

Diagnostic Role of Bronchoalveolar Lavage (BAL) in Suspected Cases of Sputum Negative Pulmonary Tuberculosis

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Summary :

Fiberoptic bronchoscopy is often used for the diagnosis of patients with suspected pulmonary tuberculosis with radiological opacities simulating tuberculosis in whom three consecutive sputum were negative, for AFB to identify acid fast bacilli on direct smear from bronchoalveolar lavage, washing, bronchial brushing and also to rule out malignancy. This study was carried out for the diagnosis of tuberculosis in sputum smear negative suspected cases by analysis of bronchoalveolar lavage fluid obtained by fiberoptic bronchoscopy procedure with Zeihl Neelsen stain in the Institute of Diseases of the chest & Hospital, Mohakhali, Dhaka. A total of 31 suspected cases were selected randomly along with 31 other patients of both sexes were selected randomly on the basis of inclusion and exclusion criteria. The patients were predominantly male. Out of 31 patients in group A, 23 (74.19%) were male and 8 (25.8%) were female. In group B, 23 (74.19%) were male and 8 (25.81%) were female. To assess the contribution of bronchoalveolar lavage with fibre optic bronchoscopy to the evaluation of suspected cases of pulmonary tuberculosis, 31 patients with 3 consecutive sputum negative for acid fast bacilli underwent bronchoscopy in group A and 31 patients control group B. In group A, exclusive means of diagnosis in 11 (35.48%) of 31 patients. In group B (control group) who were initial diagnosis nontuberculosis cases 4 (12.90%) of 31 patients were positive for acid fast bacilli in bronchoalveolar lavage third by direct smear with Ziehl Neelsen method. Direct Zeihl Neelsen staining of bronchoalveolar lavage smear revealed acid fast bacilli in 11 in group A and in 4 patients of group B.

Introduction :

Bangladesh is a high prevalence zone of tuberculosis. In practice, there is only 50% cases of sputum positive cases where radiological opacities noted pulmonary tuberculosis, other 50% cases are smear negative. According to WHO recommended guidelines in Bangladesh the modalities of treatment differ on the basis of finding acid fast bacilli in the sputum. Therefore the finding of acid fast bacilli in the sputum is important not only for rapid confirmation of diagnosis but also for treatment. Further more it helps to diagnose other diseases which simulate pulmonary tuberculosis radiologically and clinically. In a country such as Bangladesh, where the prevalence of tuberculosis is high, patients affected with pulmonary lesions compatible with tuberculosis who show a negative smear for acid fast stain will be

treated with antituberculosis drugs. This strategy is useful in most cases with the advantage of avoiding invasive diagnostic procedures. However, if this strategy was applied to non-tuberculosis cases e.g. Bronchogenic carcinoma or other infections etc. this may lead to delay in treatment resulting in poor outcome. Fiberoptic bronchoscopy represents a major advance in the diagnostic armamentarium of pulmonary physicians. Bronchoscopy and related procedure such as bronchial washing, brushing, bronchoalveolar lavage and transbronchial biopsy may be an alternative way to reach diagnosis as early as possible without serious complication. Bronchoalveolar lavage (BAL) which is known to be safe and simple may be the most useful diagnostic procedure. The procedure collect specimens for bacterial gram stain and acid fast bacilli stain, for

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fungal stain and cultures. Bronchoscopy may be performed in patients with bacterial infection of the lower respiratory tract to identify the responsible pathogen. The patients whose chest roentigenograms reveal minimal infiltration and whose sputum smear were negative for acid fast bacilli face a major problem for diagnosis in clinical practice. So, bronchoalveolar lavage may be an alternative procedure to confirm, pulmonary tuberculosis in highly suspected smear negative cases. This study is thus designed to determine the yield of fiberoptic bronchoscopy (FOB) and broncho alveolar lavage (BAL) for the diagnosis of patients suspected to have of smear negative pulmonary tuberculosis.

Materials and Methods :

This was a prospective case control study carried out in Department of Medicine, Institute of Diseases of Chest & Hospital Mohakhali, Dhaka during the period of January 1997 to June 1998, for immediate diagnosis of tuberculosis by BAL analysis using FOB in patients whose clinical and radiological features suggested pulmonary tuberculosis but whose sputum samples were repeatedly negative for AFB. The patients were selected on the basis of Criteria of inclusions having atleast one of the clinical features like, (1) persistent cough with or without sputum for more than 2 weeks (2) fever more than 2 weeks (3) Pain in the chest for more than 2 weeks, (4) Single episode of haemoptysis (5) Unexplained weight loss over one month (6) three consecutive daily sputum samples negative for AFB with Zeihl Neelsen staining (7) Radiologically suspicious specific in- filtration. The patients having the following features, were excluded from the study such as (1) pulmonary tuberculosis getting anti-TB drugs or had taken anti TB drugs with in the previous 2 years (2) COPD with corpulmonale (3) Poorly controlled asthma (4) Pulmonary abscess (5) Tracheal stenosis (6) Patients with heart diseases.

From a total of 410 consecutive patients attending IDCH, 156 patients had clinical features suggesting of pulmonary tuberculosis. Among them 116 patients were negative for AFB in sputum samples on 3 consecutive days. Of them, 31 were suspected to have pulmonary tuberculosis on radiological grounds and they served as cases and were categorised as group A. From the remaining 85 patients, 31 were taken as controls and referred to as group B. The controls were selected so as to match the cases in

respect of age, sex and occupation. They differed from cases only in radiological findings. Cases had patchy infiltrations on chest X-ray, whereas the controls had well circumscribed consolidation. Three consecutive daily sputum samples were collected from patients. The samples were sent for identification of AFB by Zeihl Neelsen stain. Only those patients who were negative for AFB in all their sputum samples where taken for the study and the others excluded. 30 ml or more of BAL fluid was collected by aspirating during FOB with normal saline and processed for analysis and search for AFB with Zeihl Nelsen stains. All the data were recorded in a proforma. Patients whose BAL smear revealed AFB with Zeihl Neelsen staining were given a short course 4 drug (2 RHZE + 4 RH) regimen of antitubercular chemotherapy and followed up monthly. The clinical & radiological improvement were recorded.

Results :

31 patients of both sexes were selected randomly on the basis of inclusion and exclusion criteria. The patients were of different ages ranging from 25 to 84 years with a mean age of 56.6 years in group A (SD=14.9) and 55.1 years in group B (SD = 14.28). The patients were predominantly male in both the groups. 23 (74.19%) were male and 8 (25.8%) where female. The difference in age and sex distribution between the two groups as assessed by chi-square test is not statistically significant ($0.>0.05$). The age and sex distribution of the patients of the series is shown in table-I.

The diagnostic yield of BAL in favour of tuberculosis in the current series was analysed. AFB was found by Ziehl-Nelson method in 11 patients (35.48%) of the initially 31 suspected cases of pulmonary tuberculosis. The diagnosis of tuberculosis was not supported by this method in the remaining 20 (64.52%) patients in this group Four (12.90%) patients in group B, who were initially suspected to have lung cancer, were also positive for AFB in their BAL fluids. This result is shown in table-II.

The ultimate diagnosis after BAL in all the patients was analysed. BAL principally helped in the diagnosis of pulmonary tuberculosis and malignancy. No other disease could be suspected or established by BAL smear and was assumed to be cases of PT. In the remaining 20 (64.52%) cases in this group, neither malignancy nor any other diagnosis could be reached

at. In group B with 31 subjects, analysis of BAL smear by Zeihl Nelson staining revealed 4 (12.9%) AFB positive cases. The difference in diagnostic yield of BAL in favour of tuberculosis between the two groups was highly significant ($P=0.03294$) at chi-square test. The results are shown in table-III.

The cellular components of BAL fluid in patients of the two groups were studied. In group A, the mean

total cell count was 125 with lymphocytes constituting 45.66%, neutrophils 15.41% and macrophages 37.35% of the cell on the average.

In group B, the mean total cell count was 144 of which lymphocytes were 45.18%, neutrophils 19.37% and alveolar macrophage 34.64%. The cell composition differed between two groups only in the lymphocyte component ($P=0.0246$ by chi square method) The results are shown in table-IV.

Table-I
Age distribution of patients according to sex

Age group (Years)	Group A						Group B					
	Male	%	Female	%	Total	%	Male	%	Female	%	Total	%
25-64	2	6.45	4	12.90	6	19.35	2	6.45	3	9.68	5	16.19
65-84	11	35.48	3	9.68	14	45.16	11	35.48	4	12.90	15	48.39
65-84	10	32.26	1	3.23	11	35.48	10	32.26	1	3.23	11	35.48
Total	23	74.19	8	25.81	31	100	23	74.19	8	25.81	31	100.00

Table-II
Exclusive diagnostic yield of BAL

	Group A (n=31)		Group B (n=31)		Group A (n=62)	
	No	Percentage	No	Percentage	No	Percentage
BAL Positive	11	35.48	4	12.90	15	24.19
BAL Negative	20	64.52	27	87.10	47	75.81

Table-III
Diagnosis after BAL smear examination

Diagnosis	No. in group A	Percentage	No in group B	Percentage
PT	11	35.48	4	12.90
Malignancy	0	0.00	3	9.68
No Diagnosis	20	64.52	24	77.42
Total	31	100.00	31	100.00

$P = 0.03$

Table-IV
Cell component of BAL Fluid

Cellular Component	Group A (mean total Cell count =125 (%))	Group B (Mean total Cell count = 125 (%))	P
Lymphocyte	15.41	19.37	0.0246
Neutrophil	45.66	45.18	0.8522
Alveolar macro	37.35	24.64	0.9446
Others	1.58	0.81	

Discussion :

The use of fiberoptic bronchoscopy in an attempt to diagnose tuberculosis in patients with suspicious radiographic lesions but negative sputum specimens has not been widely reported. Only few papers have described its value in many details^{1,2,3}.

In this study 21 patient (67.74%) of 31 suspected cases were above 44 years of age (Table-I). This bespeaks of a higher age prevalence of tuberculosis in the world. This however can not be taken as representative of the whole population because the study was carried out in a specialised centre where only the obscure and difficult cases are referred for management. In this study mean age was 56.6 years in group A, age range 25-84 years and 55.1 years in group B age range 25-84 years. In S. Chareonratanakul et al³, Bangkonk and H Levy et al⁴ studies showed mean age 65 years, range 16-78 years and mean age were 46.8 years, age range 18-71 years respectively. In this study age range and mean age almost consistent with other studies mentioned above.

Bronchoalveolar lavage was the exclusive means of diagnosis in 11 patients of 31 (35.48%) in Group A (Table-II) of the suspected cases. This finding in this series is inconsistent with study of Al-Kashmiri et al² who found exclusive means of diagnosis in 11 patients 27 (41%) suspected cases. In other studies, Danek and Bower found 10 cases of 41 patients (24.39%) by fiberoptic bronchoscopy (bronchoalveolar lavage). The cases of 41 patients (5%) was exclusive means of diagnosis. In S. Chareonratanakul et al³ study found 3 cases of acid fast bacilli positive in bronchoalveolar lavage out of 40 cases (7.55). Wallace et al⁵ found 11 cases of bronchoalveolar lavage acid fast bacilli positive on direct smear of bronchoalveolar lavage out of 23 cases (48%). This study is also consistent with the study of this series. AP willcolox et al⁶ found 56 cases acid fast bacilli positive on direct smear of bronchoscopic specimen out of 89 (62.5%) cases. This findings is also consistent with this series. The diagnosis was excluded in others in this group. All these 31 patients finding is also consistent with this series.

The diagnosis was excluded in others in this group. All these 31 patients were suspected cases of pulmonary tuberculosis and a diagnosis would not be excluded without a possible therapeutic trial with

antituberculosis chemotherapy. Twenty out of 31 suspected cases (64.62%) (Table-II) were spared the hazards of this unnecessary trial when bronchoalveolar lavage smear was found to contain no acid fast bacilli. This corresponds with the study of Al-Kashimi et al⁵. In this study 40-60% patients suspected tuberculosis were found to have active disease. They mentioned that if the treatment for all policy is adopted, many patients, would be treated unnecessarily with increase risk of antituberculosis drug side effect furthermore, 4 (12.90%) patients in group B, who were initially suspected to have pulmonary malignancy, had acid fast bacilli in their bronchoalveolar lavage smear and imposed on antitubercular therapy. The diagnosis of pulmonary tuberculosis could not have been reached in these patients without this method. They would have otherwise been left to their fate to die of a false cancer and delay in diagnosis would result more destruction. Although analysis of bronchoalveolar lavage was not of great help in the diagnosis in other controls subjects, except 4 of 31 patients (9.68%) who were diagnosed as non small cell carcinoma (Table-III) it was probably life saving for these 4 patients. This is consistent with the study of M. IP et al⁷. They found 13 patients of 95 cases (13.68%) having tuberculosis. Thirteen cases initially diagnosed as having using cancer turned out to have only tuberculosis, 4 of them had endobroncheal tuberculosis. This finding is consistent with these study MIP et al. It may be mentioned that the high similarity between lung cancer and endobronchial tuberculosis bronchoscopically has been highlighted in recent reports^{7,8} and sputum examination is not always diagnostic but histology often gives an early diagnosis while bronchial aspirate examination may establish or confirm it. The patients who were acid fast bacilli positive in bronchoalveolar lavage smear did have pulmonary tuberculosis and not some atypical mycobacterial infection is corroborated by the observation that almost all of these patients improved considerably both clinically and radiologically. There is always a real possibility of finding atypical mycobacteria in bronchoalveolar lavage smear in the form of acid fast bacilli but this possibility is presumably quite small and was incidentally zero in the current series. Regarding the cellular components of bronchoalveolar lavage in pulmonary tuberculosis. The neutrophils (45.66%) and lymphocytes (15.41%) (Table-IV), increased than normal cell count in

bronchoalveolar lavage fluid neutrophil is increased than the lymphocytes. But, tuberculosis is a chronic disease. So lymphocytes should be more. Why neutrophil is more is yet to be determined. This increase in number of cellular component, particularly neutrophil than lymphocytes is consistent with the study of S. Chareonratanakul³. In this study neutrophils was 46%, lymphocyte 16%, eosinophil 1%, and Macrophage 37%.

Conclusion :

From the above study it can be concluded that analysis of BAL for AFB with Zeihl Nelison staining by using FOB can be used in early diagnosis of pulmonary tuberculosis in sputum negative cases. It can identify patients with smear negative pulmonary tuberculosis before the result of sputum culture are available which usually require 6-8 weeks. The early detection of PT in smear negative suspected cases enables early institution of treatment and thereby will prevent extension of the disease and prevent complication.

References :

1. Danek SJ, Bower JS. Diagnosis of pulmonary tuberculosis by flexible fiberoptic bronchoscopy. *Am Rev respir dis*; 1979; 119-677-697.
2. Al-Kashimi FA, Azhar M, Al-Majed S. Diagnostic role of fiberoptic bronchoscopy in tuberculosis in the presence of typical x-ray pictures and adequate sputum. *Tubercle*; 1991; 72 : 145-148.
3. S. Charoenratanakul, W. Dejsomritrai, A. Chaiprasert Diagnostic role of fiberoptic bronchoscopy in suspected smear negative pulmonary tuberculosis. *Respiratory Medicine*; 1995; 89 : 621-623.
4. Bangkok, OE and H Levy : Bronchoalveolar lavage constituents in healthy individuals, idiopathic pulmonary fibrosis and selected comparison groups. *Am Rev Respir Dis*; 1990; 141 : (Suppl); 169-202.
5. Wallace JM, Deutsch MD, Harcl JH. Bronchoscopy and transbronchial Biopsy in evaluation of patients with suspected active tuberculosis. *Am J Med* 1981; 70 : 1189-1194.
6. Willcox PA, Potgieter PD, Bateman ED, Nenatar SR. Rapid diagnosis of sputum negative miliary tuberculosis using the flexible fiberoptic bronchoscope. *Thorax* 1985; 41 : 681-684.
7. IPM, Char PY, So SY, Lam KiK. The value of routine bronchial aspirate culture at fiberoptic bronchoscopy for the diagnosis of tuberculosis. *Tubercle*; 1989; 70 : 281-85.
8. Smith LS, schillaci RF, Sarln RF. Endobronchial tuberculosis and fiberoptic bonchoscopy and natural history. *Chest* 1987; 91 : 644-7.