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Microbiology

DRUG SUSCEPTIBILITY PROFILE OF TUBERCULOSIS IN HIV INFECTED INDIVIDUALS

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ABSTRACT **Background:** In many parts of the world, tuberculosis is the most frequent and dangerous opportunistic infection that affects persons with HIV (TB). The HIV-positive population is particularly prone to catching TB due to overlapping risk groups and a generally greater risk of developing TB disease due to more evident immunodeficiency. MTB and HIV coinfection is thus rising in frequency. Drug-resistant tuberculosis, in particular, continues to be a severe concern to public health (MDR-TB). The deleterious effects of TB in PLHIV can be significantly reduced by early diagnosis, efficient TB treatment, timely connection to HIV care, and early commencement of ART. **Methods:** Study was Prospective and Observational conducted in tertiary care hospital, during a period of Jan 2021 to June 2022. Ethical clearance was received from the Ethical Committee of institution. Inclusion criteria: All HIV positive individual with MDR TB and EPTB. **Exclusion criteria:** HIV negative MDR TB. A total of 260 HIV positive samples from ART OPD patients in tertiary care hospitals underwent 4S screening for TB, or screening for 4 TB symptoms (adults: fever, cough, weight loss, night sweats; children: fever, cough, poor weight gain/reported weight loss, h/o contact with a TB case). Following screening of these HIV positive patient, pulmonary and extrapulmonary samples were sent to TB lab & drug susceptibility profile was studied. **Results:** Out of 260 HIV positive samples MTB was detected in 50 (19.23%) samples, (i.e., 31 AFB smear positive & 19 CBNAAT positive). Total number of samples tested by First line LPA are 37 (31 AFB smear positive + 6 Culture positive) of which 31 were sensitive to both INH and Rifampin & 6 were sensitive to INH but resistant to Rifampin. These 6 samples were tested by Second Line LPA having susceptibility pattern as, 4 samples were sensitive to both FQs and SLIDs, 1sample was resistant to FQs but sensitive to SLIDs and 1 sample showed sensitive to FQs and resistant to SLIDs. **Conclusion:** HIV infection may not be linked to drug-resistant tuberculosis, as evidenced by the lower prevalence of drug-resistant M. tuberculosis isolates among HIV seropositive tuberculosis patients in our tertiary care hospital.

KEYWORDS : Tuberculosis, HIV infected individuals, drug susceptibility.

INTRODUCTION

TB is a contagious illness that significantly contributes to ill health and is one of the leading causes of death worldwide. Tuberculosis (TB) has surpassed HIV/AIDS as the most prevalent infectious cause of mortality prior to the coronavirus (Covid-19) epidemic. The estimated number of PLHIV in India is 2.3 million, and the adult population's overall HIV prevalence is 0.22%.[1]

It is still unclear exactly how HIV infection and the emergence of MDR-TB are related. Whether HIV infection is a standalone risk factor for the emergence of MDR-TB is one of the most significant unanswered concerns. Numerous studies have revealed that people with HIV experience higher rates of drug-resistant TB.[2] In addition to being the main cause of death for HIV-positive individuals, TB also significantly increases the risk of developing antibiotic resistance [3]. MDR-TB outbreaks in HIV infected individuals are a result of the accelerating and amplifying effects of HIV infection as well as the delayed recognition and diagnosis of tuberculosis.[4] Due to the challenges of adhering to polypharmacy, overlap in the adverse effects of antituberculosis and antiretroviral medications, immune reconstitution inflammatory syndrome, and drug-drug interactions, treating tuberculosis and HIV at the same time is challenging. There is a considerable danger of using inadequate treatment regimens with a small number of active medications when susceptibility patterns are unavailable and patients are treated empirically. This could result in the development of drug resistance.

AIMS AND OBJECTIVES

Drug susceptibility profile of tuberculosis in HIV infected individuals

MATERIALS AND METHODS

This is a prospective and observational study conducted at Department of microbiology from January 2021 to June 2022. Total number of samples studied were 260.

- **Inclusion criteria**:

All HIV positive individual with MDR TB and EPTB.

- **Exclusion criteria:** HIV negative MDR TB.

SAMPLE COLLECTION:

After pretest counselling and obtaining informed consent, blood was drawn for HIV testing following all aseptic precautions from patients coming to ART OPD. Following NACO guidelines these samples were tested by Rapid test which detect Antibodies against HIV 1 & HIV 2. Three different test kits of three different principle were used for HIV testing & confirmation of positive results. These are

1) COMBAIDS : Principle → Immuno dot Assay
2) MERISCREEN : Principle →Immuno chromatography
3) **SIGNAL** : Principle →immuno dot Assay

Samples reactive to HIV after 4S screening of TB (i.e., Cough, Weight loss, Night sweats & Fever) were sent to TB Lab. Three sputum samples were collected from each patient, either 2 on the spot samples with one early morning sample.

Specimen decontamination: When the sample is received in the laboratory it is decontaminated by equal amount of fresh NALC-NaOH-sodium citrate working solution.

PROCESSING OF SAMPLE:

- **Microscopy:**

Microscopy was done to diagnose pulmonary tuberculosis from sputum sample [5]. For microscopy smear were prepared in the biosafety cabinet. Let it air dry and then shifted to the room where Flourescent staining was to be done. All the smears were scanned by Z Technique and grading was done according to the guidelines provided by the RNTCP. Reporting of the smear microscopy is done on the same day.

- **LPA (Line Probe assay):** All smear positive samples were subjected to LPA.

- **Xpert MTB/RIF:**

The smear negative sputum samples or grade scanty samples by microscopy and EP samples were processed by Xpert MTB/RIF assay. The results were available in approximately 2 hrs. The results were displayed on computer in graphical form. Depending upon the

bacillary load the computer displayed the report as MTB detected high/medium/low and the presence or absence of RIF resistance.

- **CULTURE:**

All extra pulmonary samples were inoculated on the LJ media in the biosafety cabinets.

Culture on LJ Media: Two LJ media kept at 37 ^{0}C (one wrapped and other unwrapped) One at 45 ^{0}C and one at room temperature. Samples were simultaneously inoculated on the LJ containing NaCl, PNB and on the Mac Conkey agar. Slopes were observed for presence of growth every day till first week and then every week till 8 weeks.

RESULTS AND DISCUSSION

A total of 260 HIV positive samples from patients attending ART OPD of Tertiary care hospital, were undergone 4S screening of TB i.e., 4 symptom screening for TB (Adults: fever, cough, weight loss, night sweats; Children: fever, cough, poor weight gain/reported weight loss, h/o contact with a TB case). Following screening of HIV patients, samples were sent to TB lab & drug susceptibility profile was studied.

Smear was prepared from all the samples & stained by Auramine rhodamine stain and examined under fluorescent microscope. Among these 31 (11.9%) samples were Smear positive & 229 (88.1%) were smear negative. (Table 1)

Table – 1: Distribution of smear positive & smear negative patients among HIV reactive patients:

Total no of samples of HIV patients	Smear Positive	Smear Negative
260	31 (11.9%)	229 (88.1%)

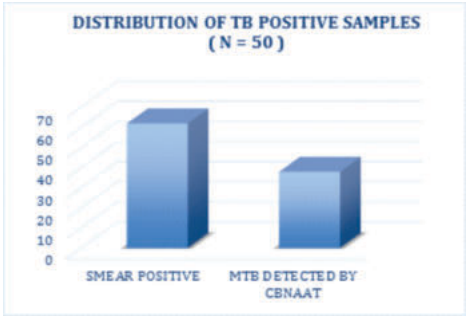
Total 206 samples were tested by CBNAAT among which MTB was detected in 19 (9.23%) samples & MTB was not detected in 187 (90.77%). (Table 2)

Table - 2: Distribution of samples tested by CBNAAT in HIV reactive patients:

Total no of samples	MTB detected	MTB not detected
206	19 (9.23%)	187 (90.77%)

Total number of samples which were positive for TB were 50 of which 31 (62%) were smear positive and 19 (38%) were detected by CBNAAT. (Fig 1)

Fig 1: Distribution of TB positive samples:



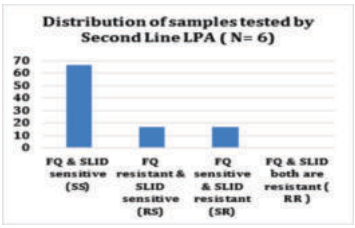
Total number of samples tested by First Line LPA were 37 of which 31 were smear positive samples and 6 were Culture positive samples. Their susceptibility pattern is shown below. (Table 3)

Table – 3: Distribution of samples tested by first line LPA:

Total no of samples for first line LPA	37
INH & Rifampin are sensitive (SS)	31 (83.78 %)
INH is sensitive &Rifampin is resistant (SR)	6 (16.22 %)
INH & Rifampin resistant (RR)	0
INH is resistant & Rifampin sensitive (RS)	0

Samples which were Rifampin resistant on First Line LPA were tested by Second Line LPA. 6 samples which were tested by second line, 4 samples were sensitive to both FQ and SLID, 1 sample was FQ resistant and SLID sensitive ,1 sample was FQ sensitive and SLID resistant as shown in fig -2

Fig -2: Distribution of samples by second line LPA:



Drug susceptibility profile of HIV reactive patients is shown below. (Table 4)

Table -4: Distribution of drug susceptibility profile in HIV reactive patients:

TYPE OF DRUG RESISTANCE	TOTAL NO OF PATIENT	PERCENTAGE (%)
DRUG SUSCEPTIBLE TB	42	84
MONORESISTANT TB	6	12
MDR – TB	1	2
Pre – XDR TB	1	2

DISCUSSION

In our study we evaluated 260 HIV reactive samples for diagnosis of TB, in which we got 31 (11.9%) samples smear positive and 229 (88.1 %) samples were smear negative which is approximately similar to study documented by Hind Satti et al [6] which reported smear positive of 8.51% and smear negative as 91.49 %. Petros Isaakidis et al [7] also conducted study among adults attending the ART centres and found that percentage of smear positive as (5.2 %) which is comparatively less than our study and percentage of smear negative as (95.80 %) which is greater than our study.

Hariom Gupta [8] conducted prospective study on 160 samples which were tested by CBNAAT showing positivity 72 (45%) which is comparatively higher than our study (9.23 %). R Dewanetal [8] documented study showing positivity of (40%) which is also higher than our study. Shilpa [9] conducted study of the 502 smear negative samples, of which 63 (12.5%) were detected as TB positive by CBNAAT which is similar with our study (9.23 %).

HIV infection has been identified as a significant risk factor for drug-resistant TB in settings characterised by relatively low TB case rates and focal ongoing outbreaks of MDR-TB among specific HIV-infected subgroups (e.g., hospitalised patients, prisoners, substance abusers) [10–13].As people with HIV infection are more prone to develop new infections, the increased prevalence of MDR-TB in this group may point to more recent transmission of drug-resistant strains as opposed to reactivation of infection acquired in the distant past in the non-HIV-infected population[14].

In our study drug susceptibility pattern was studied in which indicates Monoresistance as (12%) which is similar as that of H Gautam et al [4] (12.3 %). Petros Isaakidis et al [7] also documented the Monoresistance of 16.2% which is slightly higher than our study . In our study MDR was found to be 2% which is lower as compared to H Gautam et al [4] (26.7 %) and Petros Isaakidis et al [7] (38.2%). However, MDR prevalence is slightly greater in C N Deivanayagam [15](4.42 %). In our study Pre -XDR prevalence was found to be 2% which is lower as compared to Petros Isaakidis et al [7](20.6%) and H Gautam et al [4](6.7 %).

CONCLUSION

The pattern of first- and second-line anti-tuberculosis drug resistance among patients who have both pulmonary tuberculosis and HIV is described in this study This study may aid in a better understanding of MDR TB in HIV-positive patients and may significantly improve the management of MDR TB in HIV-positive individuals, which would ultimately aid the nation in meeting its MDG health goals. The deleterious effects of TB in PLHIV can be significantly reduced by early diagnosis, efficient TB treatment, timely connection to HIV care, and early commencement of ART

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