, 4.88 - 13) and the duration of exposure were significantly higher in the group with anthracosis/anthracofibrosis than that of without anthracosis/anthracofibrosis (both P < 0.001; Table 1). In addition, most patients in the group with anthracosis/anthracofibrosis lived in rural areas (65.6%), which was significantly higher than the group without anthracosis/anthracofibrosis (25%; OR = 5.33; 95% CI, 3.37 - 8.45). The bronchoscopic and CT imaging results were compared (Table 2).

Positive pulmonary TB was significantly higher in patients than those without anthracosis/anthracofibrosis (17.6% vs 4%; OR = 5.09; P < 0.001), and among 33 patients with positive TB, 22 patients (67%) had anthracosis/anthracofibrosis, and 11 patients (33%) did not. The effect size was 0.86 according to the Cohen d formula and was a large effect size. Degrees of freedom was 396. A comparison of variables in these 33 patients with positive TB between the groups with and without anthracosis/anthracofibrosis showed significant differences between the groups in terms of age and sex. Patients in the group with anthracosis/anthracofibrosis were older and had a higher proportion of women compared to the group without anthracosis/anthracofibrosis (P < 0.001 and P = 0.009, respectively; Table 3). Also, homemakers had a higher odds of positive anthracosis/anthracofibrosis (OR = 12; 95% CI, 1.99 - 72.35), and those with an official job had a lower odds (OR = 0.04; 95% CI, 0.01 - 0.77; both P = 0.008). There were also significant differences between the groups in the frequency and duration of biomass exposure (as well as the type of biomass and wood smoke), and charcoal increased the odds of anthracosis/anthracofibrosis (OR = 20.25; 95% CI, 3.1 - 132.2 and OR = 12; 95% CI, 1.99 - 72.35, respectively), while tobacco use was not different between the groups (P > 0.05). Among clinical signs, only fever and dyspnea had a higher frequency in the group with anthracosis/anthracofibrosis than in the group without anthracosis/anthracofibrosis (P = 0.002 and 0.005, respectively), and the CT findings were not different between the groups.

The involvement site and the CT findings were compared between the groups with anthracosis and anthracofibrosis. The results showed no significant differences between the groups in terms of CT findings. In contrast, the frequency of involvement of the upper and middle lobes of the right lung and diffuse/bilateral involvement was higher in the group with anthracosis than in the group with anthracofibrosis (P < 0.001, 0.004, and < 0.001, respectively; Table 3).

Finally, logistic regression was used to evaluate the association of variables with the chance of positive TB. The results showed female sex (P = 0.038), age (P = 0.003), duration of tobacco use (P = 0.016), and anthracosis/anthracosis (P = 0.006) as significant associated factors, while bakery or farming (P = 0.999 and 0.102, respectively), tobacco use (P = 0.153), positive exposure to biomass smoke and duration (P = 0.957 and 0.778, respectively), and living place (P = 0.164) were not associated with TB (Table 4).

5. Discussion

The present study aimed to investigate the prevalence of anthracosis/anthracofibrosis in patients undergoing bronchoscopy for other reasons and its association with pulmonary TB. The results showed that 31.17% (125/401 patients) had anthracosis or anthracofibrosis, and the rest did not. This prevalence seems higher than in previous reports. As to the evidence, the prevalence of anthracosis/anthracofibrosis is lower in developed countries than in developing countries, especially Iran (4). In the study by Mirsadraee and Saeedi, simple anthracosis was observed in 21% and anthracofibrosis in 11.7% of patients undergoing bronchoscopy (20), which is consistent with the results of the present study. In addition, the prevalence of anthracosis/anthracofibrosis was significantly higher in older women in the present study. Previous studies have also confirmed this finding (12), which might be associated with prolonged exposure to indoor and outdoor biomass smoke (3).

Generally, anthracosis is considered mild asymptomatic pneumoconiosis, and most patients have minor symptoms; meanwhile, the most common presenting symptoms include dyspnea, cough, wheezing, and hemoptysis (6). Consistently, the results of the present study indicated that most patients had a cough (76%), less than half had dyspnea (43.2%), a few had weight loss (24%), and fever (20%), hemoptysis or chest pain (13.6%). However, the frequency of patients' clinical symptoms may vary based on the severity of the disease and the underlying diseases. For instance, in this study, patients with TB and anthracosis/anthracofibrosis had a higher frequency of dyspnea and fever than those without anthracosis/anthracofibrosis. The frequency of subjective symptoms was significantly lower in the group of patients

Table 2. Comparison of the Results of the Bronchoscopic and Cytologic Examination and Computed Tomography Between Tuberculosis Patients with and Without Anthracosis [a]

Variable and Category	Patients with Anthracosis (n = 22)	Patients Without Anthracosis (n = 11)	P Value
Computed tomography findings			
Normal	0	1 (9.1)	0.333
Focal consolidation	6 (27.3)	2 (18.2)	0.687
Emphysema	0	1 (9.1)	0.333
Atelectasis	3 (13.6)	1 (9.1)	1
Single nodule	5 (22.7)	1 (9.1)	0.329
Calcification	0	0	-
Bronchiectasis	3 (13.6)	0	0.534
Pleural effusion	1 (4.5)	0	1
Mosaic pattern	0	0	-
Fibrosis	0	2 (18.2)	0.104
Cavity	4 (18.2)	4 (36.4)	0.391
Diffuse or bilateral infiltration [b]	7 (31.8)	5 (45.5)	0.471
Bronchoscopy findings			
Normal	0	10 (90.9)	< 0.001
Endobronchial masses	6 (27.3)	1 (9.1)	0.387
Positive cytology findings	2 (9.1)	0	0.542

[a] Values are expressed as No. (%).
[b] Consolidation + nodular and reticular pattern + interstitial pattern + ground-glass-opacity

with anthracosis because other patients referred for bronchoscopy had more severe lung diseases such as malignancy, interstitial lung diseases, and cavitary lung lesions.

As to the present study results, a positive history of exposure to biomass smoke increased the chance of anthracosis/anthracofibrosis up to 8 folds, which can justify the 4-fold increased chance in patients occupied in the bread and pastry cooking industry and a 3-fold increased chance in farmers and housekeepers. The role of biomass smoke and occupational risk in anthracosis/anthracofibrosis has been emphasized by previous studies (8, 11). This led to the suggestion of this disease as an occupational lung disorder (22). In the study by Hemmati et al., the smoke from bread cooking in women and the smoke from smoking in men caused anthracofibrosis (23). Although their results confirm the present study on the role of cooking as a cause of this disease and emphasize reducing the use of biomass fuel for reduction of this condition, the results by Hemmati et al. conflicted with the results of the present study concerning the role of smoking, as in the present study, the frequency and duration of smoking did not increase the chance of anthracosis/anthracofibrosis (23). Konno et al. also suggested that the anthracotic index was not correlated with tobacco smoking (12), confirming the present study results. Other studies have also suggested that smoking did not cause anthracosis/anthracofibrosis and considered this factor the main difference between this condition and COPD (4, 20). One study has also reported significantly less smoking in the group with anthracosis/anthracofibrosis than those without anthracosis/anthracofibrosis (24).

In the present study, the frequency of positive pulmonary TB was significantly higher in patients with anthracosis/anthracofibrosis than those without anthracosis/anthracofibrosis (17.6% vs 4%), and TB increased the chance of anthracosis/anthracofibrosis to 5 folds. Previous studies have also suggested the association between active pulmonary TB and anthracosis/anthracofibrosis (15-17, 24). Notably, all these studies have emphasized the relationship between anthracosis/anthracofibrosis and TB, which, in line with the results of the present study, indicates the significance of assessing other underlying diseases, especially TB, in patients with anthracosis/anthracofibrosis for appropriate management and prevention of TB-associated complications. The reason for this increased association is not fully understood, but explanations, such as interference of hazardous materials in wood smoke with the respiratory system's defense mechanisms and

Table 3. Comparison of Findings of Bronchoscopy, Computed Tomography, and Pathology Between Patients with Anthracosis and Anthracofibrosis [a]

Variable and Category	Total	Anthracosis (n = 93)	Anthracofibrosis (n = 32)	P Value
Computed tomography findings	-			
Normal		0	1 (3.1)	-
Focal consolidation		34 (36.6)	9 (28.1)	0.386
Emphysema		3 (3.2)	1 (3.1)	1
Atelectasis		11 (11.8)	6 (18.8)	0.324
Single nodule		24 (25.8)	9 (28.1)	0.797
Calcification		3 (3.2)	0	0.589
Bronchiectasis		6 (6.5)	2 (6.3)	1
Pleural effusion		4 (4.3)	4 (12.5)	0.202
Mosaic pattern		2 (2.2)	1 (3.1)	1
Fibrosis		10 (10.8)	2 (6.3)	0.729
Cavity		5 (5.4)	4 (12.5)	0.232
Diffuse or bilateral infiltration [b]		25 (26.9)	10 (31.3)	0.635
Bronchialinvolvement based on bronchoscopy findings				
Right main stem	12 (9.6)	10 (10.8)	2 (6.3)	0.729
Right upper lobe	36 (28.8)	34 (36.6)	2 (6.3)	0.001
Right middle lobe	31 (24.8)	29 (31.2)	2 (6.3)	0.004
Right lower lobe	27 (21.6)	24 (25.8)	3 (9.4)	0.079
Left main stem	9 (7.2)	8 (8.6)	1 (3.1)	0.445
Left upper lobe	26 (20.8)	18 (19.4)	8 (25)	0.497
Left lower lobe	22 (17.6)	20 (21.5)	2 (6.3)	0.061
Lingula	13 (10.4)	7 (7.5)	6 (18.8)	0.094
Diffuse or bilateral	46 (36.8)	26 (28)	23 (62.5)	0.001
Positive cytology	-	13 (14.4)	2 (6.5)	0.35

[a] Values are expressed as No. (%).
[b] Consolidation + nodular and reticular pattern + interstitial pattern + ground glass opacity (GGC)

gradual release of anthracotic materials from lymph nodes to the adjacent bronchial wall in patients with previous pulmonary TB, have been postulated (8, 16, 20, 22).

According to the present study results, patients with anthracosis/anthracofibrosis had variable chest CT findings that are not specific according to the previous studies (5, 25). Findings on imaging did not differ between the group with and without anthracosis/anthracofibrosis or between the group with anthracosis and those with anthracofibrosis. This suggests that the diagnosis of anthracosis/anthracofibrosis is not possible by imaging techniques. A bronchoscopy can appropriately diagnose this condition, consistent with previous reports (10, 16).

The present study clearly defined the symptoms, CT findings, and factors associated with anthracosis/anthracofibrosis, but the results cannot reflect the epidemiology of anthracosis/anthracofibrosis in the general population, only studied patients undergoing bronchoscopy for other reasons. Nonetheless, performing bronchoscopy only for diagnosis of anthracosis/anthracofibrosis does not seem rational; thus, many studies, like ours, have considered the disease symptoms, imaging findings, and associated factors in patients undergoing bronchoscopy for other reasons. In addition, this study was retrospective, and there were some cases of missing or incorrect data recorded in medical records.

5.1. Conclusions

Anthracosis and anthracofibrosis cause mild pneumoconiosis, and most patients have minor symptoms and few findings on imaging; bronchoscopy is suggested as an appropriate diagnostic tool. Nonetheless,

Table 4. Association Between Variables and Tuberculosis

Variable	Adjusted P Value [a]
Sex	0.038
Age	0.003
Bread and pastry cooking	0.999
Farmer or stockbreeder	0.102
Smoking	0.153
Duration of smoking	0.016
Biomass exposure	0.957
Duration of biomass exposure	0.778
Habitation	0.164
Anthracosis/anthracofibrosis	0.006

[a] Logistic regression, significance level < 0.05

as the direct complications of this condition are still unclear and as the present study results indicated, in line with previous studies, the association of this disease with TB is of great importance. Therefore, patients diagnosed with anthracosis/anthracofibrosis should be further evaluated for the diagnosis of TB. In addition, as exposure to biomass smoke played a pivotal role in anthracosis/anthracofibrosis, more attention should be paid to diagnosing this condition in old homemakers, bakers, and farmers. The treatment of anthracosis/anthracofibrosis is controversial, and the general disease trend is unclear. Hopefully, future studies can shed light on the best treatment choice for anthracosis/anthracofibrosis and the complications directly related to this condition. Increasing public awareness about the risk of biomass smoke can be an essential step toward reducing the risk of anthracosis/anthracofibrosis and associated pulmonary diseases, especially TB.

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Footnotes

Authors' Contribution: S. M. designed the study. S. M. and N. A. were responsible for data collection. S. M. and N. A. wrote the initial draft of the manuscript. S. M. and N. A. conducted the analyses. S. M. contributed to writing the manuscript. All authors contributed to the draft and approved the final version of the manuscript.

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