

Systematic Review

Frequency of Tuberculosis in Anthracosis of the Lung: A Systematic Review

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Abstract

Introduction: Anthracosis of the lung is the blackening of bronchial tissues which can lead to chronic bronchial obstruction. Many studies have shown association of bronchial anthracosis and tuberculosis. The aim of this study was accumulation of scattered studies and getting the definite conclusion about the association between anthracosis and tuberculosis.

Materials and Methods: We conducted a systematic search that included studies with sufficient information about the frequency of tuberculosis in anthracosis (anthracofibrosis) patients and non-anthraccotic control group. Moreover, tuberculosis should be confirmed by microbiologic (smear or culture) or histopathological methods.

Results: Twelve studies (eight studies on anthracofibrosis and four studies on anthracosis as a general term) comprising of 6280 patients was entered into our meta-analysis. The frequency of tuberculosis in all anthracosis patients was 22.5 % (32.3 % for anthracofibrosis and 16.6 % for anthracosis), which was significantly higher than the control group. Determination of risk showed that the cumulated odds ratio of tuberculosis in all studies of anthracosis was 3.16 (95 % CI = 2.49 – 6.85), which revealed significantly higher risk than the control group. The analysis of the subgroups showed that the cumulated odds ratio of tuberculosis in subgroups of anthracofibrosis (3.28; 95 % CI = 2.16 – 9.12) was significantly higher than anthracosis as a general term (2.85; 95 % CI = 1.73 – 6.61).

Discussion: The association of tuberculosis with all types of anthracosis of the lung was confirmed and a proper mechanism should be defined.

Keywords: Acid- fast bacilli, anthracofibrosis, anthracosis, tuberculosis

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Introduction

Anthracosis of the lung is the black discoloration of bronchial mucosa that sometimes causes bronchial obstruction.¹ It is an ancient disease for which still no effective treatment has been defined. Earlier reports showed that there was an association between tuberculosis (TB) and anthracosis, and patients who had experienced worsening clinical conditions required an evaluation that included a bronchoscopy^{2,3} but later a larger series could not prove this association.^{1,2} Regarding this controversy, several studies were subsequently performed. Most researchers used traditional methods such as acid-fast bacilli (AFB) and culture.¹⁻¹⁹ Some studies evaluated the frequency of TB in anthracosis as a general term that consisted of limited anthracosis to wide spread anthracofibrosis or evaluated it in only anthracofibrosis patients. Moreover, some reports used the control group¹⁻¹³ and many of them did not compare the frequency of TB with the control group.¹⁴⁻¹⁹ According to these findings the question that has been raised for many researchers and experts is “whether TB is an underlying cause of anthracosis or there is an association between anthracosis and TB”. By performing a meta-analysis and estab-

lishing the association of TB with available studies, we could appraise this finding and finishing future scattered studies.

The objective of this study was to determine the presence of TB in patients who demonstrate simple anthracosis and/or anthracofibrosis during routine bronchoscopy with a systematic review and meta-analysis of previous studies.

Materials and Methods

Systematic review and inclusion criteria

A comprehensive search was performed on case-control studies which evaluated the frequency of active TB in anthracosis patients. The systematic search was performed using the key words “anthracosis, anthracofibrosis, fibroanthracosis, anthracostenosis, TB, AFB, Ziehl-Neelsen, Kinyoun, auramine-rhodamine staining, Löwenstein-Jensen, and Middlebrook culture” from 1980 through 2011. The domain searches were Pubmed, Embase, Scopus, Oxford, Blackwell, Index Copernicus, Current Content, EMRO (Medline of the Middle Eastern region), Indmed, Pakmedinet, Iran Medex, the Korean Medical Citation Index, and from the proceedings of the European Respiratory Congresses. A manual search was performed for especial journals such as Tanaffos and Respirology, and through references of related published articles. In case of incomplete data, the authors were contacted directly by e-mail or telephone. Results of AFB direct smear (i.e., stained by Ziehl-Neelsen and Kinyoun), standard Mycobacterium TB culture (i.e., Löwenstein-Jensen), and histopathology were considered for the diagnosis of TB. Then, an overall final diagnosis of TB was used in meta-analysis.² Since the enrolled articles should

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Table 1. Summary of characteristics of studies enrolled in meta-analysis of frequency of TB in anthracosis

Study	Study duration	Mean age (range)	No. anthracosis	No. control	TB anthracosis (%)	TB control (%)
Anthraco-fibrosis						
Towhidi, et al. 2003 ³	1999–2001	71±3.6	93	1024	31	3
Mirsadraee, et al. 2010 ⁶	2008–2010	68±16	80	40	27	5
Mirsadraee, et al. 2005 ¹	2003	61±7	22	167	19	28
Chung, et al. 1998 ²	1994–1995	64†	28	831	60	8
Hemmati, et al. 2008 ⁹	2003–2006	61.8±3.2	34	173	44	17
Razi, et al. 2007 ⁷	1999–2002	50–90	51	464	25	5
Najafizadeh, et al. 2003 ⁸	2001–2002	70±12	47	243	27	7
Kim, et al. 2004 ⁴	1999–2003	59.5 (21–97)	37	26	40	38
Total (average)	---	---	392	2968	32.3	7.5
Anthracosis						
Mirsadraee, et al. 2009 ¹⁰	2006–2008	68±17.2	23	30	34	6
Amoli, et al. ¹¹	1975–2000	61 (40–77)	102	103	26	22
Fekri, et al. 2010 ¹²	2003–2007	(27–87)	333	1261	6.9	2.7
RezaeeTalab, et al. 2007 ¹³	2003–2005	65±12	225	775	25	5.6
Total (Average)	---	---	683	2169	16.6	4.6
Total (average) of both groups	---	63±3.8‡	1075	5137	22.5	6.3

† Median age was mentioned in the article; ‡ Determined by meta-analysis assay; § Determined by meta-analysis assay.

have enough information about the frequency of TB in anthracosis and non-anthraco-sis control groups for statistical analysis, those studies which did not contain enough information were excluded from our meta-analysis.

Meta-analysis of traditional TB assay and statistical analysis

All studies that provided enough data to compute effective size were coded by two persons who were blind to the previous results. Effects of exclusion of data or studies were evaluated by sensitivity analysis. Inter-rater reliability was evaluated by the Phi (Φ)-statistic. Reliability of coding the studies was evaluated by intraclass correlation. Heterogeneity between studies were evaluated by Cochrane's Q test. If heterogeneity was detected, a random model was used.

Odds ratio (OR) was measured to report the strength of association between TB and anthracosis (anthracofibrosis).

A funnel plot was used for determining the likely presence of publication bias. NCSS software was used for statistical analysis. Significance was accepted at $P < 0.05$.

Results

Description of studies

Twenty studies which evaluated the frequency of TB in anthracosis were entered into this study. Twelve studies that presented enough detail about TB in anthracosis and control groups were enrolled in our meta-analysis (eight studies chiefly on anthracofibrosis^{1–4,6,7,8,9} and four studies on anthracosis as a general term (pooled data about both anthracofibrosis and simple anthracosis)^{3–6} (Table 1). The studies that did not report TB in non-anthraco-tic control groups were excluded from our meta-analysis.^{7–15} Furthermore, one research used a different method (non-anthraco-tic the frequency of AF in the TB subjects), which was excluded.³ The total number of participating patients (anthracosis and control groups) was 6284. Intraclass correlation of the coding of the studies between the two groups was 0.81. The cumulated mean age of anthracosis patients was 63 ± 3.8 years, which was significantly more than the non-anthraco-tic control group (52 ± 6.4 years) ($t = 3.43$, $P = 0.02$).

Frequency of TB

Cumulated frequency of TB in the anthracosis group was 22.5 % (95 % CI = 11 – 56), (Table 1). The frequency of TB in anthracosis was significantly higher than the non-anthraco-sis control group (6.3 %, 95 % CI = 6 – 28), ($X^2 = 214$, $P < 0.00001$). Subgroup analysis showed that the frequency of TB in anthracofibrosis (32.3 %, 95 % CI = 21 – 57) was significantly higher than the anthracosis group as a general term (16.6 %, 95 % CI = 8.5 – 31), ($Q = 33$, $P < 0.0001$), (Table 1). Among the eight studies on anthracofibrosis and the four studies on anthracosis, six and three studies respectively showed a significantly higher frequency of TB in comparison to the control groups (Table 2).

Risk ratio of TB

The cumulated Odds Ratio (OR) of TB in all studies of anthracosis was 3.16 (95 % CI = 2.49 – 6.85), which revealed a significantly higher risk than the control group (Figure 1). Statistically significant heterogeneity was found (Cochrane's $Q = 61$, $P = 0.00001$) and the random model was used. The cumulated OR of TB in subgroups of anthracofibrosis and anthracosis as a general term was 3.28 (95 % CI = 2.16 – 9.12) and 2.85 (95 % CI = 1.73 – 6.61) respectively which were significantly higher than the control groups. The OR in the anthracofibrosis group was significantly higher than anthracosis as a general term (Cochrane's $Q = 52$, $P = 0.00001$).

Discussion

In this study, almost all studies which determined the frequency of TB in anthracosis (anthracofibrosis) were accumulated and analyzed by the meta-analysis method. The most comprehensive studies were found among Iranian and Korean literature. The total number of patients was 6284 in the case and control groups which seemed to be sufficient to end the study about the frequency of TB in anthracosis by traditional methods worldwide. The results of this analysis showed a significantly higher frequency (OR = 3.16) of TB in anthracosis (anthracofibrosis) patients, whom underwent bronchoscopy. This result was discovered by the earliest reports,^{2,3} but later were hesitated by others.^{1,4} Later investigators, who believed that there was an association between TB and anthracosis, began to explore this relationship and most have been able to

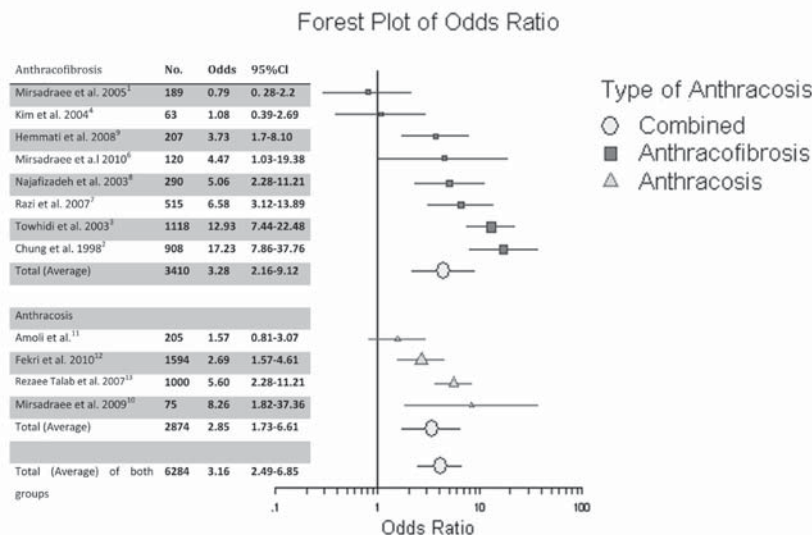


Figure 1. Forest plot of studies estimating OR of TB in patients with anthracosis (both simple anthracosis and anthracofibrosis) and anthracofibrosis.

Table 2. Summary report of meta-analysis risk of TB in anthracosis patients

	Number of subjects	OR	95% CI of OR	Weight	P- value
Anthracofibrosis					
Towhidi, et al. 2003 ³	1118	12.93	7.44–22.48	9.6	<0.001
Mirsadraee, et al. 2010 ⁶	120	4.47	1.03–19.38	5.6	0.05
Mirsadraee, et al. 2005 ¹	189	0.79	0.28–2.2	7.5	NS
Chung, et al. 1998 ²	908	17.23	7.86–37.76	8.6	<0.001
Hemmati, et al. 2008 ⁹	207	3.73	1.7–8.10	8.7	0.01
Razi, et al. 2007 ⁷	515	6.58	3.12–13.89	8.8	0.001
Najafizadeh, et al. 2003 ⁸	290	5.06	2.28–11.21	8.6	0.005
Kim, et al. 2004 ⁴	63	1.08	0.39–2.69	7.6	NS
Total (average)	3410	3.28	2.16–9.12	65	0.02
Anthracosis					
Mirsadraee, et al. 2009 ¹⁰	75	8.26	1.82–37.36	5.5	0.01
Amoli, et al. ¹¹	205	1.57	0.81–3.07	9.2	NS
Fekri, et al. 2010 ¹²	1594	2.69	1.57–4.61	9.7	0.02
Rezaee, Talab et al. 2007 ¹³	1000	5.60	2.28–11.21	8.5	0.01
Total (average)	2874	2.85	1.73–6.61	35	0.02
Total (average) of both groups	6284	3.16	2.49–6.85	100	0.02

show an association.⁶⁻²³ Most of them used traditional methods, such as smear and culture,^{1-4,6-20} which were useful as sources of our meta-analysis. Three types of researches did not use these similar methods, which were excluded from our meta-analysis: 1) Control group were not used in their studies.¹⁴⁻¹⁹ 2) Presence of anthracosis was evaluated in TB patients, which was contrary to other studies that evaluated TB in anthracosis subjects.²⁰ 3) Different methods like the polymerized chain reaction (PCR) were used.³

Na, et al.²¹ reported the frequency of positive PCR for TB in anthracofibrosis patients to be at 37 %, which is higher than the traditional method evaluated in that study (30 %) and in most of the studies reviewed (32.3 %). But we should consider that the frequency of TB in the non-anthracois group was also high (38 %) in a similar study by Kim, et al.⁴

Other indirect evidence in favor of TB such as upper lobe localization was also reported in anthracosis patients. Upper localization during bronchoscopy and imaging usually did not match together in one patient. In some studies more than 90 % of subjects showed upper lobe anthracosis during bronchoscopy.¹⁶ Using imaging, some studies reported the upper lobe as the most significant site of involvement¹⁸ and others reported right middle lobe as the

site most involved.^{7,9,20} Nonetheless, most of these studies did not show the results of control non-anthracois subjects; therefore, meta-analysis could not be used for accumulation and comparison of their information. Moreover, this evidence (upper localization) is not as diagnostic as bacteriologic and histological evaluation. Therefore, the meta-analysis mentioned above evaluated the most practical method for the evaluation of TB in anthracosis, but in future advanced diagnosis procedures, such as the PCR method, may yield more information about the presence of TB in anthracosis patients.

In this regard anthracosis subjects are very vulnerable to TB and close contact to active TB is very harmful. In a recent study, close contact was approved in 75 % of anthracosis subjects suffering from active TB.³

In conclusion, significant association between anthracosis and TB was shown in this meta-analysis, and we hope that we replied to some of the unanswered questions about anthracosis³ and close further study about association of anthracosis and TB, using traditional method. Future studies should be conducted to find a proper mechanism for susceptibility of anthracosis to TB and defining a preventive strategy.

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