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Original Research Article

"A STUDY ON SPUTUM INDUCTION IN THE DIAGNOSIS OF SMEAR NEGATIVE OR SPUTUM -SCARCE PRESUMPTIVE TUBERCULOSIS IN HIV PATIENTS IN A TERTIARY CARE CENTER"

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ABSTRACT:

Background: HIV infection and TB are two major public health problems in most of the developing countries including India. TB also the most common opportunistic infection seen in HIV infected patients in India 1,2. Tuberculosis is a significant increase in the worldwide incidence of TB which is contributed majorly by HIV infection.

AIM: To study the role of Sputum Induction to aid in the diagnosis of Smear Negative or Sputum Scare Presumptive Pulmonary Tuberculosis in adults with HIV.

OBJECTIVES:

1. By doing the Sputum Induction using the Hypertonic Saline Nebulisation
2. Performing the AFB Direct Smear and CBNAAT tests in that Induced Sputum sample.

MATERIAL & METHODS: Study Design: Prospective hospital based observational study. **Study area:** The present study was conducted in the department of TB & Respiratory medicine, Osmania Medical College, Hyderabad. **Study Period:** Mar. 2021 – Feb. 2022. **Study population:** The subjects of the study were selected among the HIV positive with Presumptive Pulmonary Tuberculosis patients who visited the outpatient department or had been admitted in our hospital who agreed for voluntary participation **Sample size:** A total of 50 Presumptive Pulmonary Tuberculosis with HIV co- infection were taken as sample size. **Sampling method:** Simple random Sampling Technique.

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Results: In the present study 74% of cases were having scarce sputum & 26% of cases were having smear negative samples where the sputum specimen acquisition by sputum Induction needed for diagnosis of Pulmonary Tuberculosis.

CONCLUSION: Sputum induction is a safe, simple and valuable procedure to obtain adequate sputum samples in suspected cases of pulmonary tuberculosis and can obviate the need for much sophisticated and invasive procedures like bronchoscopy. Sputum induction improves the diagnostic yield for AFB in patients unable to expectorate adequate sputum sample.

Keywords: SPUTUM INDUCTION, SPUTUM -SCARCE PRESUMPTIVE TUBERCULOSIS, Cursed Duet

INTRODUCTION:

HIV infection and TB are two major public health problems in most of the developing countries including India. TB also the most common opportunistic infection seen in HIV infected patients in India [1,2]. Tuberculosis is a significant increase in the worldwide incidence of TB which is contributed majorly by HIV infection. Dual epidemic of HIV and TB (HIV-TB) is a concern for India where these are prevalent in epidemic proportions[3]. Although HIV related tuberculosis is both treatable and preventable, incidence rates continue to increase in developing nations where HIV infection and Tuberculosis are endemic and resources are limited. TB and HIV are intricately linked to Malnutrition, Drug abuse, Alcoholism, Poverty, Homelessness[4]. Cost of both these diseases are enormous, estimated to be more than 30% of the annual household income of the developing nations and have a deep impact on the economy of the developing world[5]. HIV-TB is not only a medical malady but social and economic disaster and aptly described as "Cursed Duet" [6].

One third of the people living with HIV worldwide are infected with latent TB[7]. 1.1 million HIV positive new TB cases were reported globally in 2018. People living with HIV are 18(15-21) times more likely to develop TB than persons without HIV[8].

TB can occur at any stage of HIV disease and any CD4 count, although median CD4 count range from 150-300 cells/$\mu\ell$[9]. TB from latent infection to disease progresses faster in HIV infected people.

Presentation of TB is same in both HIV positive and negative cases during early stages. But in late stages extra pulmonary and disseminated form become more common. The presentation of the disease is related to the level of immune suppression of the patient[10].

The diagnosis of patients suspected of tuberculosis (TB) who are sputum smear-negative for acid-fast bacilli or who are unable to produce sputum (sputum scarce) is a daily challenge for clinicians in HIV-endemic settings. In developing countries facing the dual epidemics of TB and HIV, the burden of smear-negative or sputum-scarce TB is large and accounts for approximately every second notified TB case.

Sputum induction, performed using the ultrasonic nebulisation of hypertonic saline, is a relatively simple and safe procedure suitable for use in resource-limited decentralised settings. Induction has been shown to offer similar TB case detection rates to more invasive techiques such as bronchoscopy as an aid to TB diagnosis. It has shown particular utility for

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diagnostic sampling in children and for TB screening in asymptomatic patients prior to the initiation of antiretroviral.

AIM: To study the role of Sputum Induction to aid in the diagnosis of Smear Negative or Sputum Scare Presumptive Pulmonary Tuberculosis in adults with HIV.

OBJECTIVES:

1. By doing the Sputum Induction using the Hypertonic Saline Nebulisation
2. Performing the AFB Direct Smear and CBNAAT tests in that Induced Sputum sample.

MATERIAL & METHODS:

Study Design: Prospective hospital based observational study.

Study area: The present study was conducted in the department of TB & Respiratory medicine, Osmania Medical College, Hyderabad.

Study Period: Mar. 2021 – Feb. 2022.

Study population: The subjects of the study were selected among the HIV positive with Presumptive Pulmonary Tuberculosis patients who visited the outpatient department or had been admitted in our hospital who agreed for voluntary participation

Sample size: A total of 50 Presumptive Pulmonary Tuberculosis with HIV co- infection were taken as sample size.

Sampling method: Simple random Sampling Technique.

Inclusion criteria:

1. Aged >18 years.
2. HIV reactive with smear negative or sputum scarce presumptive pulmonary tuberculosis patients.
3. Able and willing to give written informed consent (or a relative or carer is able and willing to give informed consent).

Exclusion criteria:

1.Those who did not meet the inclusion criteria.

2. Alternative diagnosis like possible Pneumocystis jiroveci infection or Malignancy were excluded.

3. Participation in another study within 30 days.

Ethical consideration: Institutional Ethical committee permission was taken prior to the commencement of the study.

Study tools and Data collection procedure:

Patients included in the study were selected according to the inclusion and exclusion criteria. After taking the written consent of the patient, detailed history of present and past illness was recorded. Thorough clinical examination was done.

All necessary investigations were carried out.

1. Chest X-ray PA view/ CT chest
2. CD4+ count
3. Sputum AFB stain microscopy & Sputum CBNAAT
4. Induced Sputum sample- AFB Stain Microscopy & Sputum CBNAAT

(Sputum Induction Procedure: Sputum Induction was performed by using the Hypertonic Saline Nebulisation and Induced Sputum sample could be collected)

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Statistical analysis:

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Results with a p value of <0.05 was considered statistically significant.

OBSERVATIONS & RESULTS:

TABLE 1: AGE DISTRIBUTION IN THE STUDY

Age	Frequency (n=50)	Percent
21 – 30	9	18.0
31 – 40	19	38.0
41 – 50	17	34.0
> 50	5	10.0
Total	**50**	**100.0**

The majority of cases (38 %) were in the age group of 31-40 yrs. Mean age of the study group population is 39.76 ± 9.24.

TABLE 2: GENDER DISTRIBUTION IN IP & OP PATIENT

Sex	IP		OP		Total	
	Count	%	Count	%	Count	%
Female	13	32.5%	3	30.0%	16	32.0%
Male	27	67.5%	7	70.0%	34	68.0%
Total	40	100.0%	10	100.0%	50	100.0%
P-value = 0.60						

In the present study males (68%) were more than females.

TABLE 3: CLINICAL FEATURES

Symptoms	Frequency (n=50)	Percent
Cough	42	84.0
SOB	33	66.0
Chest pain	8	16.0
FEVER	43	86.0
Loss of appetite	46	92.0
Loss of weight	45	90.0

The predominant symptom in the present study was loss of appetite.

Out of 50 patients 34% (17 patients) were known Diabetic and 10% (5 patients) were known Hypertensive. Most of the patients in my study are smokers (40%).

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TABLE 4: CD4 COUNT IN IP & OP PATIENTS

CD4 Count	Minimum	Maximum	Mean
	31.0	655.0	182.68

	IP		OP		P-value
	Mean	SD	Mean	SD	
Age	39.95	10.13	39.00	4.50	0.78
CD4 count	180.45	142.49	191.60	59.56	0.81

The mean CD4 count in the present study is 182.68.

Majority (72%) of patients in the present study did not have previous history of TB.

On General examination majority of the patients had Lymphadenopathy.

TABLE 5: REASON FOR SPUTUM INDUCTION

Reason for sputum induction	Frequency	Percent
Sputum- Scarce	37	74.0
Sputum AFB smear & Sputum CBNAAT - Negative	13	26.0

In the present study 74% of cases were having scarce sputum & 26% of cases were having smear negative samples where the sputum specimen acquisition by sputum Induction needed for diagnosis of Pulmonary Tuberculosis.

TABLE 6: SPUTUM INDUCTION SAMPLING OUTCOMES IN IP & OP CASES

Sampling outcomes	IP		OP		Scare		Negative	
	Count	%	Count	%	Count	%	Count	%
Adequate	37	92.5%	8	80.0%	32	71.1%	13	28.9%
Failed	1	2.5%	1	10.0%	2	100.0%	0	0.0%
Insufficient	2	5.0%	1	10.0%	3	100.0%	0	0.0%
P-value	0.045				0.038			

TABLE 7: INDUCED SPUTUM AFB

Induced sputum AFB	Frequency (n=45)	Percent
Negative	40	89.0
Positive	5	11.0
Total	45	100

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Out of 45 adequate Induced sputum cases, 89% (40 cases) were Negative for Sputum AFB and whereas 11% (5 cases) were Positive for Sputum AFB.

TABLE 8: INDUCED SPUTUM CBNAAT

Induced sputum CBNAAT	Frequency(n=45)	Percent
MTB not detected	34	76.0
MTB detected	11	24.0
Total	45	100.0

Out of 45 adequate Induced sputum cases, 76% (34 cases) were MTB not detected by CBNAAT and where as 24% (11 cases) MTB was detected by CBNAAT.

DISCUSSION:

HIV is one of the risk factor for TB. Direct sputum smear microscopy remains a fundamental tool of TB diagnosis but it may be negative in 50% of active TB cases. In developing countries facing dual epidemics of TB & HIV, the burden of smear-negative or sputum scarce TB is large. In this scenario, sputum induction facilitates microbiological confirmation of TB, as well as drug susceptibility testing.

In the present study mean age for HIV-PTB co-infection was 39.76. Maximum range of age is 31- 40 yrs (38%). Minimum age of 23 yrs & Maximum age of 65 yrs. Christopher C et al [11] reported mean age was 40yrs & highest prevalent age is 30-39yrs (38%) which was comparable to present study. A study by Purushottam Giri et al [12] reported mean age of 38.1yrs & highest prevalent age was 30-40 yrs (34.30%) which was in accordance to present study. A study by Jonathan G. Peter et al [13] reported mean age is 40 yrs & highest prevalent age is 30-53 yrs. (70%).

A study by Yvana Maria et al [14] reported mean age was 33.5 yrs & highest prevalent age was 20-53 yrs (39.30%). A study by Maria de Fátima et al [15] reported mean age was 30 yrs & highest prevalent age was 15-34 yrs (59%). A study by Mahesha Padyana et al [16] reported mean age was 37.4 yrs & highest prevalent age is 31-40 yrs. (59%). A study by Henry DN Nyamogoba et al [17] reported mean age was 30 yrs & highest prevalent age was 25-34 yrs (40.9%).

In the present study male predominance was observed with males (68 %) and females (32 %) giving a male to female ratio of 2.12. A study by Henry DN Nyamogoba et al [17] male predominance was observed with 55.4 % males and 44.5% females. A study by Yvana Maria et al [14] male predominance was observed with 52.4% males and 47.6% females. A study by Purushottam A Giri et al [12] reported 50.58 % males and 49.42%females. A study by Jonathan G. Peter et al [13] reported 52.4% males and 47.6% females. A study by Christopher C. et al [11] reported 43 % males and 57 % females.

In the present study most common symptom is loss of appetite in 92% of patients followed by loss of weight (90%), fever (86%), cough (84%), shortness of breath (66%) and chest pain (16%). Christopher C. et al study [11] shows loss of weight (96.4) as a most common constitutional symptom and cough (83.9 %) as a most common specific symptom. Yvana Maria et al study [14] shows fever (85.7) as a most common constitutional symptom and cough (81%) as a most common specific symptom.

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In the present study most of the patients are having diabetes (34%) followed by hypertension (17%). In a study by Gomes et al [18] diabetes was present in 4 % patients. In a study by Gounden et al [19] diabetes was present in 10 % patients. Poverty, smoking, alcoholism, HIV-1 and DM are known drivers of the TB epidemics. Incidence of TB is greatest among patients with impaired immunity. Both HIV and DM are strongly associated with immuno suppression resulting in impaired phagocytosis and cellular immunity.

In the present study most of the patients are smokers (40%) followed by alcohol addiction (38%). In a study by Gounden et al [19] alcoholics & smokers was seen 63.2 % of patients. In a study by Fiske et al [20] 20.3% were Alcoholics.

In the present study minimum CD4 count is 31 & maximum being 655 with the mean CD4 count is 182.68. In a study by Jonathan G. Peter et al [13] mean CD4 count was 155. In a study by Lusiba et al [21] mean CD4 count was 154. In a study by Christopher C. et al [11] mean CD4 count was 150.6. In a study by Aurobindo Behera et al [22] mean CD4 count was 173.33. In a study by Yvana Maria [14] mean CD4 count was 216.

In the present study 74% of cases were having scarce sputum & 26% of cases were having smear negative samples. In a study by Jonathan G. peter et al [13] 74% of cases were having scarce sputum & 26% of cases were having smear negative samples. In a study by C. M. Parry C [23] et al study 65 % of cases was having scarce sputum & 35 % of cases were having smear negative samples.

In the present study 90 % of induced samples were adequate which is comparable to a study by Jonathan G. peter et al [13], where it was 82.3%. In the present study 10 % of cases had failed sputum induction & insufficient sputum production after induction. In a study by Jonathan G. peter et al [13] 17.7 % of cases had failed sputum induction & insufficient sputum production after induction.

In a study by C. M. Parry C. et al [23] 89 % of induced samples were adequate & 11% of cases had failed sputum induction & insufficient sputum production after induction. In a study by Muhammad et al [24] 80.48% of induced samples were adequate & 19.5% of cases had failed sputum induction & insufficient sputum production after induction.

In the present study 11 % of induced sputum cases were Positive Sputum AFB microscopy where as 89% of induced sputum cases were Negative for Sputum AFB microscopy. In a study by C. M. Parry C. et al [23] 76 % of induced sputum cases were Negative for Sputum AFB microscopy where as 24 % of induced sputum cases were Positive Sputum AFB microscopy.

In a study by M. Morse et al [25] 68% of induced sputum cases were Negative for Sputum AFB microscopy where as 32 % of induced sputum cases were Positive Sputum AFB microscopy. In a study by Muhammad et al [24] 78.79% of induced sputum cases were Negative for Sputum AFB microscopy where as 21.21% of induced sputum cases were Positive Sputum AFB microscopy. In a study by Jonathan G. peter et al [13] 15% of sputum induced cases were culture positive.

In the present study 24 % of Induced sputum cases were MTB detected by CBNAAT and where as 76 % cases MTB not detected by CBNAAT. A study by Prem Prakash Gupta et al reported 17% cases MTB was detected by CBNAAT. A study by R Dewan et al reported 17% cases MTB was detected by CBNAAT.

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CONCLUSION:

Sputum induction is a safe, simple and valuable procedure to obtain adequate sputum samples in suspected cases of pulmonary tuberculosis and can obviate the need for much sophisticated and invasive procedures like bronchoscopy. Sputum induction improves the diagnostic yield for AFB in patients unable to expectorate adequate sputum sample.

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