DIAGNOSTIC YIELD OF FIBREOPTIC BRONCHOSCOPY IN SMEAR NEGATIVE NEW CASES OF PULMONARY TUBERCULOSIS

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Study Objective: To assess the diagnostic yield of bronchial washings for detection of AFB in clinically suspected new smear negative cases of pulmonary tuberculosis.

Design: Non-interventional analytical

Settings: Combined Military Hospital Quetta and Fatima Jinnah General & Chest Hospital Quetta, Pakistan.

Material and Methods: From outpatient departments of these two hospitals, fifty smear negative new cases of pulmonary tuberculosis (PTB) were included in whom diagnosis was made on the basis of clinical findings and x-ray. All these patients underwent fibreoptic bronchoscopy for collection of bronchial washings from the lobe/segment where lesions were evident on plain chest x-ray. These secretions were sent to microbiology department for preparation of smear and detection of acid-fast bacilli (AFB) with Ziehl-Nelson staining.

Results: Out of 50 patients, 33 (66%) were males and 17 (34%) were females. On smear of bronchial washings, 21 (42%) were positive for AFB while 29 (58%) were still negative.

Conclusion: Bronchial washings were found to have better diagnostic yield of AFB on direct smears as compared to standard sputum smear examinations. Moreover, clinical suspicion of PTB is not always correct, as significant numbers of clinically suspected cases did not yield AFB in bronchial washings. Where feasible, fibreoptic bronchoscopy and direct washings should be employed for confirming the clinical impression of PTB in smear negative cases.

Keywords: *pulmonary tuberculosis, *fiberoptic bronchoscopy, *bronchial washings, *sputum smear negative, mycobacterium tuberculosis, *acid fast bacilli

Introduction:
Tuberculosis (TB) is an important public health problem. According to population commission report, TB is fourth major cause of death in Pakistan¹ with 0.36 million new cases in 1995 and an estimated 4.2 million cases over the next 10 years.² For epidemiological reasons, pulmonary tuberculosis is the most important form of tuberculosis, as it is responsible for transmission of tuberculosis in community. It is important that every effort should be made to diagnose and treat

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cases of pulmonary tuberculosis. Diagnosis of pulmonary tuberculosis is straightforward when a
typical history and a characteristics radiograph are coupled with detection of AFB in sputum smears.
A sputum smear examination for AFB is by far most the important investigation for diagnosis of
pulmonary tuberculosis. Since a large numbers of bacilli (>10⁹/ml) need to be present in the
sputum specimen for their detection by Ziehl Neelson’s stain of smear, ³ Consequently, a number
of patients of active tuberculosis may be smear negative especially in early course of disease.
There are many other reasons for failure to detect AFB in sputum smear. These include, failure to
produce sputum by the patient, faulty collection of sputum by medical staff, and inadequate trans-
fer and storage of sputum samples to laboratory. Improper handling of samples by laboratory staff
and their lack of expertise are other sources of false negative reports. Even on properly collected
samples, the sensitivity of Ziehl Neelsen stain is variable and ranges between 20-80%. ⁴ ⁵ Presence
of AFB in sputum confirms active disease and denotes that patient is an open case of tubercu-
losis and is infectious to others.

Diagnosis of PTB on the basis of history and the chest x-ray alone have serious limitations. In
clinical practice, we encounter number of patients who have received multiple courses of antitu-
berculous drugs in spite of the fact that AFB were never detected in their sputum. There is definite
case to make diagnosis of “smear negative pulmonary tuberculosis” in a new case but one should
resist repeat course of antituberculous chemotherapy in re-treatment group without finding AFB in
their sputum. Even in new case of PTB, clinical diagnosis is not always correct. It is necessary
that every effort should be made to confirm tuberculosis by detecting AFB in lung secretions. As
sputum smear examination is not always rewarding and can be false negative in number of cases,
fibreoptic bronchoscopy and washings / lavage offer an additional method of sputum collection
directly from lungs. Logically one should expect higher yield of AFB because sputum is directly
collected from the infected site and these special samples are handled and analyzed carefully by
more experienced laboratory staff. To evaluate diagnostic yield of bronchial washings in detection
of AFB in smears, this study was carried out in clinically suspected new smear negative cases of
pulmonary tuberculosis.

Material and methods:
This prospective, non interventional /analytical study was carried out in Department of Medicine,
Combined Military Hospital Quetta in collaboration with Department of Pulmonology, Fatima Jinnah
General and Chest Hospital, Quetta. Fifty patients were enrolled from outpatient settings of these
two hospitals. All these patients were consistently negative for AFB on direct microscopy of three
consecutive sputum smears. They were labeled as “smear negative new cases of pulmonary
 tuberculosis” by two of the authors on the basis of history, clinical examination and chest x-ray.

Inclusion Criteria
- Smear negative, untreated, strongly suspected cases of pulmonary tuberculosis on ac-
  count of history and chest X-ray.
- No clinical and radiological response to two weeks course of antibiotics (combination of
  Clarithromycin and Amoxicillin -clavulanic acid)
- Age: 15-70 years
- Either sex

Exclusion Criteria: Those unwilling or unfit for bronchoscopy

- History of recent MI or unstable angina.
Brittle or moderate-severe bronchial asthma
Drug abuser
Immunocompromised (HIV & on cytotoxic drugs).
Respiratory insufficiency with moderate to severe hypoxia and/or any degree of hypercarbia.
Debility, malnutrition.

All enrolled patients underwent fibreoptic bronchoscopy at one of the two hospitals. An informed consent was taken from each patient. The two of authors themselves did bronchoscopies. No pre-medication or sedation was given to any of these patients. Trans-nasal route was employed in all patients for insertion of fibreoptic bronchoscope after spraying nasal passages and throat with 6-10 ml of 2% lignocaine; Small amount of lignocaine gel was also applied to the tip and distal shaft of bronchoscope to facilitate insertion. Vocal cords were sprayed with 4% of lignocaine. After passage through vocal cords 2-ml boluses of 2% lignocaine were sprayed on main carina and on both sides of bronchial tree. Tip of the bronchoscope was lodged in the most affected segment of the lung and twenty ml of sterile solution of normal saline was instilled through biopsy channel and subsequently sucked in to the trap attached in between suction unit and bronchoscope. Depending upon x-ray findings, procedure was in other involved segments. The bronchial washings thus collected were sent to laboratory for detection of AFB by direct microscopy of smears with traditional ZN stain.

After each procedure, bronchoscope was rinsed in water and detergent and then immersed in orsalex solutio (disinfectant) for ½ hour, which is effective killing time for AFB. To check adequacy of sterilization of bronchoscope, washings from the bronchoscope channel were routinely sent to laboratory for microscopy and culture to avoid false positive results.

Results:
Out of 50 patients 33(66%) were male and 17 (34%) were females, with age ranging from 15-70 years [Fig:1]. All of them presented with complex of symptoms related to pulmonary tuberculosis. Most commonly encountered symptoms were [Fig:2]: productive cough (96%), fever (94%), weight loss (74%), haemoptysis (36%), tiredness/ fatigue (32%), and night sweat (30%). Forty percent patient had bilateral changes in their chest x-rays while predominantly right and left sided changes were observed in 32% and 28% of cases. Out of these fifty sputum smear negative cases of PTB, 42% yielded presence of AFB on direct smears while 58% were still negative for AFB [Fig: 3].

Discussion:
Diagnosis of a "new case of pulmonary tuberculosis" in patients with repeated sputum smears negative for AFB is a challenging job and should only be taken up by those who have reasonable level of experience of handling of tuberculosis cases. No symptom, sign or radiological feature is pathognomonic for tuberculosis as similar features are encountered in number of other respiratory illnesses. There is no diagnostic role of erythrocyte sedimentation rate (ESR). Tuberculin test/ Mantoux test has no significant diagnostic value particularly in adults and in communities where tuberculosis is in abundance and BCG vaccination is routinely carried out. Definitive diagnosis of tuberculosis requires detection of acid-fast bacilli in sputum on direct microscopy of smears and subsequent confirmation on culture. Sputum smear is a simple test but its yield for AFB is poor and is dependent upon of variety of factors. Most of the sampling errors can be overcome, if sputum is directly collected from the suspected segment/ lobe of lung through fibreoptic bronchoscope.
In our study, fifty patients qualified criteria and underwent fibreoptic bronchoscopy for collection of washings from the involved segment/lobe of lung. These bronchial washings were sent to microbiologist for direct microscopy of smears with ZN stain. 21 (42%) out of 50 were found to be positive, while 29 (58%) were still negative for AFB. Result of our study are comparable with other similar studies, Petty TL et al who first conducted his study in 1976 and then repeated in 1997 documents 36.4% yield of AFB on bronchial washing. Similar results were reported by Charoenratanakul S and colleagues in Thailand (1995). In their study, overall yield of bronchoscopy in diagnosing pulmonary tuberculosis was 32.5%. Miro AM and colleagues (New York 1992), revealed 37% yield on bronchial washings. This study consisted of two groups with and without risk of HIV. The diagnostic yield in both these groups were not significantly different. Rao S (India 1993) studied 55 patients with radiological shadows of suspected malignancy and bronchial washings were obtained to exclude PTB. Prior sputum smear had been negative for AFB. Bronchial washings were examined for AFB and malignant cells. AFB was seen in 15/55(28%) smears made of bronchial washings. Study by Kennedy DJ and colleagues (Los Angeles 1992) compared bronchoscopic yield of mycobacterium tuberculosis in HIV infected with non-infected one and the results were 35% in HIV infected and 43% in non-HIV infected patients. Results of our study are also comparable with Smith LS et al who conducted his study in 1987 and William DJ et al in 1988 and study by Ahmed S et al conducted in Pakistan in 2000.

Conclusions:
Sputum smear examination for acid fast bacilli is the first and most important screening test for PTB suspect patients. In smear negative cases of PTB, fibreoptic bronchoscopy can be employed to improve the diagnostic yield and to confirm clinical impression of PTB. Those who are still negative for AFB on direct smears of bronchial washings, culture of these washings should be incorporated to improve yield. Consistent absence of AFB on direct smears and in culture of sputum and fibreoptic bronchial washings casts serious doubts on the clinical diagnosis of tuberculosis and invites physician involved to revise their clinical diagnostic criterion.

References:
9. Rao S, Significance of bronchial washing smear negativity in suspect pulmonary tubercu-


References:


30. Cowl CT, Prakash UB, Kruger BR. The role of anticholinergics in bronchoscopy, a randomized clinical trial. Chest 2000; 118:188.


McCune, RM, Tompsett, R, McDermott, W. Fate of Mycobacterium tuberculosis in mouse tissues as determined by the microbial enumeration technique. II. The conversion of tuberculous infection to the latent state by the administration of 104:763.


57. Centers for Disease Control. National action plan to combat multidrug-resistant tubercu-
Boston, 1952.
60. Lurie, MB. Resistance to Tuberculosis: Experimental Studies in Native and Acquired De-
1982; 3:5.
monary Diseases and Disorders, vol 3, 2nd ed, Fishman, AP (Ed), McGraw-Hill, New York, 
63. Barnes, HL, Barnes, IR. The duration of life in pulmonary tuberculosis with cavity. Am Rev 
Tuberculosis 1928; 18:412.
64. Finlay, BB, Cossart, P. Exploitation of mammalian host cell functions by bacterial patho-
gens. Science 1997; 276:718.
66. Jarvis, KG, Giron, JA, Jerse, AE et al. Enteropathogenic Escherichia coli contains a puta-
tive type III secretion system necessary for the export of proteins involved in attaching and 
67. Mecas, J, Strauss, EJ. Molecular mechanisms of bacterial virulence: Type III secretion 
68. Ainsa, JA, Martin, C, Gicquel, B. Molecular approaches to tuberculosis. Mol Microbiol 2001;
42:561.
69. Balasubramanian, V, Pavelka, MS Jr, Bardarov, SS, et al. Allelic exchange in Mycobacte-
70. Pellicci, V, Reyрат, JM, Gicquel, B. Generation of unmarked directed mutations in mycobac-
American Sociey for Microbiology 2000.
72. Camacho, LR, Ensergueix, D, Perez, E, et al. Identification of a virulence gene cluster of 
Mycobacterium tuberculosis by signature-tagged transposon mutagenesis. Mol Microbiol 
1999; 34:257.
73. Pierce, CH, Dubos, RJ, Schaefer, WB. Multiplication and survival of tubercle bacilli in the 
74. Derbyshire J. TB out of control?. The mitchell lecture 1995. J. Royal college of physicians 
75. WHO Global tuberculosis programme. Tuberculosis: the greatest killer in the history of 
76. Dannenberg AMJ. Pathogenesis of pulmonary tuberculosis. Am rev respir dis: 1982; 125:
25-30.
78. Bjortuf O, Brosstad F, Boe J. Bronchoscopy with transbronchial biopsies. Measurement of


### TABLE- 18 CHEST X-RAYS FINDINGS

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<thead>
<tr>
<th>SITE</th>
<th>NUMBER OF CASES</th>
<th>PERCENTAGE</th>
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<tbody>
<tr>
<td>BILATERAL CHANGES</td>
<td>20</td>
<td>40%</td>
</tr>
<tr>
<td>MAINLY RIGHT SIDED CHANGES</td>
<td>16</td>
<td>32%</td>
</tr>
<tr>
<td>MAINLY LEFT SIDED CHANGES</td>
<td>14</td>
<td>28%</td>
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### TABLE- 17 SEX DISTRIBUTION

<table>
<thead>
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<th>Total patients</th>
<th>Sex</th>
<th>No of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>Males</td>
<td>33</td>
<td>66%</td>
</tr>
<tr>
<td></td>
<td>Females 17</td>
<td></td>
<td>34%</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>50</td>
<td>100%</td>
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</tbody>
</table>

**ENDOBRONCHIAL WASHINGS FOR AFB**
### TABLE- 18

<table>
<thead>
<tr>
<th>BRONCHOSCOPY RESULTS</th>
<th>NUMBER OF CASES</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>POSITIVE</td>
<td>21</td>
<td>42%</td>
</tr>
<tr>
<td>NEGATIVES</td>
<td>29</td>
<td>58%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>50</td>
<td>100%</td>
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</table>

### TABLE- 16

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Productive Cough of &gt; 3 weeks</td>
<td>48</td>
<td>96%</td>
</tr>
<tr>
<td>Fever</td>
<td>47</td>
<td>94%</td>
</tr>
<tr>
<td>Weight loss</td>
<td>37</td>
<td>74%</td>
</tr>
<tr>
<td>Tiredness/ fatigue</td>
<td>16</td>
<td>32%</td>
</tr>
<tr>
<td>Night sweet</td>
<td>15</td>
<td>30%</td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>18</td>
<td>36%</td>
</tr>
</tbody>
</table>

### PROFORMA

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<th>S. NO.</th>
<th>D-O-A.</th>
<th>WARD</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAME.</td>
<td>AGE.</td>
<td>SEX.</td>
</tr>
<tr>
<td>ADDRESS</td>
<td></td>
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</tr>
</tbody>
</table>

Symptoms

- Productive Cough of > 3 weeks
- Fever
- Weight loss
- Tiredness/ fatigue
- Night sweet
- Haemoptysis

Report of Radiologist and Comments of Chest Physician on Chest x-ray

**AFB STATUS ON ASPIRATION**

Bronchoscopic aspiration

AFB +Ve AFB -Ve