

# Smoking/Chest X-Ray Severity Effect on Sputum Culture Conversion in Multi Drug Resistant Tuberculosis Patient

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## Abstract

**Background:** Smoking is a known risk factor for development of active tuberculosis but its effect has not been evaluated well in India. This study was conducted to evaluate the direct effects of cigarette smoking and chest x-ray severity on culture conversion following chemotherapy in patients with multi drug resistant pulmonary tuberculosis (MDR PTB). **Methods:** The prospective observational study was conducted in 97 MDR PTB patients. They were grouped into smokers (Group 1) =41 patients and never smokers (Group 2) = 56 patients. They were followed up upto 6 months and were assessed for the effects of smoking and severity on chest x-ray on sputum culture conversion. **Results:** Out of 97 patients, 38, 42, 53 and 60 patients were culture converted at end of 3rd, 4th, 5th and 6th month respectively. In Group 1 patients culture conversion was significantly ( $p < 0.05$ ) lower than Group 2 at 3rd, 4th, 5th month. Patients with minimal chest x-ray lesions had significantly (0.001) higher culture conversion. Group 1 had significantly (0.02) low culture conversion compared to Group 2 with far advanced chest x-ray lesions at 3rd and 4th month. Patients with cavity had significantly (0.001) low culture conversion. Group 1 had significantly (0.01) low culture conversion compared to Group 2 with cavity at 3rd month. **Conclusion:** Smoking had an adverse effect and was significantly associated with lower culture conversion. Far advanced lesion and presence of cavity on chest x-ray were significantly associated with lower culture conversion. Thus, emphasis on smoking cessation and early detection of MDR PTB in patients may help in better treatment and outcome of the patients.

**Keywords:** Pack Years, Cavitation, Far Advanced Lesion

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**Received:** 07<sup>th</sup> April 2022

**Accepted:** 15<sup>th</sup> December 2022

**How to Cite this Article:** Kumar A, Gupta A, Bhatnagar AK. Smoking/Chest Xray Severity Effect On Sputum Culture Conversion In Multidrugresistant Tuberculosis Patient. J Int Med Sci Acad 2023;36(2):204-207.

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## Introduction

Tuberculosis (TB) is a contagious airborne bacterial infection caused by the organism *Mycobacterium tuberculosis*. Tuberculosis remains a major global health problem mainly due to emergence of drug resistant TB. By definition, resistance to isoniazid and rifampicin is known as Multidrug resistance tuberculosis (MDR-TB). MDR/RR-TB cases in India is estimated as 1, 24,000 (9.1/lakh population). In recent years, tuberculosis has been imposing a major health issue in curing tuberculosis in many countries majorly due to increase in the development of resistance to many drugs which are been used to treat tuberculosis [1].

Tobacco smoking has various hazardous effects on different organs of the body especially in lungs where it causes inflammation and variable fibrosis in peribronchial region along with destructive effects in the epithelial wall and vasculature affecting the alveolar function thus causing abnormalities in permeability of epithelium and vasculature, capacity to filter the pathogens and other inhaled substances. In the development of active tuberculosis, smoking

plays one of the major risk factors specially in India but its effect has yet to be evaluated [2].

This study was conducted to evaluate direct effect of smoking and radiological severity on culture conversion following proper chemotherapy in patients with multi drug resistant pulmonary tuberculosis.

## Materials and Methods

This study was conducted in Department of Respiratory Diseases & Tuberculosis, Rajan Babu Institute for Pulmonary Medicine and Tuberculosis, Delhi and were newly diagnosed of having Rifampicin Resistant/MDR PTB and registered under PMDT during intake period from 1<sup>st</sup> July 2014 to 31<sup>st</sup> July 2015.

The sample size was determined to be 40 by applying two tailed test and using alpha value of 0.05 and beta value of 0.2 considering applicable difference of culture conversion during treatment between smokers (group 1) and never smokers (group 2) to be 30% and taking into account the exclusion criteria.

**Patient Inclusion Criteria**

- All newly diagnosed MDR/Rifampicin resistant Tuberculosis Adult Patient (>18years) in RBIPMT Kingsway camp hospital register under PMDTRNTCP
- All relatively stable and ambulatory patients.
- All patients who were willing to take part in our study and gave informed written consent.

**Patient Exclusion Criteria**

- Pregnant and lactating women
- Patient with co-morbid conditions like HIV seropositivity and diagnosed case of diabetes mellitus, chronic renal, heart or liver disease and IV drug user.
- Patient with history of significant alcohol intake.

**Methodology**

A prospective observational study was performed with approval from institutional ethical committee among newly diagnosed MDR/Rifampicin resistant patients who were enrolled after giving informed consent and their demographic data was noted. Smoking history of patient was taken as per IUATLD/ amended WHO core questionnaire for low-income countries [3] and chest x-ray was done at presentation and were classified as mild, moderately advanced and far advanced [4].

Patients were put on treatment and followed up with sputum culture at 3rd, 4th, 5th and 6th month. They were divided into Group 1 who smoked greater than 100 cigarettes or beedi in their life time and patients who did not have history of smoking or in their lifetime have history of smoking not more than 100 cigarettes or beedi. Patients smoking history, chest x-ray findings and sputum culture conversion [2] were noted and studied for possible correlation among them in patients of newly diagnosed Rifampicin resistant/Multi-Drug resistant pulmonary tuberculosis.

**Statistical Analysis**

SPSS version 21.0 software was used for statistical analysis of the

data. The various risk factors and predisposing conditions were expressed as frequencies and percentages. The data was expressed as mean or median for Continuous variables. Chi-square test was used to compare the data among groups for Nominal categorical data. Significant difference was indicative by using p value to be less than 0.05.

**Results**

Out of 97 patients included in our study, the range was 18 to 63 years for the age with mean (31.7 ± 11.35). 60.8 % (59) were male and 39.2 % (38) were female.

39.2% (38), 43.3% (42), 54.6% (53) and 61.9% (60) of patients had their sputum culture conversion out of the total at the 3<sup>rd</sup>, 4<sup>th</sup>, 5<sup>th</sup> and 6<sup>th</sup> month respectively.

In this study, there was significant (p=0.01) lower culture conversion rate in Group 1 than Group 2 at 3<sup>rd</sup>, 4<sup>th</sup> and 5<sup>th</sup> month. There was no significant (p>0.05) difference in the number (%) of patients who culture converted out of the total number at the end of the months among pack years of smoking at all the time periods as shown in table-1.

As shown in table-2, at the end of the month, the number (%) of patients who culture converted out of the total number were statistically significantly (p=0.001) higher in whom chest x-ray was minimal at all the time intervals. The culture conversion was significantly (p=0.001) lower in patients with cavity on chest x-ray at all the time intervals.

As shown in table-3, patients with cavity on chest x-ray, Group 1 had significantly lower culture conversion at 3<sup>rd</sup> month (0%) as compare to Group 2 (25%) (p value =0.01). In Patients without cavity, culture conversion among Group 1 was low as compare to Group 2 however it was not statistically significant (p value >0.05) at all intervals.

In table-4, patients with far advanced lesions on chest x-ray, Group 1 had lower culture conversion at 3<sup>rd</sup> and 4<sup>th</sup> month as compare to Group 2 (p value =0.02). Among patients with minimal chest x-ray, the culture conversion was also lower in patient with Group 1 as compare to Group 2 but it was not statistically significant.

**Table 1 : Association of No. (%) of patients who converted out of the total no. at the end of the months with smoking habit**

Smoking habit	No. of patients	No. (%) of patients who converted out of the total no. at the end of the months				
		3 <sup>rd</sup> month	4 <sup>th</sup> month	5 <sup>th</sup> month	6 <sup>th</sup> month	
		No. (%)	No. (%)	No. (%)	No. (%)	
Duration of Smoking	Group 1	41 (100)	10 (24.4)	12 (29.3)	17 (41.5)	21 (51.2)
	Group 2	56 (100)	28 (50.0)	30 (53.6)	36 (64.3)	39 (69.6)
p value			0.01	0.01	0.02	0.06
<b>Pack years</b>						
	≤10 pack years	20 (100)	6 (30.0)	7 (35.0)	9 (45.0)	11 (55.0)
	11-20 pack years	15 (100)	3 (20.0)	4 (26.7)	7 (46.7)	8 (53.3)
	>20 pack years	6 (100)	1 (16.7)	1 (16.7)	1 (16.7)	2 (33.3)
P value			0.70	0.66	0.40	0.63

**Table 2: Association of No. (%) of patients who converted out of the total no. at the end of the month with Chest X-ray PA**

Chest X-ray PA		No. of patients	No. (%) of patients who converted out of the total no. at the end of the month			
			3 <sup>rd</sup> month	4 <sup>th</sup> month	5 <sup>th</sup> month	6 <sup>th</sup> month
			No. (%)	No. (%)	No. (%)	No. (%)
Extent of lesion	Minimal	37 (100)	23(62.2)	27(73.0)	32(86.5)	33(89.2)
	Moderate	31 (100)	12(38.7)	12(38.7)	15(48.4)	18(58.1)
	Far advanced	29 (100)	3(10.3)	3(10.3)	6(20.7)	9(31.0)
p value			0.001	0.001	0.001	0.001
Chest X-ray PA		No. of patients	No. (%)	No. (%)	No. (%)	No. (%)
Cavity	Yes	37 (100)	4(10.8)	5(13.5)	9(24.3)	13(35.1)
	No	60 (100)	34(56.7)	37(61.7)	44(73.3)	47(78.3)
p value			0.001	0.001	0.001	0.001

**Table 3: Effect of smoking and cavity on chest x-ray on culture conversion out of total no. at end of the months**

Cavity on chest x ray	Smoking	No. of patients	No. of patients who converted out of the total no. at the end of the month			
			3 <sup>rd</sup> month	4 <sup>th</sup> month	5 <sup>th</sup> month	6 <sup>th</sup> month
			No. (%)	No. (%)	No. (%)	No. (%)
Yes	Group 1	21	0 (0.0)	1 (4.8)	5 (23.8)	8 (38.1)
	Group 2	16	4 (25.0)	4 (25.0)	4 (25.0)	5 (31.2)
	p value		0.01	0.07	0.93	0.66
No	Group 1	20	10 (50.0)	11 (55.0)	12 (60.0)	13 (65.0)
	Group 2	40	24 (60.0)	25 (65.0)	32 (80.0)	34 (85.0)
	p value		0.46	0.45	0.09	0.07

**Table 4: Effect of smoking and chest x-ray on culture conversion out of total no. at end of the months**

Extent of lesion on chest x-ray	Smoking	No. of patients	No. of patients who converted out of the total no. at the end of the month			
			3 <sup>rd</sup> month	4 <sup>th</sup> month	5 <sup>th</sup> month	6 <sup>th</sup> month
			No. (%)	No. (%)	No. (%)	No. (%)
Minimal	Group 1	7	4 (57.1)	5 (71.4)	5 (71.4)	5 (71.4)
	Group 2	30	19 (63.3)	22 (73.3)	27 (90.0)	28 (93.3)
	p-value		0.76	0.91	0.19	0.09
Moderate	Group 1	17	6 (35.3)	7 (41.2)	9 (52.9)	11 (64.7)
	Group 2	14	6 (42.9)	5 (35.7)	6 (42.9)	7 (50.0)
	p-value		0.66	0.75	0.57	0.40
Far Advanced	Group 1	17	0 (0.0)	0 (0.0)	3 (17.6)	5 (29.4)
	Group 2	12	3 (25.0)	3 (25.0)	3 (25.0)	4 (33.3)
	p-value		0.02	0.02	0.63	0.82

## Discussion

This study was done at Rajan Babu Institute for Pulmonary Medicine and Tuberculosis, a tertiary level institute & DR-TB centre in Delhi.

The study group consisted of 97 patients who were diagnosed MDR/RR-TB irrespective of gender, who satisfied the inclusion and exclusion criteria and gave informed and written consent. Among 97 patients 41 had smoked (group 1) and 56 patients were never smoker (group 2).

On chest x-ray, patients with minimal lesion were 38.1% [37], moderate 32% [31] and far advanced lesions were 29.9% [29]. Pazarli P et al [5] also found extensive radiological involvement in 21.4% of cases.

In group 2 patients, 20.6% [20] had smoked <10 pack years and 21.7% [21] had smoked >10 pack years. In the patient with history of smoking >10 pack years of cigarettes was significantly associated with far advanced lesion on chest x-ray. It suggests that smoking causes cumulative lung damage of MDR-TB patients. Thus, smoking can affect the disease progression in MDR-TB patients if

it is responsible for the quicker advancement of MDR-TB lesions and patients present with far advanced lesions when they are smoking.

In this study, 38.1% [37] of cases had cavity on the chest x-ray. In study done by Magee MJ et al<sup>6</sup> 26.9% of non-diabetic patients had lung cavity. Because lungs cavities are efficiently aerosolized, cavities contain large numbers of bacilli which have advantage to the spread of *M. tuberculosis*.

Cavity was present only in 28.6% of group 2 where as 51.2% in group 1. Presence of cavity was more significantly associated with Group 1 than Group 2.

As discussed before, smoking decreases lung defense which may lead to increased damage during pulmonary infection and subsequent cavity formation.

In this study 38, 42, 53, 60 patients had Culture conversion at 3<sup>rd</sup>, 4<sup>th</sup>, 5<sup>th</sup>, and 6<sup>th</sup>, month respectively. Majority of the patients [63.33% (38 of 60)] had culture converted within first 3 months which is similar to the study done by Jain K. et al [7] where 82% of sputum culture converted patients achieved it by first 3 months. This may be explained by the fact that patients detected as DR-TB under the national programme are often on anti-TB therapy at the time of diagnosis and due to prior treatment, the bacillary load is less.

The fraction of Group 1 patients who converted was significantly lower than Group 2 at 3<sup>rd</sup>, (24.4% vs 50%) [p value-0.01], 4<sup>th</sup> (29.3% vs 53.6%) [p value-0.01], 5<sup>th</sup> (41.5% vs 64.3%) [value 0.02] month. In study done by Magee M.J. [7] current smokers had 65.2% conversion as compare to 75.5% in those who do not currently smoke. Due to various organic compounds in the cigarette smoke which can have adversely affect the enzymes which help in drug metabolism thus may cause delay in sputum culture conversion, hence may cause unfavorable effects on drug pharmacokinetics and proper treatment and management [8]. Cigarette smoking is a nitric oxide synthase (NOS) inhibitor [9]. For the defense mechanism in response to the intracellular organism, nitric oxide (NO) plays a major role. Further, activated macrophages that are involved in the defense against *M. tuberculosis* express nitric oxide synthase (NOS). Thus, smoking decreases multiplication/killing of bacilli and it may delay clearance of multiplying bacilli and thereby culture conversion.

The culture conversion of patients with far advanced chest x-ray findings were 10.3% (3), 10.3% (3), 20.7% (6), 31.0% (9) compared to 89.7% (35), 89.7% (35), 79.3% (39) and 69% (47) in patients with minimal to moderate-ray findings at 3<sup>rd</sup>, 4<sup>th</sup>, 5<sup>th</sup> and 6<sup>th</sup> respectively. The findings were statistically significant (p value-0.001). From this it is seen that smoking status and x-ray changes both influence culture conversion. This shows that even in patients with Far Advanced x-ray, exposure to tobacco smoke was an independent factor in Delayed culture conversion.

The culture conversion of patients with cavity on chest x-ray were 10.8% (4), 13.5% (5), 24.3% (9) and 35.1% (13), which were significantly (p value- 0.001) lower and were 56.7% (34), 61.7% (37), 73.3% (44) and 78.3% (47) in patients without cavity at 3<sup>rd</sup>, 4<sup>th</sup>, 5<sup>th</sup> and 6<sup>th</sup> respectively. From this it is seen that smoking status and cavity both influence culture conversion.

To evaluate whether smoking has independent adverse effect from cavity, Group 1 and Group 2 patients with cavity were compared. Out of 37 patients with cavity, 21 patients who were in group 1- 0.0% (0) and 4.8% (1) converted as compared to 16 patients of group 2 where 25% (4) and 25% (4) at 3<sup>rd</sup> month and 4<sup>th</sup> month

respectively had converted which was significantly lower (p value- 0.01 at 3<sup>rd</sup> month and 0.07 at 4<sup>th</sup> month). This shows that even in patients with cavity, smoking was an independent factor in delayed culture conversion.

This may be explained by the fact that iron content of alveolar macrophages among smokers is about twice that of non-smoker [10]. In presence of excess iron levels, harmful radicals are released when there is interaction between iron sulfur clusters and NO in enzymes which may cause impairment in the functioning of alveolar macrophages due to intracellular proteins which may get damaged, thus smoking may act as an independent risk factor for delayed culture conversion.

## Conclusion

Smoking independently and cavitation and far advanced lesions on chest x-ray with smoking history were associated with delayed culture conversion in patients of multidrug resistant tuberculosis. Thus, it's imperative that an active early case detection of multidrug resistant tuberculosis in suspected patients and counseling for smoking cessation may help in early sputum culture conversion and thus may lead to better outcome.

<b>Conflict of Interest:</b>	All authors declare no COI
<b>Ethics:</b>	There is no ethical violation as it is based on voluntary anonymous interviews
<b>Funding:</b>	No external funding
<b>Guarantor:</b>	Dr. Ankita Gupta will act as guarantor of this article on behalf of all co-authors.

## References

1. *Guidelines for Programmatic Management of Drug Resistant Tuberculosis in India.* Available from- <https://tbcindia.gov.in/showfile.php?lid=3590>.
2. Aubry M C, Wright J L, Myers J L. *The pathology of smoking- related lung diseases.* Clin Chest Med 2000; 21:11–35.
3. *Tobacco control and prevention a guide for low income countries.* International Union Against Tuberculosis and Lung disease (IUATLD) 1998.
4. *National Tuberculosis Association of USA. Diagnostic standard and classification of tuberculosis.* New York, 1961;(11thed) :14-43.
5. Pazarlı P., Duman D.Y., Moçin O.Y., et al. *The Effect of Smoking on Treatment Outcome of Multidrug-Resistant Tuberculosis.* Turk ToraksDerg 2013;14:93-7.
6. Magee MJ, Kempker RR, Kipiani M, et al. *Diabetes mellitus, smoking status, and rate of sputum culture conversion in patients with multidrug-resistant tuberculosis: a cohort study from the country of georgia.* PLoS One. 2014 Apr 15;9(4):e94890.
7. Jain K, Desai M, Solanki R, et al. *Treatment outcome of standardized regimen in patients with multidrug resistant tuberculosis.* Journal of Pharmacology and Pharmacotherapeutics. 2014;5(2):145.
8. O'Malley M, King AN, Conte M, et al. *Effects of cigarette smoking on metabolism and effectiveness of systemic therapy for lung cancer.* J ThoracOncol. 2014 Jul;9(7):917-26.
9. Chan J, Xing Y, Magliozzo RS, et al. *Killing of virulent Mycobacterium tuberculosis by reactive nitrogen intermediates produced by activated murine macrophages.* J Exp Med 1992;175:1111e22.
10. Mateos F, Brock JH, Pérez-Arellano JL. *Iron metabolism in the lower respiratory tract.* Thorax 1998;53:594e600.

