International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2024: 7.101

Role of Induced Sputum and Bronchoalveolar Lavage in Diagnosis of Sputum Smear Negative Pulmonary Tuberculosis

Dr. Robin Varughese John [1], Dr. Hafiz Deshmukh[2], Dr. Rutuja Prabhudesai[3], Dr. Shivprasad Kasat[4], Dr. Ashish Deshmukh[5], Dr. Sunil Jadhav[6]

[1] Senior Resident, Department of Pulmonary Medicine, MGM Medical College & Hospital, Chhatrapati Sambhajinagar

[2]Associate Professor, Department of Pulmonary Medicine, MGM Medical College & Hospital, Chhatrapati Sambhajinagar

[3]Resident, Department of Pulmonary Medicine, MGM Medical College & Hospital, Chhatrapati Sambhajinagar

[4]Assistant Professor, Department of Pulmonary Medicine, MGM Medical College & Hospital, Chhatrapati Sambhajinagar

[5]Professor & Head, Department of Pulmonary Medicine, MGM Medical College & Hospital, Chhatrapati Sambhajinagar

[6]Professor, Department of Pulmonary Medicine, MGM Medical College & Hospital, Chhatrapati Sambhajinagar

Abstract: ***Introduction: Tuberculosis is an illness of antiquity which is caused by acid fast bacillus, Mycobacterium tuberculosis. It affects mainly the lungs however can likewise affect other organs in the body. Transmission usually takes place through air borne spread of droplet nuclei from patients of known cases of pulmonary tuberculosis. Present study was conducted to determine the diagnostic yield of induced sputum and bronchoalveolar lavage in diagnosis of sputum smear negative pulmonary tuberculosis. Materials and Method: The present study is a Non-Randomized Prospective Cross-Sectional study from October 2019 to September 2021. Patients with clinical suspicion of pulmonary tuberculosis were selected from OPD (Outpatient Department) and admitted to IPD (Inpatient department). Clinical specimens were submitted to the microbiology laboratory of MGM Medical College and Hospital Aurangabad. Results: A total of 36 patients were selected in the study, a majority of the cases i. e.12 (33.33%) were in age group of 21-30 years. BAL AFB was positive in 20 patients giving a sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy for BAL AFB were 86.96%, 100%, 100%, 81.25% and 91.67% respectively. Out of 23 cases that were positive for BAL for CBNAAT, only 10 cases were positive on induced sputum for CBNAAT, which is a concordance of 43.47%. All 13 negative cases on BAL for CBNAAT and for AFB were detected negative on induced sputum too with a concordance of 100%. Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy for BAL CBNAAT was 90%, 100.00%, 100.00%, 96.30% and 97.22% respectively. Conclusion: For diagnosis of pulmonary tuberculosis, a adequate sputum sample is one of the most important requirement. In patient's that fail to produce such a sample, induction of sputum, is a cheap, safe, reliable procedure with greater patient comfort, no age restriction and less time consuming. It should be carried out in patients as an initial procedure prior to advising and subjecting them to invasive diagnostic procedures like bronchoscopy.***

Keywords: pulmonary tuberculosis, sputum sample, bronchoscopy, bronchoalveolar lavage, AFB/CBNAAT

1. Introduction

Tuberculosis is an illness of antiquity which is caused by acid fast bacillus, Mycobacterium tuberculosis. It affects mainly the lungs, however can likewise affect other organs in the body. Transmission usually takes place through air borne spread of droplet nuclei from patients of known cases of pulmonary tuberculosis. Early finding and treatment of patients is significant for the prevention of spread of infection in the community. Worldwide tuberculosis is a significant health concern, with an estimated eight million new cases and two million deaths occurring every year (1). In India, the illness affects around 1.78 million people every year. As per the Ministry of Health and Family Welfare of India about 2.15 million new cases were reported in the year 2018 (2). With the onset of HIV infections in the mid 1980's there has been an increase in both pulmonary and extra pulmonary cases of tuberculosis as well as infections due to non-tuberculous mycobacteria. Disseminated form of tuberculosis is quite common in HIV infected individuals. India positions second after South Africa in assessing HIV related TB cases (3).

In majority of tuberculosis centers, even after fastidious hunt, the positive yield from sputum is only around 16% to 50% with a large proportion of samples remaining negative, despite clinico-radiological suspicion of PTB. For a long-time sputum smear microscopy and conventional sputum AFB culture have been the pillar of diagnosis of PTB. Downsides of smear microscopy are poor sensitivity and quality control issues (4). Another issue faced by patients is making multiple visits to healtcare facilities for giving multiple sputum specimens over several days.

Conventional light microscopy of Z-N-stained sputum smears is a generally accessible test for diagnosing tuberculosis in resource limited settings. Z-N microscopy, although highly specific, its sensitivity is variable (20%to 80%). Fluorescence microscopy, a more sensitive test than Z- N as staining takes less time, the significant expense of mercury fume light sources, customary support and the dull room prerequisite are its constraints (8). Culture on LJ medium provides myocobacterial isolates which can be recognised by basic phenotypic tests. It is the most widely recognized strategy for isolation of mycobacteria from clinical specimens. Its major

limitation is the amount of time taken for the results (5) and its inability to identify drug resistant strains. Microbiologists have been educated to acquire cultural confirmation of tuberculosis whenever possible which not only confirms the diagnosis but also provides information regarding drug susceptibility testing (4, 5, 8).

On account of these shortcomings, more rapid and reliable methods have been introduced. During the past ten years, many Nucleic Acid Amplification methods have been developed for quick detection and identification of Mycobacterium tuberculosis from clinical specimens. (5, 6) A nucleic acid analysis is a technique that is used to detect a particular nucleic acid sequence in order to identify species or organisms like viruses or bacteria. Nucleic acid test varies from other tests in that they detect hereditary materials (RNA/DNA) rather than antigens or antibodies. Recognition of these genetic materials enormously helps in the early diagnosis of a disease since simple identification of antigens or antibodies takes time for their appearance in the bloodstream (7). The measure of hereditary material acquired is typically tiny; hence nucleic acid analysis has incorporated a stage for enhancement of hereditary material. Multiple copies of genetic material are obtained through such amplification tests. Such nucleic acid test is called nucleic acid amplification tests. There are different methods of doing such tests namely, polymerase chain reaction, strand displacement assay or transcription mediated assay (8).

Nucleic acid amplification assays use specificity of Watson Crick base pairing. Single stranded probe or primer molecules capture DNA or RNA target molecules of complementary strands. Hence, the design of probe strands is highly significant for the sensitivity and specificity of the detection. Besides identifying Mycobacterium tuberculosis and detecting rifampicin resistance different applications of amplification tests includes diagnosis of Gonococcal and other Neisserial infections, urogenital Chlamydial trachomatis infections (9). WHO has supported use of nucleic acid amplification tests in tuberculosis laboratories since December 2010 and in India it has been embraced in 2012 and started as a pilot project in Maharashtra state (10). Nucleic acid amplification assay comprises of a closed system based on RT-PCR. Its benefit lies in the fact that it requires minimal technical expertise and helps in diagnosing tuberculosis and rifampicin resistance within 2 hours (11).

Bronchoalveolar lavage has been utilized with great success as a tool for recovering pathogenic micro-organisms from the lower respiratory tract of individuals with pulmonary infiltrates. The procurement of BAL is technically straight forward, although the best yields and least complications are obtained by a gifted bronchoscopist. As BAL is a somewhat protected and quick technique, it's indicative use in immunocompromised patients and immunocompetent patients with pulmonary infiltrates may, in selected circumstances, offer an option in contrast to more invasion and dangerous procedures. BAL has potential use for the study of infectious disease of the lung from the point of detailing the host's local inflammatory and immune responses to pulmonary infection. Cell populations present in lavage fluid during the intense period of bacterial contamination show a predominance of neutrophils, while lymphocytic expansion is seen during the resolution phase. The lavage fluid of patients with chronic infectious processes such as tuberculosis is that there is a shortfall of neutrophils and an increment in lymphocyte number (12). Bronchial washing for bacteriological assessment expands the worth of bronchoscopy to acquire the most accurate diagnostic results. Macroscopic and histopathological examination complements the framework of tuberculosis pathology and also makes differential determination of different pathologies, particularly that with bronchial carcinoma. With this point of view this cross sectional, non-randomized prospective study of 'Role of Induced Sputum and Bronchoalveolar Lavage in Diagnosis of Sputum Smear Negative Pulmonary Tuberculosis' to understand the efficacy of diagnosing sputum smear negative pulmonary tuberculosis through induced sputum and bronchoalveolar lavage was conceived and thus samples obtained were subjected to AFB smear microscopy as well as CBNAAT.

2. Aims and Objectives:

Aims: To determine the diagnostic yield of induced sputum and bronchoalveolar lavage in diagnosis of sputum smear negative pulmonary tuberculosis.

Objectives: To compare the efficacy of both induced sputum and bronchoalveolar lavage in diagnosis of sputum smear negative pulmonary tuberculosis.

3. Material and Methods

Approval of institutional ethics committee was taken prior to commencement of this study. The study was undertaken in the Department of Respiratory Medicine, MGM Medical College and Hospital, Aurangabad.

Study Design: The present study is a Non-Randomized Prospective Cross-Sectional study.

Study Duration: The study was conducted from October 2019 to September 2021.

Source of patient: For this study patients with clinical suspicion of pulmonary tuberculosis were selected from OPD (Outpatient Department) and simultaneously admitted to IPD (Inpatient department). Clinical specimens were then submitted to the microbiology laboratory of MGM Medical College and Hospital Aurangabad.

Inclusion criteria: Patients with clinical and radiological features suggestive of pulmonary tuberculosis whose sputum samples are negative for AFB by florescence smear were included in this study. The presenting complaints of patients were

1) Cough with or without expectoration for > 2 weeks.
2) Weight loss
3) Fatigue.
4) Hemoptysis.
5) Loss of appetite.
6) Fever

Radiological features seen were, cavitations, fluffy or nodular infiltrate & miliary pattern.

Exclusion criteria

1) Patients<18 years of age.
2) Patients where bronchoscopy is difficult to perform (difficult airway, trismus, unstable patients).

Selection of participants: Subjects were screened through a detailed history, general and systemic examination until desirable sample size was achieved.

Data analysis and Statistical Analysis: The data was entered in Microsoft Excel sheet and analysed using Epiinfo software. SPSS version 25 and EPI Info version7.3 was used for analysis. Comparison of Categorical variables was done by using counts and percentages and Chi square test for significance. Validity parameters like Sensitivity, Specificity, Positive predictive value, Negative predictive value and Diagnostic accuracy were used to compare tests with gold standard test. P-value<0.05 was considered to be significant.

Study Procedure: Complete procedure was explained to the volunteers and properly informed as well as written consents were obtained before the procedure. A detailed history was taken regarding complaints, past history, and family history. Detailed General and systemic examination was performed.

Sample Size:

N=36

Sample Size: N=76 ɳ= Z2× p (1-p) ε2

Where p= population proportion 0.217; Z= z score 1.96 for 95% confidence interval margin of error 1%.

Protocol of Sputum Induction:

A definite clarification of the methodology would be told to every patient. In order to avoid the contamination, all patients would be asked to over and again flush and wash their mouth until the returned liquid was free from debris.5 mL of 3% hypertonic saline would be filled into the nebulizer reservoir device. The assembly would be connected to the jet nebulizer. The procedure would be completed in a sufficiently ventilated room with windows open and staff having followed all protection measures. Patients would be told to breathe in and breathe out the mist of the nebulized solution through the mask only. The inhalation of hypertonic saline would be intruded every 5 mins, so that the patient could expectorate the sputum into a clean sterile sputum container. The methodology would be continued until a sufficient amount of sputum (2 mL or more) was obtained or a maximum of 15 mins had passed without success or the patient has complained of breathlessness or wheeze. The patient would be closely monitored all throughout the procedure, furthermore 1 hour after the procedure. The sputum samples would be stained with florescence stain and examined for AFB using the oil immersion lens as well as CBNAAT.

Protocol for bronchoscopy procedure:

Around the same time, preceding the bronchoscopy procedure an informed written consent would be obtained from the patient. The procedure would be carried out electively with the patient being nil by mouth for about six hours prior to procedure. Patients would be pre-medicated 15-30 minutes prior to bronchoscopy with nebulization of two per cent xylocaine via jet nebulizer and bronchodilators. Bronchoscopy would be carried out under local anesthesia. Olympus BF 150 bronchoscope would be utilized.

Bronchial washing would be performed by adding a liquots of 0.9% isotonic saline at room temperature through the internal channel of the fibre optic bronchoscope and aspirated into a trap connected to suction tubing. Normally 15-30 ml of fluid would be instilled with each washing and about one-fourth to half of this volume would be recovered in the suction trap. Up to one-fourth of the instilled amount retrieved would be considered as a successful procedure. No studies, however, in any case, have set up the best volume of liquid for ideal outcomes. The bronchial washings would be sent for AFB florescence- stained smear and CBNAAT.

Smear preparation: Blood stained, opaque, greyish or yellowish portion of the sputum are used for smear preparation. An appropriate portion of the specimen is transferred to a new, clean, scratch-free glass slide and is spread over an area of approximately 2 cm by 1cm. It is allowed to air dry for 15 minutes and fixed by passing the slide through a flame 3 or 4 times. After allowing it to cool, it was stained by Ziehl-Neelsen method of staining.

Z-N staining: The slide is kept on a staining rack and is flooded with dilute carbol fuchsin stain. The slide is gently heated until vapor rises. Carbol fuchsin is left on the slide for 5 minutes. The slide is then gently rinsed with tap water and decolorized with 25% sulphuric acid for 2 to 4 minutes. The slide gently rinsed again with tap water and the decolorization process is repeated until the smear looked colorless. The slide is then counter stained with 0.1% methylene blue for 30 seconds and air dried.

Microscopic Examination of the slide: The slide is focused under oil immersion lens (100 X). A linear pattern is followed and a minimum of 100 fields are examined systematically. The slides are reported as negative, scanty (AFB1+, AFB2+, AFB3+) or positive.

1) **Cartridge based nucleic acid amplification test (CBNAAT):** The cartridge based nucleic acid amplification test using Xpert MTB/RIF assay is performed on all sputum specimens irrespective of AFB smear positivity or negativity to detect tuberculosis and to determine rifampicin susceptibility. Procedure of Cartridge based nucleic acid amplification test (CBNAAT) includes:

a) Firstly, the Xpert MTB/RIF cartridge is labeled with the sample id.
b) The XpertMTB/RIF sample reagent is added to the respiratory specimens in the ratio 2: 1 in a conical screw capped tube.
c) The tube is shaken vigorously 10 to 20 times or vortexed for at least 10 seconds.
d) It is then incubated for 10 minutes at room temperature and is shaken vigorously again for 10 to 20 times or vortexed for at least 10seconds.
e) Following that, the mixture is incubated at room temperature for an additional 5 minutes.
f) Using a transfer pipette 2 ml of the mixture is then

transferred to the test cartridge and the test cartridge is then loaded to the Gene Xpert instrument (Cepheid).

g) The rest of the steps are fully automated. Within 2 hours the instrument gives the result as MTB Detected or Not Detected and Rifampicin sensitive or not.

2) Decontamination of sputum (Petroff's method)

Sputum was decontaminated since it would be contaminated with oral nasopharyngeal flora. To a centrifuge tube of 15 ml capacity, 3 to 4 ml of sputum is mixed thoroughly with 4% sodium hydroxide (double the quantity of sputum) and kept at 37^0 C for 20 minutes, shaking the tube in between. At the end of20 minutes, the tube was opened slowly avoiding aerosols and 2-3 drops of bromothymol blue indicator was added and mixed well. With a sterile pipette, sterile 8 % HCL was added slowly until a definite yellow color was obtained. Then it was back titrated with sodium hydroxide until the first blue tinge appeared. The contents of the tube were mixed well and centrifuged at 4000 rpm for 20 minutes. The supernatant was discarded into the discard jar with disinfectant.

4. Results and Observations

Table 1: Demographic profile of patients

		No. of patients [n=36]	Percentage
Age-Group	21-30	12	33.33
	31-40	7	19.44
	41-50	4	11.11
	51-60	5	13.89
	61-70	5	13.89
	>70	3	8.33
	Mean ± SD	43.13±17.90	
Gender	Male	20	55.56
	Female	15	41.67
Occupation	Student	08	22.22
	Homemaker	11	30.56
	Farmer	11	30.56
	Shopkeeper	03	8.33
	Laborer	01	2.78
	Engineer	02	5.56

Majority 12 (33.33%) cases were in age group of 21-30 years followed by 07 (19.44%) cases in age group of 31-40 years. There were 5 (13.89%) cases each in age group of 51-60 and 61-70 years. Mean age was 43.13±17.90 years ranging from 21-77 years. Maximum 20 (55.56%) cases were males followed by 15 (41.67%) cases were females. Majority 11 (30.56%) cases were homemaker and farmers respectively followed by 08 (22.22%) cases were students and 03 (8.33%) cases were shopkeepers.

Table 2: Distribution of study subjects according to symptoms

Symptoms	Number	Percentage
Cough	29	80.56
Fever	30	83.33
Chest pain	03	8.33
Breathlessness	16	44.44
Weight loss	17	47.22
Loss of appetite	21	58.33

Many cases had multiple symptoms out of which majority 30 (83.33%) cases had fever followed by 29 (80.56%) cases with cough, 21 (58.33) cases with loss of appetite, 17 (47.22%) cases with weight loss and 16 (44.44%) cases with breathlessness.

Table 3: Distribution of study subjects according to past history of tuberculosis

		No. of patients [n=36]	Percentage
Past history of TB	Yes	8	22.22
	No	28	77.78
Family history of TB	Yes	00	00
	No	36	100

Maximum 28 (77.78%) cases had no past history of tuberculosis. All cases 36 (100%) had no family history of tuberculosis.

Table 4: Distribution of study subjects according

		No. of patients [n=36]	Percentage
Abnormal Side in Chest Radiology	Left	10	27.78
	Right	17	47.22
	Bilateral	5	13.89
	Normal	4	11.11
Main abnormality on Chest Radiology	Consolidation	19	52.78
	Cavities	2	5.56
	Bronchiectasis	1	2.78
	Fibrocavitatory disease	4	11.11
	Pleural effusion	2	5.56
	Nodular opacity	3	8.33
	Grossly normal	4	11.11
Induced sputum for AFB	Positive	9	25.00
	Negative	27	75.00
Sputum induced CBNAAT	Positive	10	27.78
	Negative	26	72.22
BAL for AFB	Positive	20	55.56
	Negative	16	44.44
BAL for CBNAAT	Positive	23	63.89
	Negative	13	36.11

Majority 17 (47.22%) cases had abnormality on right side followed by 10 (27.78%) cases with abnormality on left side, bilateral were 5 (13.89%) cases and 4 (11.11%) cases were normal in findings.

Majority cases 19 (52.78%) cases had consolidation followed by 4 (11.11%) cases of fibrocavitatory disease and grossly normal radiograph respectively. There were 3 (8.33%) cases of nodular opacity and 2 (5.56%) cases of cavities and pleural effusion each. There was 1 (2.78%) case of bronchiectasis only.

Majority 27 (75%) cases had negative result on induced sputum for AFB. Only 9 (25%) cases came positive on induced sputum. Majority 26 (72.22%) cases had negative result on induced sputum for CBNAAT. Only 10 (27.78%) cases came positive on induced sputum for CBNAAT. Majority 20 (55.56%) cases had positive result on BAL for AFB. And rest 16 (44.44%) cases came negative for BAL for AFB. Majority 23 (63.89%) cases were positive for BAL for CBNAAT and rest 13 (36.11%) cases were negative.

Table 5: Sensitivity and Specificity for BAL for AFB

Induced Sputum for AFB	BAL for AFB		
	Positive	Negative	Total
Positive	09	00	09
Negative	11	16	26
Total	20	16	36

Validity of BAL for AFB	
Sensitivity	86.96%
Specificity	100.00%
Positive predictive value	100.00%
Negative predictive value	81.25%
Diagnostic accuracy	91.67%

Out of 20 cases that were positive on BAL, only 9 cases were positive on induced sputum for AFB, which is a concordance of 45%. All 16 negative cases on BAL for AFB were detected negative on induced sputum too with a concordance of 100%. Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy for BAL AFB was 86.96%, 100%, 100%, 81.25% and 91.67% respectively.

Table 6: Sensitivity and Specificity for BAL for CBNAAT

Induced Sputum for CBNAAT	BAL for CBNAAT		
	Positive	Negative	Total
Positive	10	00	10
Negative	13	13	26
Total	23	13	36

Validity of BAL CBNAAT	
Sensitivity	90%
Specificity	100%
Positive predictive value	100%
Negative predictive value	96.30%
Diagnostic accuracy	97.22%

Out of 23 cases that were positive for BAL for CBNAAT, only 10 cases were positive on induced sputum for CBNAAT, which is a concordance of 43.47%. All 13 negative cases of BAL for CBNAAT and for AFB were detected negative on induced sputum too with a concordance of 100%. Sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy for CBNAAT AFB was 90%, 100.00%, 100.00%, 96.30% and 97.22% respectively.

5. Discussion

Microbiological affirmation of pulmonary tuberculosis (TB) is currently progressively significant because of emergence of multi-drug resistance and increased incidence of TB among patients with human immunodeficiency virus (HIV) infection. However rapid and precise diagnosis will decrease the danger of nosocomial transmission of TB. Direct sputum smear microscopy remains a fundamental tool for diagnosis but may be negative up to 50% case of active pulmonary TB. Alternative methods of obtaining sputum specimens are frequently needed in those patients with radiological suspicion of TB who are unable to expectorate or are smear negative. The methods include – sputum induction (SI), bronchoalveolar lavage (BAL) and gastric washings (GW) specimens [13].

The study was carried out on 36 cases of sputum smear negative pulmonary tuberculosis out of which 20 were males and 15 were females. Mean age was 43.13±17.90 years ranging from 21-77 years.

Age incidence: In present study, majority 12 **(33.33%)** were in age group of 21-30 years followed by 07 **(19.44%)** cases in age group of 31-40 years. Mean age was **43.13± 17.90** years ranging from **21-77** years.

Table 7: Showing comparison of most common age group in various studies

Studies	N	Most common age group (in years)	Mean age	Range
Biswas et al (13)	100	18-40	-	-
Shubhkaran et al (14)	57	21-60	43.07±14.22	-
Balakrishna et al (15)	70	51-60	-	-
Park et al (16)	39	-	45.2±19.8	-
Madas et al (17)	50		35.58	18-60
Gopathi et al (18)	120	31-40	38	
Ahmad et al (19)	190	-	33±10	-
Chakradhar et al (20)	55	41–60	-	-
Kim et al (21)	92	-	BAL group-50.9 ±14.9	-
Present study	36	21-30	43.13□17.90	21-77

Above table shows studies like Shubhkaran et al (14), Gopathi et al (18) having most common age group of 21-40 years which is similar to present study findings. Mean age was similar in Shubhkaran etal (14), Park et al (16) with present study. It was less in studies like Madas et al (17), Gopathi et al (18) and Ahmad et al (19).

Gender: In our study, maximum 20 (55.56%) were males followed by 15 (41.67%) were females.

Table 8: Showing comparison of most common gender in various studies

Studies	N	Most common gender
Biswas et al (13)	100	Males (65%)
Shubhkaran et al (14)	57	Males (87.7%)
Balakrishna et al (15)	70	Males (66%)
Park et al (16)	39	Males (48.7%)
Madas et al (17)	50	Males (74%)
Gopathi et al (18)	120	Male (65%)
Ahmad et al (19)	190	Males (85%)
Chakradhar et al (20)	55	Males (65%)
Kim et al (21)	92	Males (54%)
Dubey et al (22)	100	Males (55%)
Present study	36	Males (55.6%)

All studies in above table shows males as majority gender which is similar to present study findings. This is majorly because tuberculosis is more prevalent in males in India.

Occupation: In present study, out of 36 cases, majority 11 (30.56%) cases were homemaker and farmers respectively followed by 08 (22.22%) students and 03 (8.33%) were engineers. In a similar study by Ahmed et al (19), unskilled workers were maximum (85.6%), semi skilled workers (9.1%) which is higher than present study finding.

Symptoms: In present study, many cases had multiple symptoms out of which majority 30 (83.33%) had fever followed by 29 (80.56%) with cough, followed by 21 (58.33%) with loss of appetite, 17 (47.22%) with weight loss and 16 (44.44%) with breathlessness.

Table 9: Showing comparison of various symptoms in various studies

Studies	n	Cough	Fever	Weight loss	Loss of appetite	Chest pain	Breathlessness
Biswas et al (13)	100	42%	-	-	-	-	-
Shubhkaran et al (14)	57	98.24%	71.9%	-	56.14%	56.14%	66.66%
Park et al (16)	39	51.3%	7.7%	-	-	17.9%	2.6%
Madas et al (17)	50	80%	60%	-	-	-	20%
Gopathi et al (18)	120	95%	80%	-	75%	32%	63%
Ahmad et al (19)	190	5.8%	1.6%	-	-	-	-
Present study	36	80.56%	83.33%	47.22%	58.33%	8.33%	44.44%

Above table shows that cough and fever were most common findings followed by chest pain, breathlessness in majority of similar studies.

Past history of tuberculosis: In present study, maximum 28 (77.78%) cases had no past history of tuberculosis and rest 22.22% cases had history of TB. In a similar study by Balakrishna et al (15), out of 70 cases, 28 (40%) cases were put on RNTCP category II regimen since all of them had a previous history of Anti- tuberculosis treatment. This finding is higher than present study findings. Chakradhar et al (20) in their study from Kurnool found that out of 55 patients, 18 patients were previously treated for Pulmonary tuberculosis (32.72%), remaining patients 37/55 (67.27%) were new cases. This finding is also higher than present study findings. Dubey et al (22) in contrast, found only 5% cases with previous history of TB. Also, Park et al (16) from Korea observed 19% cases with previous history of TB which is lower than present study findings.

Abnormal side of disease: In our study we found majority 17 (47.22%) cases had abnormality on right side followed by 10 (27.78%) cases with abnormality on left side.

Table 10: Showing comparison of abnormal side in similar studies

Studies	N	Right	Left	Bilateral
Shubhkaran et al (14)	57	35.08%	21.05%	9.3%
Madas et al (17)	50	36%	40%	24%
Chakradhar et al (20)	55	80%	15%	5%
Dubey et al (22)	100	39%	35%	24%
Present study	36	47.22%	27.78%	13.89%

Above table shows right side being the most affected side in similar studies like Shubhkaran et al (14), Madas et al (17), Chakradhar et al (20) and Dubey et al (22).

Main abnormality in chest radiology: Majority cases 19 (52.78%) had consolidation followed by 4 (11.11%) cases of fibrocavitatory disease and grossly normal radiograph respectively. There were 3 (8.33%) cases of nodular opacity and 2 (5.56%) cases of cavity and pleural effusion each. There was 1 (2.4%) case of bronchiectasis. Similarly Chakradhar et al (20) reported 36.36%, Shubhkaran et al (14) reported 59.64%, Biswas et al (13) 91% of majority of Consolidation.

Induced sputum yield of AFB: SI has performed well both in resource-poor and resource-rich countries. [7-10] In these studies, SI provided adequate samples for diagnosis was cost-effective and about 25-42% patients were smear positive on SI samples. But some studies in developed countries showed that SI added little to overall diagnosis and was deemed costly.

In present study, majority cases 27 (75%) had negative result on induced sputum for AFB. Only 9 (25%) cases came positive on induced sputum. In a study by Biswas et al (13), out of 100 cases, SI gave an additional yield in diagnosis of who were smearing negative with spontaneous adequate sputum, 21 (34%) were found positive on induced sputum culture examination. SI culture was successful in confirmation of diagnosis in 14 (33%) out of 42 patients with no/adequate sputum. In a study by Gopathi et al (18), of the total 120 patients, induced sputum smear examination for acid fast bacilli was positive in 76 cases (63.3%) which is higher than present study findings. BAL yield of AFB in our study, majority 20 (55.56%) cases had positive result on induced sputum BAL for AFB. And rest 16 (44.44%) cases came negative on induced sputum BAL.

BAL CBNAAT yield for AFB: In a present study, majority 23 (63.89%) cases were positive for BAL CBNAAT and rest 13 (36.11%) cases were negative. Dubey et al (22) observed that out of 100 BAL sent for CBNAAT testing 15% detected mycobacterial TB, 2% detected mycobacterial TB with Rif resistance. These findings are lower than present study findings. Mohantyet al (23) in their study on 100 patients, found BAL CBNAAT yield in 38/71 (54%) cases which slightly lower than present study findings.

Concordance of induced sputum yield and BAL yield of AFB: In present study, out of 20 cases that were positive on BAL, only9 cases were positive on sputum induced AFB, which is a concordance of 45%. All 16 negative cases on BAL for AFB were detected negative on induced sputum too with a concordance of 100% and out of 23 cases that were positive for BAL CBNAAT, only 10 cases were positive on sputum induced CBNAAT, which is a concordance of 43.47%. All 13 negative cases on BAL CBNAAT for AFB were detected negative on induced sputum too with a concordance of 100%.

Mohanty et al (23) observed that out of 71 patients who were SI smear negative SI CBNAAT was positive in 23 (32%) patients. CBNAAT conducted on BAL fluid in the same 71 patients had a yield of 54% (38/71). BAL culture, which was accepted as the gold standard had a yield of 59% (42/71). Fadaii et al (24) found that out of 18 patients who had positive lavage samples, 16 patients had positive induced-sputum results. Park et al (16) discussed that of the four PTB patients who were BAL culture positive, three were also induced sputum culture positive. Thus, addition of bronchoscopy enabled bacteriologic diagnosis of PTB possible in 20%.

Validity of BAL CBNAAT: In our study, sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy for BAL CBNAAT was 86.96%, 100%, 100%, 81.25% and 91.67% respectively. Kim et al (21) observed that the BAL AFB had sensitivity of 85.7% and negative predictive value of 88%. Dubey et al (22) found that BAL CBNAAT testing had 78.57% sensitivity, 93.02% specificity, 64.71%PPV, 96.39% NPV and 91% diagnostic accuracy. Shin et al (25) obtained 75.9%, 97.2%, 95.3% and 84.3% sensitivity, specificity, PPV and NPV of BAL, respectively. Jacomelli et al (25) reported 60% sensitivity and 100% specificity of BAL.

6. Conclusion

For diagnosis of pulmonary tuberculosis, sputum sample is one of the most important and an absolute requirement. In patients that fail to produce adequate sputum, induction of sputum, which is a cheap, safe, reliable procedure with greater patient comfort and safe, no age restriction and less time consuming, should be carried out in patients as an initial procedure prior to advising and subjecting them to invasive diagnostic procedures like bronchoscopy. Induced sputum is also successful in diagnosis of pneumocystis carinii infection as well as diagnosis of suspected pulmonary tuberculosis in a HIV individual. Induced sputum requires less patient cooperation and complications like pneumothorax, risk of bleeding appears to be absent as compared to invasive diagnostic procedures like bronchoscopy. In my present study the sensitivity and diagnostic accuracy of induced sputum for AFB/CBNAAT is much higher than that compared to bronchoscopy for bronchial washings for AFB/CBNAAT.

Ethics Approval and Consent to Participate: Ethical approval for conducting the study was obtained from MGM Medical College and Hospital, Aurangabad, Maharashtra. Written informed consent was obtained from the patient for their participation in the study.

Consent for Publication: The patient's informed consent has been acquired for the publication of the case details, clinical images, and relevant medical information. All efforts have been made to ensure patient confidentiality, and any identifying information has been appropriately anonymized.

Competing Interests: The authors declare nocompeting interests, financial or otherwise, that could have in fluenced the content or interpretation of this study.

Funding: This research received no specific grant from any funding agency, commercial entity, or not-for-profit organization. The study was conducted solely as part of the authors' academic and clinical activities.

References

[1] GlobalTuberculosisReport2017. Geneva, World Health Organization, 2017.
[2] Ministry of Health and Family Welfare 2018.
[3] ShenoiSV, Escombe AR, Friedland G. Transmission of Drug-Susceptible and Drug- Resistant Tuberculosis and the Critical Importance of Airborne Infection Control in the Era of HIV Infection and Highly Active Antiretroviral Therapy Rollouts. Clin Infect Dis.2010.
[4] Steingart KR, Ng V, Henry M, Hopewell PC, Ramsay A, Cunningham J et al. Sputum processing methods to improve the sensitivity of smear microscopy for tuberculosis: a systematic review. Lancet Infect Dis.2006; 6: 664–74.
[5] World Health Organization. Automated real-time nucleic acid amplification technology for rapid and simultaneous detection of tuberculosis and rifampicin resistance: Xpert MTB/RIF assay for the diagnosis of pulmonary and extrapulmonary TB inadults and children: policy update [Internet] Geneva: World Health Organization; 2013.
[6] Krysl J, Korzeniewska-Kosela M, Muller NL, FitzGerald JM. Radiologic features of pulmonary tuberculosis: an assessment of 188 cases. Can Assoc Radiol J.1994; 45: 101–107.
[7] Grossman RF, Hsueh PR, Gillespie SH, Blasi F. Community-acquired pneumonia and tuberculosis: differential diagnosis and the use of fluoroquinolones. Int JInfect Dis.2014; 18: 14– 21.
[8] National Institute for Health and Clinical Excellence. Tuberculosis: clinical diagnosis and management of tuberculosis, and measures for its prevention and control. London: National Institute for Health and Clinical Excellence; 2011.
[9] What is the nucleic acid test (NAT)?. American Red Cross.
[10] Peter A. Leone, Joseph A. Duncan. Tropical Infectious Diseases: Principles, Pathogens and Practice (Third Edition). Philadelphia: Elsevier.2011; 184–190 10.
[11] Dewan R, Anuradha S, Khanna A, Garg S, Singla S, Ish P, et al. Role of cartridge-based nucleic acid amplification test (CBNAAT) for early diagnosis of pulmonary tuberculosis in HIV. JIACM.2015; 16 (2): 114-7.
[12] Sulis G, Roggi A, Matteelli A, Raviglione MC. Tuberculosis: epidemiology andcontrol. Mediterr J Hematol Infect Dis.2014; 6 (1): e2014070 1.
[13] Biswas, S., Das, A., Sinha, A., Das, S. K., & Bairagya, T. D. The role of induced sputum in the diagnosis of pulmonary tuberculosis. Lung India: official organ of Indian Chest Society.2013; 30 (3): 199–202.
[14] Sharma Shubhkaran, Luhadia S. K., Gupta N. K. Diagnostic yield of fiber-optic bronchoscopy in sputum smear negative and radiologically suspected old cases of pulmonary tuberculosis international journal of medical sciences and education, 2014; 1 (2):
[15] J. Balakrishna, P. R. Shahapur, P. Chakradhar, S. Sreedevi, Shaik HussainSaheb. Role of Fiberoptic Bronchoscope in Sputum Smear Negative, Radiological

Suspect Cases of Pulmonary Tuberculosis. J. Pharm. Sci. & Res. Vol.7 (4); 2015: 231-233.

[16] Park, Jae. Efficacy of Induced Sputum for the Diagnosis of Pulmonary Tuberculosis in Adults Unable to Expectorate Sputum. Tuberculosis and respiratory diseases.2015; 78: 203-9.

[17] MadasS, ReddyMC, BinduHM, KoutamK. Role of Induced Sputum, Bronchial Aspirate and Post Bronchoscopic Sputum in the Diagnosis of Sputum Smear Negative Pulmonary Tuberculosis. Ann. Int. Med. Den. Res.2015; 1 (3): 185-90.

[18] Nageswar Rao Gopathi, Venu Mandava, Usha Rani Namballa, andSravani Makala. A comparative study of induced sputum and bronchial washings in diagnosis of sputum smear negative pulmonary tuberculosis.

[19] Mushtaq Ahmada, Wanis H. Ibrahimb, Sabir Al Sarafandic, Khezar S. Shahzadac, ShakeelAhmedc, IrfanUlHaqc, TasleemRazad, Mansoor AliHameede, MerlinThomasc, Hisham Ab Ib Swehlic, Hisham A. Sattar. Diagnostic value of bronchoalveolar lavage in the subset of patients with negative sputum/smear and mycobacterial culture and a suspicion of pulmonary tuberculosis International Journal of Infectious Diseases 82 (2019) 96– 101.

[20] Puligunta Chakradhar, Gadde Bharath, Madduri Veerasekharaiah. Role of fiberoptic bronchoscopy and genexpert in evaluating sputum smear negative pulmonary tuberculosis suspects journal of evidence-based medicine and healthcare pISSN- 2349-2562, Vol.6/Issue 9/March 04, 2019

[21] Y. W. Kim, B. S. Kwon, S. Y. Lim, Y. J. Lee, Y. -J. Cho, H. I. Yoon, J. H. Lee, C. -T. Lee, J. S. Park. Diagnostic value of bronchoalveolar lavage and bronchial washing in sputum- scarce or smear-negative cases with suspected pulmonary tuberculosis: a randomized study, Clinical Microbiology And Infection, Volume 26, Issue 7, p911-p916, July 01, 2020

[22] Dubey, Sakshi et al. Diagnostic yield of bronchoalveolar fluid/bronchoscopy among sputum AFB and CBNAAT negative presumptive tuberculosis patients: an observational study. International Journal of Research in Medical Sciences, [S. l.], v.9, n.2, p.546-551.

[23] Thitta Mohanty, Santosh Kumar Panigrahi, Manoranjan Pattnaik, Geetanjali Panda, Deepwanweta Routray, Jeetendra Kumar Patra, Bijaya Kumar Meher. Study On Diagnostic Modalities In Smear Negative Pulmonary Tuberculosis With Special Reference To Sputum Induction (SI CBNAAT), Bronchoscopy (Bal Cbnaat And Bal Culture) J. Evid. Based Med. Healthc., pISSN- 2349-2562, eISSN- 2349-2570/ Vol.4/Issue 47/June 12, 2017, https: //doi: 10.18410/jebmh/2017/567.

[24] Abbas Fadaii, Hamid Sohrabpoor, Bahador Bagheri. Comparison between induced- sputum and bronchoalveolar lavage fluid in diagnosis of pulmonary tuberculosis Iranian Journal of Clinical Infectious Disease 2009; 4 (3): 167-170.

[25] Jung Ar Shin, Yoon Soo Chang, Tae Hoon Kim, Hyung Jung Kim, Chul Min Ahn and Min Kwang Byun Fiberoptic bronchoscopy for the rapid diagnosis of smear-negative pulmonary tuberculosis. BMC Infectious Diseases 2012 12: 141.

[26] Márcia Jacomelli, Priscila Regina Alves Araújo Silva, Ascedio Jose Rodrigues, Sergio Eduardo Demarzo, Márcia Seicento, Viviane Rossi Figueiredo. Bronchoscopy for the diagnosis of pulmonary tuberculosis in patients with negative sputum smear microscopy results J Bras Pneumol.2012; 38 (2): 167-173.