Original Article

Epidemiological Review and Sensitivity Patterns of CBNAAT Testing for Tuberculosis in a Teaching Hospital of Eastern India

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Introduction : CBNAAT facilities utilizing the molecular method of TB diagnosis yields substantially higher rates of diagnosis than conventional methods.

Methods : We conducted an observational record review study of CBNAAT samples received at a teaching hospital of Eastern India and analyzed the type of source patients, the nature of health facility sending such samples and the outcomes of CBNAAT testing across the subpopulations of TB patients.

Results : 2453 Pre DR TB and 1950 Pre TB patients comprised our study population, with 87.5% being HIV negative. 50.5% Pre DR TB and 13% Pre TB patients had CBNAAT positivity. CBNAAT positivity was 50.2% in new sputum negative and 44.5% in new sputum positive samples, while it was 74.8% in Pre DR TB and 12.9% in Pre TB samples, the figures being statistically significant. However, the incidence of Rifampicin resistance did not differ among most subpopulations in the study.

Conclusions : CBNAAT remains a crucial diagnostic tool in TB detection campaigns. Rifampicin resistance was not rare in the study and spanned all subgroups included in this study.

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Key words **: Pre TB, Pre DR TB, CBNAAT, Rif resistance.**

Tuberculosis (TB) caused by Mycobacterium tuberculosis (MTB) bacteria is an important public health issue around the globe. Routine diagnostic methods for MTB include acid-fast bacilli (AFB) microscopy, MTB culture, conventional polymerase chain reaction (PCR), and GeneXpert® MTB/RIF assay.

The efficiency of MTB culture using the LJ medium has been demonstrated to detect MTB when 10 viable bacilli per mL of sputum were present.[1] GeneXpert MTB/RIF assay is one of the most advanced and rapid PCRbased methods recommended by WHO in 2010 for the detection of MTB DNA and rifampicin resistance. It is based on a hemi-nested real-time PCR assay utilizing five molecular beacon technology spanning the rpoB gene 81-bp rifampicin resistance determining region (RRDR).[2] The early detection of the MTB and RIF/DR in TB suspects is crucial for disease management and to control the disease transmission from person to person and the emergence of drug-resistant tuberculosis (DRTB). Moreover, studies have shown that CBNAAT facilities utilizing the molecular method of TB diagnosis yields substantially higher rates of diagnosis than conventional methods.[3]

Editor's Comment :

- **CBNAAT testing for Tuberculosis yields positive results in both sputum positive as well as negative samples.**
- **Rif resistance among CBNAAT positive samples are more common in Pre DR TB than among Pre TB subjects.**
- **PLHIV are most susceptible to harbor Rif resistance.**
- **Sputum negative samples are more likely to harbor Rif resistance than sputum positive samples.**

Material and Methods

This study was conducted at Murshidabad Medical College, Berhampore, a tertiary referral center catering to large parts of West Bengal and the adjoining areas of Bihar, Jharkhand and Bangladesh. This was an observational record review study from the sputum CBNAAT test records conducted at the TB clinic of our institution. Records of all sputum samples received from June 2018 to July 2019, both inclusive were collected and tabulated to obtain information about the source and type of patients as well as of the outcome of the test results.

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The source of patient referral was either the hospital IPD or OPD, or from private facilities, Tuberculosis units (TU) or the ART center of our institution.

The patients presenting for sputum CBNAAT testing were categorized as per RNTCP guidelines into Pre TB (those with no exposure to ATD, without HIV positivity and with no contact with MDR TB) and to pre DR TB (those with previous exposure to ATD, with HIV TVB co-infection or with contact with MDR TB), into the following subgroups:

- Pre TB
  - Pre TB NSN (New sputum negative)
  - Pre TB NSP (New sputum positive)
- Pre DR TB
  - Pre DR TB Contact MDR (NSN, NSP)
  - Pre DR TB FU (Follow up) (NSN, NSP)
  - Pre DR TB PLHIV (with HIV TB coinfection) (NSN, NSP)
  - Pre DR TB RT (returned to treatment after default) (NSN, NSP)

Results

This was an observational record review study of all cases presenting for sputum CBNAAT testing at Murshidabad Medical College, West Bengal, India, during the period June 2018 to July 2019. Data regarding gender distribution, source of referral for the sputum CBNAAT testing, suspected pulmonary or extra pulmonary involvement, HIV status of the population being tested and the CBNAAT test result were recorded and analyzed to yield statistical information.

The study spanned a period of 14 months from June 2018 to July 2019, both inclusive, during which a total of 4403 patients (2953 males, 1450 females, 67.1% and 32.9%, respectively) were tested at our facility, giving a male : female ratio of 2.04 : 1.

The patients were classified into two broad groups as per the RNTCP nomenclature into Pre TB cases (1950 cases, with no prior exposure to ATD, to HIV or to contact with MDR TB) and Pre DR TB (2453 cases) with previous exposure to ATD (treatment completed on follow up or returned to treatment after treatment discontinuation), HIV positivity or contact with MDR TB (Fig 1).

These cases were further subdivided into NSN and NSP cases. It was observed that the NSN cases were significantly more among Pre DR TB PLHIV (146 *versus* 84) and Pre DR TB RT (458 *versus* 154) and equitably distributed among Pre DR TB Contact MDR (50 versus 46) and Pre DR TB FU (769 *versus* 746). However, among Pre TB cases, NSP patients outnumbered NSN cases (1151 *versus* 799) (Fig 2 and 3).

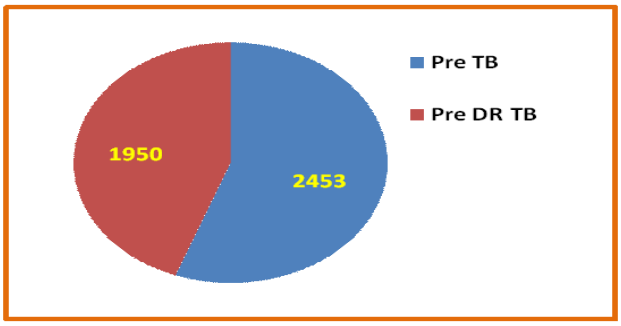

Fig 1 — Distribution of study population (n = 4403)

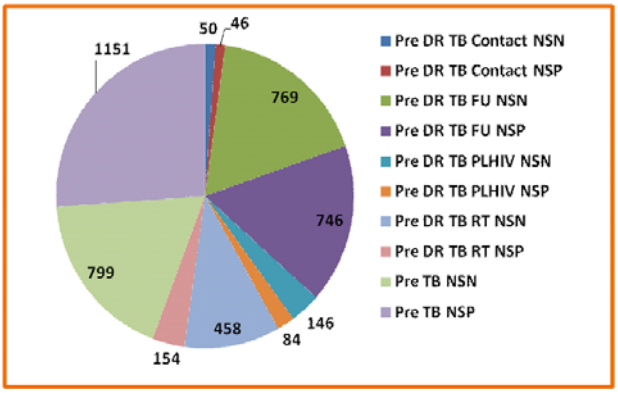

Fig 2 — Distribution of patient categories in study population (n = 4403)

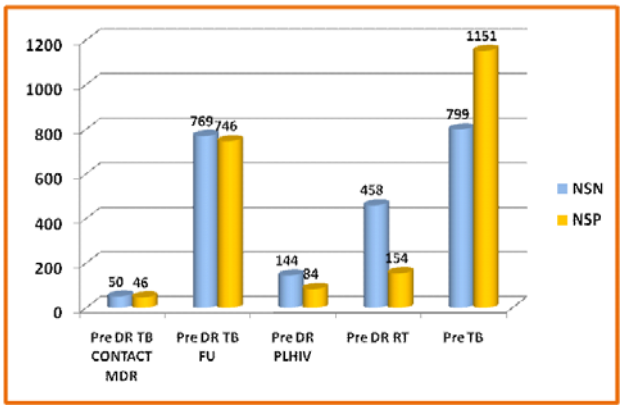

Fig 3 — Distribution of NSN and NSP cases across study sub-populations

The health facility from which patients were referred for CBNAAT testing were tabulated. 49% and 26.6% patients were referred from the OPD and IPD respectively of the study institution, followed by 11.6% from the TB units, 8.7% from private facilities and 4.1% from the ART center of our hospital. The hospital OPD generated relatively more DR TB suspects than pre TB cases (57.4% *versus* 38.4%) while the ART center referred more Pre TB cases than DR TB suspects (7.6% versus 1.3%) (Table 1).

Our study included patients who were referred for sputum CBNAAT testing. Predictably, the study

Table 1 — *Source of referral for patients tested for sputum CBNAAT*

	IPD	OPD	Private	TU	ARTC	Total
Pre DR TB Contact MDR :						
NSN	11	22	11	6	0	50
NSP	8	25	8	5	0	46
Total	19(19.8%)	4749%)	19(19.8%)	11(11.4%)	0	96(100%)
Pre DR TB FU :						
NSN	149	401	72	147	0	769
NSP	138	422	31	153	2	746
Total	287(18.9%)	823(54.3%)	103(6.3%)	300(19.8%)	2(0.1%)	1515(100%)
Pre DR TB PLHIV :						
NSN	33	68	7	16	22	146
NSP	14	50	3	9	8	84
Total	47(20.4%)	118(51.3%)	10(4.3%)	25(10.9%)	30(13%)	230(100%)
Pre DR TB RT :						
NSN	73	250	43	89	3	458
NSP	35	68	8	43	0	154
Total	108(17.6%)	318(52%)	51(8.3%)	132(21.6%)	0	612(100%)
Pre DR TB Total	561(22.9%)	1409(57.4%)	183(7.7%)	268(10.9%)	32(1.3%)	2453(100%)
Pre TB :						
NSN	196(24.5%)	343(42.9%)	38(4.8%)	142(17.8%)	80(10%)	799(100%)
NSP	413(35.9%)	405(35.2%)	163(14.2%)	101(8.8%)	69(6%)	1151(100%)
Total	609(31.2%)	748(38.4%)	201(10.3%)	243(12.5%)	149(7.6%)	1950(100%)
Study population	1170(26.6%)	2157(49%)	384(8.7%)	511(11.6%)	181(4.1%)	4403(100%)

population predominantly involved suspected PTB patients (4223 out of 4403 patients, 95.1%) with less than 5% cases with clinical suspicion of EPTB. This predominance of PTB patients was evident in all sub population in this study (94.8% in MDR Contacts, 98.4% in follow up patients, 83.3% in PLHIV, 98.4% in returned to treatment, and 94.7% in pre TB group). The highest incidence of EPTB was seen in the PLHIV population (11.7%). Excluding the patients with a prior diagnosis of HIV, the prevalence of HIV sero-positivity was 14.2% in Pre TB patients, and 3.6%% in pre DR TB RT. The overall prevalence of HIV was 11.1% in pre DR TB patients, 14.2% in pre TB patients and 12.5% in the entire study population (Table 2).

Out of the 4403 samples tested in our study, CBNAAT was negative in 50.9%, while 2207 (47.4%) of sputum samples provided positive test results. The overall CBNAAT positivity was 74.8% in pre DR TB group and 12.9% in the pre TB group, summing up to a diagnostic yield of 47.4% in the study population.

Sensitive and Rif resistant MTB was detected in 45.3% and 2.1% samples respectively. The incidence of negative CBNAAT samples was highest among Pre TB (85.5%), Pre DR PLHIV (56.1%) and Pre DR TB RT (45.9%) cases. Rif resistance was seen in 2.1% of our cases, with Pre TB and Pre DR TB sub-populations showing resistance figures of 0.5% and 3.4% respectively. The highest incidence of Rif resistance was seen in Pre DR TB PLHIV (8.3%) (Table 3). CBNAAT testing yielded highest results in follow up cases (90.2%), followed by defaulters returning to treatment and PLHIV patients (50.5% and 43% respectively).

We further analyzed our study population into sputum negative and sputum positive samples. There were 1116 new sputum negative (NSN) cases (1004 Pre DR TB, 112 Pre TB) and 971 new sputum positive (NSP) cases (831 Pre DR TB, 140 Pre TB) in our study, giving a case detection rate of 50.2% among NSN cases and 44.5% among NSP cases (Fig 5). The CBNAAT positivity rate was significantly higher among Pre DR TB patients (70.6% in NSN, 80.7% in NSP) than among Pre TB patients (14% in NSN, 12.2% in NSP) (Table 4).

Table 2 — *HIV status and pulmonary versus extra pulmonary TB*

	HIV +	HIV -	PTB	EPTB	Total
Pre DR TB Contact MDR :					
NSN	0	50	45	5	50
NSP	0	46	46	0	46
Total	0	96(100%)	91(94.8%)	5(5.2%)	96(100%)
Pre DR TB FU :					
NSN	4	765	747	22	769
NSP	18	728	744	2	746
Total	22(1.5%)	1493(98.5%)	1491(98.4%)	24(1.6%)	1515(100%)
Pre DR TB PLHIV :					
NSN	146	0	119	27	146
NSP	84	0	84	0	84
Total	230(100%)	0	203(88.3%)	27(11.7)	230(100%)
Pre DR TB RT :					
NSN	17	441	448	10	458
NSP	5	149	154	0	154
Total	22(3.6%)	590(96.4%)	602(98.3%)	10(1.7%)	612(100%)
Pre DR TB Total	272(11.1%)	2181(88.9%)	2387(97.3%)	66(2.7%)	2453(100%)
Pre TB :					
NSN	50	749	696	103	799(100%)
NSP	227	924	1151	0	1151(100%)
Total	277(14.2%)	1673(85.8%)	1847(94.7%)	103(5.3%)	1950(100%)
Study population	549(12.5%)	3854(87.5%)	4234(96.2%)	169(3.8%)	4403(100%)

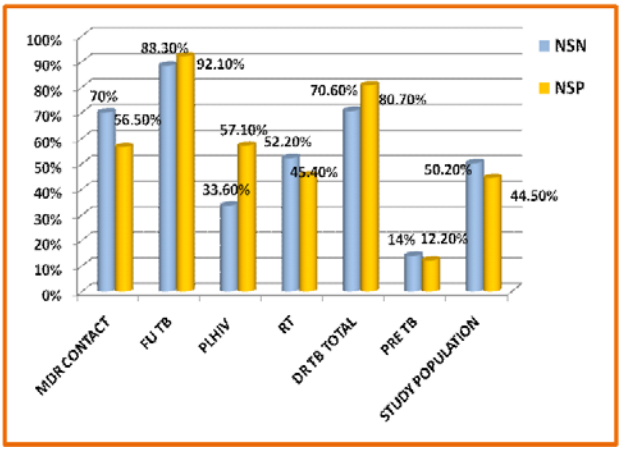

Fig 4 — CBNAAT positivity in NSN and NSP samples

We analyzed our data to see if the rate of CBNAAT positivity was different among various study subpopulations. Considering the Pre DR patients, CBNAAT positivity was higher among NSN than NSP (80.7 and 70.6) and this was statistically significant. Such statistically significant differences were also observed between Pre DR TB NSN and Pre TB NSN (70.6% and 14.0%), Pre DR TB NSP and Pre TB NSP (80.7% and 12.2%), and Pre DR TB and Pre TB (74.8% and 12.9%), but not between Pre TB NSN and Pre TB NSP (14.0% and 12.2%) patients (Table 5).

Resistance to Rif is a major area of clinical interest. This was less than 5% among all subpopulations in the study, except for a resistance of 19.2% among PLHIV and 6.5% among pre DR TB RT subjects (Table 6). Rif resistance was seen in 27.5% of Pre DR PLHIV NSN, 11.4% of Pre DR PLHIV NSP, 7.1% of Pre DR RT NSP, 6.3% of Pre DR RT NSN, 5.5% of Total Pre DR NSN cases, and 5.4% of all NSN cases in the study. In all remaining categories, the incidence of Rif resistance was less than 5% (Table 7, Fig 5). However, there was no statistically significant difference in Rif resistance between Pre TB NSN and Pre DR TB NSN, Pre TB NSP and Pre DR TB NSP, NSN and NSP or Pre TB and Pre DR TB subgroups (Table 8).

Discussion

It has been seen that, in a low-resource high-burden setting like India, CBNAAT has a great impact in holding off treatment where empiric ATD is often used [4]. The simplicity, high sensitivity and specificity for Rif resistance detection makes CBNAAT a very attractive tool for diagnostic of MTB and RIF resistance in MDR cases [5]. There has been little documentation regarding the utilization of CBNAAT from Eastern India ever since the Government of India adopted this technique and incorporated into the protocol of the RNTCP.

Our study had 44.4% of Pre TB cases suggesting that new TB suspects are yet to be routinely referred for CBNAAT testing. The predominance of Pre DR TB cases (Contact MDR, PLHIV, FU and RT) reflects the trend among clinicians to offer CBNAAT only to those

Table 3 — *Distribution of CBNAAT test result across the study subpopulations*

	Sensitive	Resistant	Not detected	Indeterminate	Error	Total
Pre DR TBContact MDR	60(62.5%)	1(1%)	32(33.3%)	3(3.1%)	0	96(100%)
Pre DR TBFU	1323(87.3%)	43(2.8%)	130(8.6%)	1(0.1%)	18(1.2%)	1515(100%)
Pre DR TBPLHIV	80(34.8%)	19(8.3%)	129(56.1%)	1(0.4%)	1(0.4%)	230(100%)
Pre DR TBRT	289(47.2%)	20(3.3%)	281(45.9%)	8(1.3%)	14(2.3%)	612(100%)
Pre DR TBTotal	1752(71.4%)	83(3.4%)	572(23.3%)	13(0.5%)	331.3%)	2453(100%)
Pre TBTotal	243(12.5%)	9(0.5%)	1668(85.5%)	6(0.8%)	24(1.2%)	1950(100%)
Study population	1995(45.3%)	92(2.1%)	2240(50.9%)	19(0.4%)	57(1.3%)	4403(100%)

Table 4 — *CBNAAT positivity in study sub-populations*

MDR Contact NSN (n = 50)	35 (70%)	MDR Contact NSP(n = 46)	26 (56.5%)
FU TB NSN (n = 769)	679 (88.3%)	FU TBNSP(n = 746)	687 (92.1%)
PLHIV NSN (n = 146)	51 (33.6%)	PLHIV NSP(n = 84)	48 (57.1%)
RT NSN (n = 458)	239 (52.2%)	RT NSP(n = 154)	70 (45.4%)
Pre DR TB Total NSN (n = 1423)	1004 (70.6%)	Pre DR TB Total NSP(n=1030)	831 (80.7%)
Pre TB NSN (n = 799)	112 (14%)	Pre TB NSP(n = 1151)	140 (12.2%)
Total NSN cases in the study (n = 2222)	1116 (50.2%)	Total NSP cases in the study(n = 2181)	971 (44.5%)

Table 5 — *CBNAAT positivity among various study subpopulations*

Variables	CBNAAT Test		Total No (%)	χ^2, df	p value
	Positive No (%)	NegativeNo (%)			
Pre DR TB NSP	831 (80.7)	199(19.3)	1030(100)	32.4981, 1	0.000
Pre DR TB NSN	1004 (70.6)	419(29.4)	1423(100)		
Pre DR TB Total	1835 (74.8)	618(25.2)	2453(100)		
Pre TB NSN	112 (14.0)	689 (86.0)	799(100)	1.3902, 1	0.238
Pre TB NSP	140 (12.2)	1011(87.8)	1151(100)		
Pre TB Total	252(12.9)	1700(87.1)	1952(100)		
Pre DR TB NSN	1004 (70.6)	419(29.4)	1423(100)	656.1168, 1	0.000
Pre TB NSN	112 (14.0)	689 (86.0)	801(100)		
NSN Total	1116(50.2)	1108(49.8)	2224(100)		
Pre DR TB NSP	831 (80.7)	199(19.3)	1030(100)	1033.1208, 1	0.000
Pre TB NSP	140 (12.2)	1011(87.8)	1151(100)		
NSP Total	971(44.5)	1210(55.5)	2181(100)		
Pre DR TB	1835 (74.8%)	618 (25.2)	2453 (100)	1668.6549, 1	0.000
Pre TB	252 (12.9%)	1698 (87.1)	1950 (100)		
Study population	2087 (47.4%)	2316 (52.4)	4403 (100)		

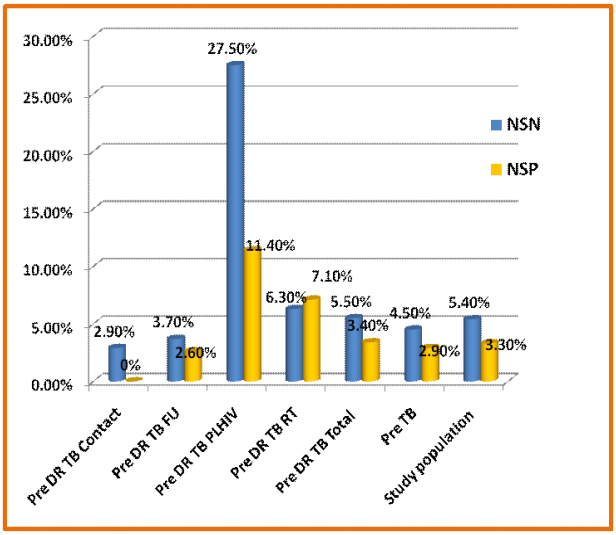

Fig 5 — Incidence of Rif resistance (n = 4403)

DR TB suspects. Further awareness generation amongst the medical and paramedical community is essential to counter this selection bias in future.

75.6% of our patients were referred from the study institution itself (49% from OPD and 26.6% from IPD services) while the neighboring TB units and private sector health facilities contributed 11.6% and 8.7% of our study patients. This is a dismal figure and indicates poor orientation to CBNAAT testing among the health care providers.

As mentioned, less than 5% of our cases were suspect EPTB cases. This raises the question of subjecting other clinical specimens for CBNAAT. Specimens that can be sent for testing include respiratory specimens such as sputum, bronchial or tracheal aspirates, broncho-alveolar lavage and gastric lavage as well as extra pulmonary specimens like tissue biopsy including lymph node, pus from abscess, CSF, ascitic and pericardial fluid, pleural fluid [6]. CB-NAAT testing for TB on other samples such as stool, urine and blood is not recommended [7].

50.9% of our patients had negative CBNAAT results, raising the question of patient selection before utilizing this facility. However, in high burden countries like India, where diagnosis of TB remains a clinician's nightmare, this figure reflects the utility of CBNAAT to rule out TB, unless histopathological examination proves otherwise.

Table 6 — *MTB detection rates by CBNAAT and incidence of Rif resistance among CBNAAT positive samples*

	CBNAAT positivity	Rif resistance (% of CBNAAT positive samples)
Pre DR TB Contact MDR (n=96)	61 (63.5%)	1 (1.6%)
Pre DR TB FU (n = 1515)	1366 (90.2%)	43 (3.1%)
Pre DR TB PLHIV Total (n =230)	99 (43%)	19 (19.2%)
Pre DR TB RT Total (n =612)	309 (50.5%)	20 (6.5%)
Pre DR TB Total (n = 2453)	1835 (74.8%)	84 (4.6%)
Pre TB NSN (n = 799)	112 ((14%)	5(4.5%)
Pre TB NSP (n = 1151)	140 (12.2%)	4(2.9%)
Pre TB Total (n = 1950)	252 (12.9%)	9 (3.6%)
Study population (n = 4403)	2087 (47.4%)	93 (4.5%)

The prevalence of HIV in our study was 12.5%, with a higher prevalence of resistance in this subgroup (19.2% among CBNAAT positive samples). In a study from Pune in Western India using line probe assay, the authors documented prevalence of MDRTB, INH mono- resistance and Rif resistance at 12.5%, 9% and 2.5%, respectively. The prevalence of MDRTB among new and relapsed patients was 8.8% and

Table 7 — *Incidence of Rif resistance in new sputum negative (NSN) and new sputum positive (NSP) samples*

New sputum negative (NSN)				New sputum positive (NSP)			
	Sensitive	Resistant	Total		Sensitive	Resistant	Total
MDR Contact NSN (n = 50)	34(97.1%)	1(2.9%)	35	MDR Contact NSP (n = 46)	26(100%)	0	26
FU TB NSN(n = 769)	654 (96.3%)	25(3.7%)	679	FU TBNSP(n = 746)	669(97.4%)	18(2.6%)	687
PLHIV NSN(n = 146)	37 (72.5%)	14(27.5%)	51	PLHIV NSP(n = 84)	43(89.6%)	5(11.4%)	48
RT NSN(n = 458)	224 (93.7%)	15(6.3%)	239	RT NSP(n = 154)	65 (92.9%)	5(7.1%)	70
Pre DR TB Total NSN (n = 1423)	949 (94.5%)	55(5.5%)	1004	Pre DR TB Total NSP (n = 1030)	803(96.6%)	28(3.4%)	831
Pre TB NSN(n = 799)	107 (95.5%)	5(4.5%)	112	Pre TB NSP(n = 1151)	136 (97.1%)	4(2.9%)	140
Total NSN(n = 2222)	1056 (94.6%)	60 (5.4%)	1116	Total NSP(n =2181)	939 (96.7%)	32(3.3%)	971

Table 8 — *Difference in the incidence of Rif resistance in study subpopulations*

CBNAAT positive	CBNAAT Test		Total No. (%)	χ^2, df	p value
	Sensitive No(%)	Resistance No(%)			
Pre TB NSN	107 (95.5%)	5 (4.5%)	112 (100)	0.2036, 1	0.651
Pre DR TB NSN	949 (94.5%)	55 (5.5%)	1004 (100)		
Total NSN	1056 (94.7)	59 (5.3)	1115 (100)		
Pre TB NSP	136 (97.1%)	4 (2.9%)	140 (100)	0.0987, 1	0.753
Pre DR TB NSP	803 (96.6%)	28 (3.4%)	831 (100)		
Total NSP	939 (96.7)	32 (3.3)	971 (100)		
NSN	1056 (94.6%)	60 (5.4%)	1116 (100)	5.3349, 1	0.020
NSP	939 (96.7%)	32 (3.3%)	971 (100)		
Total	1995 (95.6)	92 (4.4)	2087 (100)		
Pre TB	243 (96.4)	9 (5.6)	252 (100)	0.4763, 1	0.490
Pre DR TB	1752 (95.4)	83 (4.6)	1835 (100)		
Total	1997 (95.6)	92 (4.4)	2089 (100)		

23.1%, respectively[8]. More importantly, the detection rate of TB with CBNAAT is much higher than with sputum microscopy and this most evident with HIV co-infection where sputum negative TB is common. In a study of 100 patients from New Delhi, the case detection rate was 11% with microscopy and 40% with CBNAAT[9]. Apart from HIV, we also found a high prevalence of resistance in Pre DR TB RT patients who defaulted on ATD at some point of time. This trend is not unique to India and has been witnessed in Vietnam, Thailand and Rowanda[10-12].

The sub-analysis of patients into NSN and NSP categories was unique to our study. Interestingly, both Pre DR TB and Pre TB cases had higher rates of resistant organisms being detected in the NSN populations (5.5% versus 3.4% and 4.5% versus 2.9%) respectively. This deserves further analysis and research and raises the possibility of prior treatment leading to both less sputum positivity and higher rates of drug resistance. Last, but not the least, a conspicuous finding in our study is the low rates of CBNAAT positivity among Pre TB NSP cases (12.2%). Pre DR RT cases (45.4%), Pre DR Contact MDR NSP cases (56.5%) and among Pre DR TB PLHIV NSP cases (57.1%). This is a matter of serious concern and poses the strong possibility of false positive sputum microscopy and raises quality assurance issues on our minds. Further studies are essential to throw more light on this matter. The statistically insignificant differences in Rif resistance among our study subgroups indicate that Rif resistance is not isolated to any particular patient category and needs to be borne in mind across the spectrum of health care services.

Conclusion

We conclude that CBNAAT testing is essential in resource restricted setting not only to confirm the presence of MTB infection but also to rule out tuberculosis in clinically suspected cases. Moreover, an overall resistance of 2.1% in the study population from a predominantly rural part of Eastern India and a resistance figure of 3.4% among Pre DR TB suspects contributes important information to the rising incidence of drug resistance TB in this part of the world.

Lacunae

The OPD and IPD patients included in our study were not subdivided on the basis of the department of origin, which would have reflected the relative levels of sensitization among the medical personnel across the departments. This study with a sample size of more than 4000 reflects a wide population base. However multivariate analysis was not performed which could have added to the statistical power of the study.

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Conflict of Interest : None

References

1 Munir MK, Rehman S, Aasim M, *et al* — Comparison of Ziehl Neelsen microscopy with GeneXpert for detection of *Mycobacterium tuberculosis. IOSR Journal of Dental and Medical Sciences* 2015; **14(11):** 56-60.

2 Boehme CC, Nabeta P, Hillemann D, *et al* — Rapid molecular detection of tuberculosis and rifampin resistance. *The New England Journal of Medicine* 2010; **363(11):** 1005-5.

3 Rasool G, Khan AM, Mohy-Ud-Din R, Riaz M — Detection of *Mycobacterium tuberculosis* in AFB smear-negative sputum specimens through MTB culture and GeneXpert® MTB/RIF assay. *International Journal of Immunopathology and Pharmacology* 2019; **33:** 1-6.

4 YoungsJ, Patil S, Jain Y — A prospective study evaluating the impact of cartridge-based nucleic acid amplification test (CBNAAT) on the management of tuberculosis in a low-resource high-burden Indian rural setting. *J Family Med Prim Care* 2018; **7(5):** 982-92.

5 Guenaoui K, Harir N, Ouardi A, Zeggai S, Sellam F, Bekri F, *et al* — Use of GeneXpert Mycobacterium tuberculosis/ rifampicin for rapid detection of rifampicin resistant Mycobacterium tuberculosis strains of clinically suspected multi-drug resistance tuberculosis cases. *Ann Transl Med* 2016; **4(9):** 168.

6 Shah I, Gupta Y — Xpert MTB/RIF for diagnosis of tuberculosis and drug resistance in indian children. *Indian Pediatr* 2016; **53:** 837-8.

7 World health Organisation (WHO) — Xpert MTB/RIF implementation manual. Technical and operational 'how-to': Practical Considerations. 2014 apps.who.int/ iris/bitstream/ 10665/112469/1/9789241506700_eng.pdf.

8 Sadhana N, Runwal K, Ghanekar C, Gaikwad S, Sane S, Pujari S — High prevalence of multi drug resistant tuberculosis in people living with HIV in Western India. *BMC Infectious Diseases* 2019; **19:** 391-6.

9 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. *J nd Assoc Clinical Med* 2015; **16(2):** 114-7.

10 Quy HT, Lan NT, Borgdorff MW, *et al* — Drug resistance among failure and relapse cases of tuberculosis: is the standard re-treatment regimen adequate? *Int J Tuberc Lung Dis* 2003; **7:** 631-6.

11 Yoshiyama T, Yanai H, Rhiengtong D, *et al* — Development of acquired drug resistance in recurrent tuberculosis patients with various previous treatment outcomes. *Int J Tuberc Lung Dis* 2004; **8:** 31-8.

12 Rigouts L, Portaels F — DNA fingerprints of Mycobacterium tuberculosis do not change during the development of resistance to various antituberculous drugs. *Tuber Lung Dis* 1994; **75:** 160.