ORIGINAL ARTICLE

ROLE OF FIBEROPTIC BRONCHOSCOPY IN PATIENTS WITH SPUTUM SMEAR NEGATIVE FOR ACID FAST BACILLI AND CHEST X-RAY SUGGESTIVE OF PULMONARY TUBERCULOSIS

Rajesh Kumar Jain S[1], Arun B. J[2], Paramjyothi G. K[3]

HOW TO CITE THIS ARTICLE:
Rajesh Kumar Jain S, Arun B. J, Paramjyothi G. K. "Role of Fiberoptic Bronchoscopy in Patients with Sputum Smear Negative for Acid Fast Bacilli and Chest X-Ray Suggestive of Pulmonary Tuberculosis". Journal of Evidence based Medicine and Healthcare; Volume 2, Issue 2, January 12, 2015; Page: 155-164.

ABSTRACT: AIMS: To study the role of fiberoptic bronchoscopy in patients with sputum smear negative for AFB and chest X-ray suggestive of pulmonary tuberculosis**. SETTINGS AND DESIGN:** After informed consent, 60 adult patients with sputum smear negative for Acid Fast Bacilli (AFB) and chest X-ray (CXR) suggestive of pulmonary tuberculosis (PTB), underwent diagnostic fiberoptic bronchoscopy (FOB) as per British Thoracic Society (BTS) guidelines. Relevant sampling methods like bronchoalveolar lavage (BAL), brushings and biopsy were done and samples were analyzed by smear microscopy, histopathology and or culture methods on case per case basis. The values obtained were tabulated & statistically analyzed, the results with P value < 0.05 were considered statistically significant. **RESULTS:** Males constituted majority of our study population 48 (80%). The most common age group involved in the study was 40-49 years (41.7%). Cough was the most common symptom reported by all 60 patients (100%). 16 patients (26.66%) had past history of PTB. Majority of the study population, 47 patients had unilateral lesions on CXR (78.33%) had unilateral lesion on CXR. The final diagnosis of PTB was established in 42 (70%) cases. Immediate diagnosis of PTB was possible in 33 cases (55%). The diagnosis other than PTB was established in 5 cases (8.33%), which included 2 cases (3.33%) of lung cancer, 2 cases (3.33%) of fungal (Candida) pneumonia, and 1 case (1.66%) of bacterial (Klebshiella sp) pneumonia. **CONCLUSIONS:** Diagnostic yield of fiberoptic bronchoscopy was 70% in suspected cases of PTB with sputum smear for AFB negative, which makes it a necessary tool in all cases with X-ray suggestive of PTB, it's also a safe procedure considering the minimal complications in our selected cases. Considering FOB under RNTCP for diagnosis of suspected cases of sputum smear negative cases through public private partnership may add to the success of national program.

KEYWORDS: Smear negative pulmonary tuberculosis, fiberoptic bronchoscopy, LJ culture.

INTRODUCTION: Since Robert Koch's discovery of Mycobacterium tuberculosis (MTB) in 1882, microscopic detection of the bacilli in clinical specimens has remained the mainstay of tuberculosis (TB) diagnosis in developing countries.(1)

In PTB sputum is the specimen of choice.(2) Sputum smear examination is usually positive advanced disease but may be negative in advanced disease(2) but may be negative in less advanced disease.(2) Although microscopic examination is rapid, simple and economical, it is relatively insensitive, requiring more than 10,000 bacilli per millilitre to detect Acid Fast Bacilli (AFB).(3) Sputum smear examination had a sensitivity of about 50% and a specificity of greater than 99% in two reported studies, with a positive predictive value of 91-98.5%.(2) In immuno-

competent patients, sometimes, poor quality of the sputum sample, deficient preparation, staining, or examination of the sputum smear can contribute to the negative results.[4]

There are also limitations in the diagnosis of Pulmonary Tuberculosis (PTB) by Chest X-Ray (CXR) only as a diagnostic tool, such as: high inter and intra-reader variations, no shadow is characteristic of PTB, 10–15% culture - positive cases remain undiagnosed, 40% patients diagnosed as having TB by X-ray alone may not have active TB disease.[5]

When a clinician is faced with a patient having CXR suggestive of active PTB but with spontaneous or induced sputum specimens negative for AFB on direct smear examination, two courses of action are open: either start treatment empirically or wait for the results of the culture and, if these are negative, the patient may be observed with regular radiographs and further sputum examination.[6]

With the advent of the FOB, a more aggressive approach to investigation has been adopted in such patients in an attempt to diagnose PTB at an earlier stage in its natural history.[6] FOB is a useful procedure for evaluation suspected cases of sputum smear negative PTB.

The advantage of making early diagnosis prevents morbidity, progression & spread of the disease, lung damage by fibrosis and mortality. Hence this study has been undertaken to evaluate the significance of FOB in the diagnosis of PTB among patients who have CXR suggestive but remain undiagnosed because of a negative sputum smear for AFB, hence aiding in the early diagnosis and thereby prompt & accurate treatment of such patients.

SUBJECTS AND METHODS:

1. Inclusion Criteria:

i. Adult patients aged 18 years and above.
ii. Suspected patients of PTB (as per RNTCP guidelines) with initial sputum smear for AFB negative.

2. Exclusion Criteria:

i. Patients not consenting for the study.
ii. Known or suspected case of HIV infection.
iii. Patients not fit to undergo bronchoscopy.
iv. Patients on anti-tubercular therapy (ATT) for more >1 month.

After informed consent, detailed recording of history, complete physical examination and relevant investigations a presumptive diagnosis was made. FOB (STORZ 11001BN-1) was done in all these patients for confirmation of the diagnosis as per British Thoracic Society (BTS) guidelines. Sampling methods like Broncho-alveolar Lavage (BAL), Mucosal Biopsy (MB) and Bronchial brushings (BB) were done and samples were analyzed by smear microscopy, histopathological examination (HPE) and or culture methods on case per case basis. The specimens were sent for culture of MTB on Lowenstein-Jensen (LJ) medium. Post Bronchoscopy Sputum (PBS) samples were collected for smear examination for AFB.

ANALYSIS OF RESULTS: After completion of the study, the clinical data as per proforma was analyzed for all the 60 patients, observation and results were documented. Descriptive statistics like mean, SD and percentage were used to express the data. Data were presented in tabular and graphical form. Sensitivity and specificity were also calculated. Data were analyzed by software SPSS v16.0.

RESULTS:

TABLE 1: Out of total 60 patients studied, the most common age group was 40-49 years (41.7%).

Age (years)	Number of patients	%
20-29	4	6.7
30-39	16	26.7
40-49	25	41.7
50-59	13	21.7
60-69	2	3.3

Table 1: AGE DISTRIBUTION

Sex	Number	%
Male	48	80
Female	12	20

TABLE 2: SEX DISTRIBUTION

Males constituted 48 (80%) patients and 12 (20%) were females.

TABLE 3: Cough was the most common symptom being reported by all 60 patients (100%) followed by night sweats and sputum production.

Sl. No	Symptoms	Number of patients	%
1	Cough	60	100
2	Sputum	31	51.7
3	Haemoptysis	15	25
4	Dyspnoea	21	35
5	Fever	20	33.3
6	Loss of weight	29	48.3
7	Loss of appetite	28	46.7
8	Night sweating	34	56.7

Table 3: SYMPTOMATOLOGY

TABLE 4: 17 (56.66%) of them had single comorbidity and 13 (43.33%) had more than one comorbidity, past history of PTB was present in 16 patients (26.66%), followed by DM in 15 patients (25%), COPD in 13 patients (21.66%), BA in 4 patients (6.66%) and HTN in 2 patients (3.33%).

Past history	Number of patients	%
Diabetes mellitus (DM)	15	25
Hypertension (HTN)	2	3.33
Bronchial asthma (BA)	4	6.66
COPD	13	21.66
Old PTB	16	26.66

Table 4: CO-MORBID ILLNESS

TABLE 5: 15 patients (31.91%) had history of either tobacco smoking or tobacco chewing or alcoholism. 32 patients (68.08%) had history of more than one combination of tobacco smoking and /or tobacco chewing and /or alcoholism. In our study most common was tobacco smoking seen in 39 patients (65%).

Personal history	Number of patients	%
Tobacco smoking	39	65
Alcohol	24	40
Tobacco chewing	26	43.33

Table 5: HABITS

TABLE 6: CXR of our study group showed, 13 patients (21.66%) having bilateral lesions, 47 patients (78.33%) had unilateral lesions. Of these 47 patients, 30 patients (50%) had right sided lesions and the remaining 17 patients (28.33%) had left sided lesions.

Site of lesion	Number of patients	%
Right side	30	50
Left side	17	28.33
Bilateral	13	21.66
Total	**60**	**100**

Table 6: SITE OF LESION ON CHEST X RAY

TABLE 7: 20 patients (33.33%) had cavitatory lesions and 40 patients (66.67) had infiltrates.

Lesion	Total number	%	Type	Number of patients	%
Cavitatory	20	33.33	Single	9	15
			Multiple	11	18.33
Infiltrate	40	66.67	Focal	24	40
			Diffuse	16	26.67

Table 7: TYPE OF LESION ON CXR

TABLE 8: 13 patients (22%) were culture positive on pre-bronchoscopic sputum for LJ culture.

Pre-bronchoscopic sputum LJ Culture	Number of cases	%
Positive	13	22
Negative	47	78
Total	60	100

Table 8: PREBRONCHOSCOPIC SPUTUM LJ CULTURE:

TABLE 9: Congestion with hyperaemia which was observed in 40 patients (66.66%), erosions & ulceration was seen in 25 patients (41.66%), intra-bronchial bleeding in 6 patients (10%), intra-bronchial growth 3 patients (5%) and stenosis in 1 patient (1.66%) was observed.

Finding	Number of patients	%
Normal	20	33.33
Erosion/ Ulcer	25	41.66
Congestion/ Hyperaemia	40	66.66
Growth	3	5
Stenosis	1	1.66
Bleeding	6	10

Table 9: GROSS FOB FINDINGS

TABLE 10: Among 60 patients studied, the smear positive diagnosis of various FOB specimens was possible in 33 patients (55%), and LJ culture positive diagnosis of various FOB specimens was possible in 42 cases 70%.

FOB specimen	Smear positive		LJ culture positive	
	Number of cases	%	Number of cases	%
BW	14	23.3	23	38.33
BAL	4	6.66	6	10
BB	0	0	0	0
MB	2	3.33	0	0
TBNA	7	11.7	7	11.7
PBS	6	10	6	10
Total	33	55	42	70

Table 10: RESULT OF FOB IN DIAGNOSED PTB CASES

TABLE 11: Minor hemorrhage following forceps mucosal biopsy was seen only in 1 patient (1.66%). However serious complications did not occur in our study group.

Complications	Number of cases	%
Haemorrhage	1	1.66%
Hypoxia	0	0
Respiratory distress	0	0
Cardiac arrhythmia	0	0
Cardiac arrest	0	0

Table 11: COMPLICATIONS

TABLE 12: Among the 60 cases studied, the total number of PTB cases diagnosed was 42 (70%). The total number of PTB cases having smear positive (BW+ BAL+ BB+MB+TBNA+ PBS) was 33 (55%). The total number of PTB cases having positive LJ culture (BW+BAL+BB+PBS+TBNA) was 42 (70%). Diagnosis other than PTB was made in 5 (8.33%) patients, which included 2 cases (3.33%) of malignancy, 2 cases (3.33%) of fungal (Candida) pneumonia, and 1 case (1.66%) of bacterial (Klebsiella) pneumonia.

Sl.	Diagnosis	Number of cases	%
I	Total PTB cases diagnosed	42	70
A	With smear (BW+BAL+BB+MB+TBNA+PBS)	33	55
B	With culture (BW+BAL+BB+PBS+TBNA)	42	70
II	Total cases of other diseases diagnosed	5	8.33
A	Malignancy	2	3.33
B	Bacterial pneumonia	1	1.66
C	Fungal pneumonia	2	3.33

Table 12: DIAGNOSTIC YIELD OF FOB SPECIMENS

DISCUSSION: The WHO Committee on TB recommends that patients of PTB in whom the disease is not confirmed bacteriologically should be classified as "suspects" till the presence of AFB is demonstrated and a patient with persistent symptoms whose sputum does not contain AFB should be followed up and ATT should be given only if the diagnosis can be confirmed bacteriologically.[7] In areas with high transmission the risk of infectivity of SSN-PTB to young household contacts have been estimated to be quite high.[8,9,10] Published observation suggests that over 50% of patients with SSN-PTB would need ATT by the end of 12 months if untreated.[11,12] Data from longitudinal surveys from Bangalore district, India indicate that at the end of 18 months follow up the mortality rate of SSN-culture positive PTB was 14.1% compared with 34.7% observed SSP patients.[13] Many patients of PTB are co-infected with HIV, with late stage HIV disease (CD4+ counts ≤ 200/mm^3) and those who are severely immunocompromised are more likely to be SSN.[14] Thus early diagnosis of active SSN-PTB is important. On review of literature, we found few similar studies. Shin et al studied 126 patients who were SSN suspected cases of PTB, 54 patients were confirmed as having active PTB. Haemoptysis was negatively

correlated with active PTB. Tree-in-bud appearance on HRCT was significantly associated with active PTB. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of FOB alone was 75.9%, 97.2%, 95.3%, and 84.3%, respectively, for the rapid diagnosis of active PTB. The combination of FOB and HRCT improved the sensitivity to 96.3% and the NPV to 96.2%.[15]

Saif Quaiser et al made definitive diagnosis of TB in 17 (42.5%) of the 40 patients. BAL smear was exclusively positive in one case; BAL culture in 3 patients & PBS smear also had one patient exclusively positive. In various other previous studies, PBS smear revealed AFB positivity ranging from 23% to 37%.[16]

Usha Kalawat et al study revealed BAL samples positive in 82.2% of sputum smear negative samples. Culture positivity of BAL samples was 90.9% as compared to sputum culture positivity which was 26.4%. Overall diagnosis could be established in 86.6% of patients with the help of fiberoptic bronchoscopy.[17]

Arahad Altaf Bachh et al conducted a study on 75 SSN, suspected PTB patients with various bronchoscopic procedures (BW, TBLB, BAL, and PBS). Three pre-bronchoscopic sputum smears were negative for AFB in all patients but culture was positive in 20 patients and this was the only diagnostic feature in 10 patients. BW smear was positive 21 patients. The culture of bronchial washings was positive for AFB in 39 patients. Patients with positive BW smear were positive on culture also. In 29 patients, smear or culture of BW alone contributed to final diagnosis. The PBS yielded AFB in 11 patients. Total yield of bronchoscopy in diagnosis of SSN-PTB was 83.33% (50/60); FOB was the only diagnostic method in 66% (40/60) cases with BW being the only diagnostic method in 48.33%. BW smear for AFB and HPE evidence of caseating granuloma made immediate diagnosis possible in 48.33% (29/60) patients.[18]

Shingal et al reported the diagnostic yield of FOB for PTB as 35.7% (15/42).[19] Sarkar et al made definitive diagnosis in 26 of the 30 (87%) patients.[20] Willcox et al,[21] reported diagnostic yield of 67.4% (89/275) and by Purohit et al[22] of 74% (37/50). Kulpati and Hira found that FOB was diagnostic in 25 of the 33 patients (75.7%).[23] Gracia et al found bronchoscopic methods were diagnostic in 19 of the 20 patients (95%).[24] Chawla et al[25] reported the diagnostic yield of 90% (45/50) and Jaiswal et al[26] of 56% (21/50). Wongthim et al reported diagnostic yield of 63.3 % (71/112).[27] Chan et al reported the diagnostic yield of 85.2% (29/34).[28] Hence the overall yield of FOB in the diagnosis of active PTB among SSN-PTB suspects varies widely from 35.7% to 95% in the literature.

There are several limitations in this study. First, the study population and clinical setting were selective and limited, so it is difficult to generalize this result to other settings. Second, the commonly used TST was not evaluated in our study. This was based on previous studies showing the limitation of TST for evaluating TB in due to BCG vaccination. Third, to improve diagnostic accuracy and ensure safety, a well-trained Pulmonologist is essential. High cost and the complication risk limit the use of FOB in other situations. However, our study demonstrates that FOB can play an important role in the rapid diagnosis of active PTB in SSN-PTB suspects. Fourth, several studies reveal Fluorescence Microscopy (FM) is more sensitive and rapid than ZN for diagnosis of PTB. FM using Light Emitting Diode (LED) in clinical laboratories is recommended.[29,30] Fifth, instead of LJ culture, use of newer molecular diagnostic methods like

Line Probe Assays (LPA), GeneXpert can help in more rapid diagnosis and provide drug susceptibility pattern of tubercle bacilli for detection of drug resistant tuberculosis (DR-TB).

High prevalence settings for TB are often resource-limited and thus offer constraints for the use of FOB. There would be a need for further research on the feasibility and cost-effectiveness of FOB for PTB diagnosis in resource-limited settings before it can be recommended as a useful tool. Involving medical colleges as partners and implementing Public Private Partnership are ways in which big hospitals can cater to the needs of the patients. In such setups, FOB through the RNTCP can be one approach to prevent needless governmental expenditures on TB diagnosis and loss of disability-adjusted life years (DALY) in patients.

CONCLUSIONS: Diagnostic yield of fiberoptic bronchoscopy was 70% in suspected cases of PTB with sputum smear for AFB negative, which makes it a necessary tool in all cases with X-ray suggestive of PTB, it's also a safe procedure considering the minimal complications in our selected cases. Considering FOB under RNTCP for diagnosis of suspected cases of sputum smear negative cases through public private partnership may add to the success of national program.

REFERENCES:

1. Tuberculosis, Surendra.K. Sharma, 2nd ed. 2009, – Laboratory Diagnosis, page 160.
2. Crofton and Douglas's Respiratory Diseases 1, Anthony Seaton, Douglas Seaton, A. Gordon Leitch, 5th edition 2010, Pulmonary Tuberculosis: Clinical Features, page 518-519.
3. Fishman's Pulmonary Diseases and Disorders, volume 2, Fishman Elias, Fishman Grippi, Senior Pack, 4th edition, The Epidemiology, Prevention & Control of Tuberculosis in United States, page 2462.
4. Toman. K, how many bacilli are present in a sputum specimen found positive by smear microscopy? In: Frieden T, Editor- Toman's Tuberculosis Case Detection, Treatment & Monitoring: Questions & Answers, 2nd edition, Geneva: WHO; 2004; page 11-13.
5. RNTCP – Training Module For Medical Practitioners, Central TB Division, Directorate General Of Health Sciences, Ministry Of Health & Family Welfare, New Delhi; Dec- 2010: Page: 16.
6. Willcox P. A, Benatar S. R, Potgieter P. D. Use of Flexible Fiberoptic Bronchoscope in Diagnosis of Sputum Negative Pulmonary Tuberculosis, Thorax, 1982; 37; 598-601.
7. WHO Technical Report Series; No 552; ninth report of WHO Expert Committee on Tuberculosis; Geneva; World Health Organization; 1974.
8. Colebunder R, Bastian I, A review of smear negative pulmonary tuberculosis; International Journal of Tuberculosis and Lung Diseases; 2000; 4: 97-107.
9. Behrr MA, Warren SA, Salmon H, Hopewell PC, Ponce de A, Daley CA et al; Transmission of Mycobacterium Tuberculosis from patients smear- negative for acid fast bacillus; Lancet 1999; 353: 444-9.
10. Rouillon A, Perdrizet S, Parrot R, Transmission of tubercle bacilli: the effects of chemotherapy, Tubercle 1976;57: 275-99.

11. Hong Kong Chest Service/ Tuberculosis Research Centre Madras/ British Medical Research Council, Sputum Smear Negative Tuberculosis, Contrlled clinical trial of 3- months and 2-months regimen of chemotherapy, Lancet 1979, 1: 1361-3.
12. Hong Kong Chest Service/ Tuberculosis Research Centre Madras/ British Medical Research Council, A study of course and characteristics of sputum smear negative pulmonary tuberculosis, Tubercle 1981, 62: 155-67.
13. Narain R, Nair SS, Naganna K, Chandrashekar P, Rao GR, Lal P. Problems in defining a case of pulmonary tuberculosis in prevalence surveys. Bulletin World Health Organization 1968, 39: 701-29.
14. Mohan A, Sharma SK. Fiberoptic bronchoscopy in diagnosis of sputum smear negative pulmonary tuberculosis: current status. Indian Journal of Chest Diseases and Allied Sciences 2008. 50: 67-78.
15. Jung Ar Shin, Yoon Soo Chang1, 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.
16. Saif Quaiser, Anil Agarwal, Ruhi Khan, Shahzad F, Fiberoptic bronchoscopy as a valuable diagnostic option in sputum smear negative pulmonary tuberculosis: a prospective study; International Journal Of Applied & Basic Medical Research; Jul-Dec 2012,Volume 2; Issue 2.
17. Usha Kalawat, Krishna K. Sharma, Prakash N. R. Reddy, and A. Gururaj Kumar, Study of bronchoalveolar lavage in clinically and radiologically suspected cases of pulmonary tuberculosis, Lung India. 2010 Jul-Sep; 27 (3): 122–124, doi: 10.4103/0970-2113.68307.
18. Arahad Altaf Bachh et, Fiber optic bronchoscopy play a significant role in the diagnosing sputum smear negative pulmonary tuberculosis. Lung India; 2010, 220-225.
19. Sameer Singhal, Abhay. M. Use of flexible bronchoscopy for rapid diagnosis of suspected tubercular cases in rural India; J Infect Dev Ctries 2009; 3 (11): 860-864.
20. Sarkar SK, Sharma GS, Gupta PR et al. Fiberoptic bronchoscopy in the diagnosis of pulmonary tuberculosis. Tubercle 1980; 61: 97-99.
21. Willcox PA, Benatar SR, Potgeiter PD. Use of fiberoptic bronchoscope in diagnosis of sputum-negative pulmonary tuberculosis. Thorax 1982; 37: 598-601.
22. Puorhit SD, Sisodia RS, Gupta PR et al: Fiberoptic bronchoscopy in the diagnosis of smear negative pulmonary tuberculosis.Lung India 1983; 1: 143-146.
23. Kulpati DDS, Hira HS. Diagnosis of smear negative pulmonary tuberculosis by flexible fiberoptic bronchoscopy. Indian Journal of Tuberculosis; 1986; 33: 179-82.
24. De Gracia J, Curull V, Vidal R, Riba A, Orriols R, Martin N, et al. Diagnostic value of bronchoalveolar lavage in suspected pulmonary tuberculosis. Chest 1988; 93: 329-32.
25. Chawla R, Pant K, Jaggi OP, Chandrasekhar S, Thukral SS. Fiberoptic bronchoscopy in smear negative pulmonary tuberculosis. Eur Respir J 1988; 1: 804-6.
26. Jaiswal AK, Kulpati DD, Jain NK, Singh MM. Role of bronchoscopy in the early diagnosis of suspected smear negative cases of pulmonary tuberculosis. Indian J Tub 1989; 36: 223-6.

27. Wongthim S, Udompanich V, Limthongkul S, Charoenlap P, Nuchproyoom C. Fiberoptic bronchoscopy in diagnosis of patients with suspected active pulmonary tuberculosis. J Med Assoc Thai 1989; 72: 154-9.
28. Chan HS, Sun HMA, Hoheisel GB. Bronchoscopic aspiration and bronchoalveolar lavage in the diagnosis of sputum smear negative pulmonary tuberculosis. Lung 1990; 168: 215-20.
29. Khatun Z, Kamal M, Roy CK, Sultana T, Rahman MQ, Azad MBAS, Ahmed ANN. Usefulness of Light Emitting Diode (LED) fluorescent microscopy as a tool for rapid and effective method for the diagnosis of pulmonary tuberculosis. Bangladesh Medical Research Council Bulletin. 2011; 37: 7 -10.
30. Laifangbam S, Singh HL, Singh NB, Devi KM, Singh NT. A comparative study of fluorescent microscopy with Ziehl-Neelsen staining and culture for the diagnosis of pulmonary tuberculosis. Kathmandu University Medical Journal (2009), Vol. 7, No. 3, Issue 27, 226-230.

AUTHORS:

1. Rajesh Kumar Jain S.
2. Arun B. J.
3. Paramjyothi G. K.

PARTICULARS OF CONTRIBUTORS:

1. Senior Resident, Department of Pulmonary Medicine, MMCRI, Mysore.
2. Assistant Professor, Department of Pulmonary Medicine, JJMMC, Davanagere.
3. Associate Professor & HOD, Department of Respiratory Medicine, Nizams Institute of Medical Sciences, Hyderabad, Telangana.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Rajesh Kumar Jain S,
398/1, Shivaya Mutt Road,
D. R. Mohalla, Mysore-570024.
E-mail: rajesh2310@gmail.com

Date of Submission: 01/01/2015.
Date of Peer Review: 03/01/2015.
Date of Acceptance: 06/01/2015.
Date of Publishing: 09/01/2015.