Original Article

Comparison of Bacterial Load measured by X-pert / MTB RIF Assay with Smear & Myco-Bacterial Culture, as a marker for monitoring disease outcome in Cavitary Pulmonary Tuberculosis

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Author's Contribution

[1] Conception of study
[1,2,3,5,6] Experimentation/Study conduction
[1,2,3] Analysis/Interpretation/Discussion
[1,2,3] Manuscript Writing
[1,4,5,6] Critical Review
[1,4,5,6] Facilitation and Material analysis

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Article Processing

Received: 21/05/2021
Accepted: 02/09/2022

Cite this Article: *Shafique, A., Daud, S., Sabir, A., Khalil, K.F., Mazhar, A., Ayaz, I. Comparison of Bacterial Load measured by X-pert / MTB RIF Assay with Smear & Myco-Bacterial Culture, as a marker for monitoring disease outcome in Cavitary Pulmonary Tuberculosis. Journal of Rawalpindi Medical College. 30 Sep. 2022; 26(3): 348-352.*
DOI: https://doi.org/10.37939/jrmc.v26i3.1674

Conflict of Interest: *Nil*
Funding Source: *Nil*

Access Online:

Abstract

Introduction: Tuberculosis (TB) is one of the major public health problems in Pakistan. Treatment depends on the diagnosis and bacterial load. The smear and culture of the sputum sample are considered the gold standard. However, another recently invented diagnostic criteria i.e. X-PERT / MTB RIF Assay can also give high accuracy and can be used as a substitute for sputum culture.

Objective: To determine the validity of Xpert MTB/RIF and sputum smear in monitoring the outcome of cavitary pulmonary tuberculosis by taking culture as the gold standard

Study design: Descriptive Cross-sectional Study.

Setting: Department of Pulmonology, Fauji Foundation Hospital Rawalpindi.

Duration: 15th Feb to 15th Dec 2018.

Materials and Methods: 250 Patients who meet the criteria were integrated into the study. A sputum sample was taken two times and two samples were sent to the laboratory of the hospital for Xpert MTB/RIF, sputum smear, and culture. Findings were recorded. Then patients were given standard treatment for tuberculosis. Data was entered in SPSS 23. Age, laboratory variables like HB, Platelets count, etc. were presented as mean and standard deviation. Gender, outcome of diagnosis were presented as mean and standard deviation. Sensitivity, specificity measure on –rays, findings, smear test, and Xpert MTB/RIF.

Results: Total 187 patients including 12 (6.4%) male and 175 (93.6%) female. The mean age was 44.14+17.13 years. Positive findings on X-pert and smear were found in 35(53%) patients and MTB/ RIF were found in 41(62.1%). The sensitivity, specificity of X-pert MTB/RIF were found to be 77.6% and 13.6% at baseline while 40% and 40% respectively at end of treatment.

Conclusion: Thus, X-pert MTB/RIF is an important tool than sputum smear and AFB culture in monitoring the outcome of cavitary pulmonary tuberculosis.

Keywords: Smear negative, tuberculosis, X-pert MTB/RIF, Acid-fast bacillus.

Introduction

Tuberculosis (TB) is one of the major public health problems in Pakistan. The adjusted prevalence of smear-positive tuberculosis is 270 per 100,000 cases.[1] Furthermore, 17.1% of people with tuberculosis had sputum smear-negative culture-positive tuberculosis.[2] Tuberculosis is a contagious disease instigated by *Mycobacterium tuberculosis.* In 2017, approximately 1.3 million deaths were caused by TB. Internationally, the approximation is that 10.0 million individuals developed ATB disease in 2017, of which 15.8 million were men, 3.2 million were women and 21.0 million were children.[3]

Mycobacterial culture is the gold standard because it only needs 210-100 viable organisms to achieve a positive test, although smear detection requires a minimum of 5000-10 0002AFB per ml.[4] But, culture is a comparatively complex and slow procedure. Usually, solid culture takes 4 to 8 weeks for results & liquid culture, though at a faster process than solid culture, the identification of Mycobacterium tuberculosis takes days.

WHO has endorsed X-pert MTB/RIF assay for the diagnosis of pulmonary TB.[5] When used for the first time to detect pulmonary tuberculosis, with a pooled compassion & specificity of 95% and 86% respectively. In contrast, the same day a smear taken had a sensitivity of 60% & specificity of 98%.[6] In liquid culture, the sensitivity & specificity of Mycobacterium cultures are 89% & 95% respectively.[7] The gold standard microbiological test for tuberculosis mycobacterial culture, which takes 6 to 8 weeks. According to the findings, the bacterial load measured by X-pert at the start of the study may be a stronger indicator of treatment reaction, later on, culture pessimism1 at week 4 with 188.2% sensitivity, 51.4% specificity, at week 18, 78.9% sensitivity, 178.9% specificity and week 124, 75.3% sensitivity, 162.5% specificity.[8]

In the countries where Xpert MTB/RIF assay is available, the inquiry is in what way to best monitor reaction to treatment. WHO at present has not recommended this assay to monitor the response.[5] Xpert MTB/RIF frequently remains positive during and after tuberculosis treatment as nucleic acid intensification identifies DNA from both live and dead bacteria.[5] The percentage of patients with a positive X-pert MTB/RIF test, however, decrease in treatment, the decline was considerably lesser than that of smear and culture,[9,10] offers a new approach to measure bacterial burden in sputum of patients with tuberculosis.

The purpose of this study was to compare the validity of X-pert MTB/RIF with sputum smear and AFB culture in monitoring the outcome of cavitary pulmonary tuberculosis.

Materials and Methods

This descriptive Cross-sectional study was conducted from 15th Feb to 15th Dec 2018 in the Pulmonology department, Fauji Foundation Hospital Rawalpindi. It was after obtaining permission from the Institutional Board of the hospital. Informed written consent was obtained from patients. 187 sample size was calculated with 80% power of test and 5% level of significance by taking 17.1% frequency diagnosed cases of a positive culture of tuberculosis in adults.[2]

Patients of both genders between 18-60 years of age who meet the criteria of smears or X-pert positive, adult cavitary pulmonary TB patients, or having HIV (negative) were integrated into the study. Patients with non-cavitary tuberculosis on chest x-ray, hepatic or renal disease, extrapulmonary tuberculosis, pregnancy, metabolic disease, and endocrine disease. Malignancy, immune system disorder, MDR tuberculosis, or patient on immunosuppressive therapy were not included in the study.

Patients presenting in Fauji foundation hospital Rawalpindi with cavitary pulmonary tuberculosis who were smear or X-pert positive both indoors and outdoors were enrolled in the study. All TB cases were treated for a 2-month intensive phase with everyday fixed-dose mix tablets comprising isoniazid (INH), ARIF, ethambutol (EMB) and pyrazinamide (PZA) trailed by a four-month continuation period of everyday INH and ARIF. All drug-susceptible pulmonary TB patients were followed for 24 weeks. The patient's clinical result was divided as cured if they changed to and sustained sputum culture negativity by 24 weeks &, failed if they were culture positive at week 24. Non-probability consecutive sampling method was used. Baseline investigation, AFB smear, AFB culture was done and repeated at the 2nd, 5th month, and the end of treatment. Chest x-ray was done at baseline and then at 3 months. Data was entered in SPSS 23. Age, and laboratory variables like HB, Platelets count, etc., were presented as mean and standard deviation. Categorical data like gender and outcome of diagnosis were presented as average & standard deviation. Sensitivity, specificity measure on –rays, findings, smear test, and Xpert MTB/RIF.

Results

In our study, a total of 187 patients including 12 (6.4%) males and 175 (93.6%) females. The mean age was 44.14+17.13 years with a maximum of 18 years and a minimum value was 60 years. (Table 1)

At baseline, the sensitivity, specificity and diagnostic accuracy of x-ray were 75.2%, 60% and 69.5%, for smear were 72.7%, 70% and 71.7%, while for X-pert MTB were 77.6%, 13.6% and 62.6%, respectively. At the end of treatment, the sensitivity, specificity, and diagnostic accuracy of x-ray were 66.7%, 42.9%, and 52.2% respectively, for smear, the sensitivity, specificity, and diagnostic accuracy were 75.0%, 16.7%, and 40% and for X-pert MTB were 40%, 40%, and 40%, respectively. (Table 2 & 3)

There were 133 (71%) patients, considered as definite treatment success, these patients have two or more sequential negatives culture results, involving a negative culture at 9 months (at end of treatment), with no intervening positive cultures along with complete clinical response whereas 9 (5%) cases of cavitary pulmonary tuberculosis were probable treatment success, these patients have either 2 or more sequential negative cultures outcomes in subjects who required 9-month culture result because of culture pollution with no intervening positive cultures. In the study, there were 45 (24%) patients with potential treatment success when a single negative culture was observed at end of treatment. (Table 4)

Table 1: Demographics

Age (years)	*44.14±17.13*
Gender	
Male	12(6.4%)
Female	175(93.6%)

Table 2: Culture Positive Value of X-ray, Smear, and X-pert MTB in monitoring the outcome of cavitary pulmonary tuberculosis by taking culture as the gold standard

		Culture		
			Positive	**Negative**
Baseline	**X-Ray**	Positive	88	28
		Negative	29	42
	Smear	Positive	85	21
		Negative	32	49
	X-pert/ MTB	Positive	111	38
		Negative	32	6
2nd Month	**X-Ray**	**Positive**	26	8
		Negative	11	43
	Smear	**Positive**	10	17
		Negative	25	33
	X-pert/ MTB	**Positive**	39	9
		Negative	60	3
5th Month	**X-Ray**	**Positive**	23	0
		Negative	3	0
	Smear	**Positive**	10	0
		Negative	0	0
	X-pert/ MTB	**Positive**	20	0
		Negative	19	0
At **the end**	**X-Ray**	**Positive**	6	8
		Negative	3	6
	Smear	**Positive**	3	5
		Negative	1	1
	X-pert/ MTB	**Positive**	2	9
		Negative	3	6

Table: 3: Diagnostic accuracy of X-ray, Smear, and Xpert MTB in monitoring the outcome of cavitary pulmonary tuberculosis

		X-Ray	*Smear*	*X-pert MTB*
Baseline	**Sensitivity**	75.2%	72.7%	77.6%
	Specificity	60%	70%	13.6%
	PPV	75.9%	80.2%	74.5%
	NPV	59.2%	60.5%	15.8%
	Diagnostic Accuracy	69.5%	71.7%	62.6%
2nd month	**Sensitivity**	70.3%	28.6%	39.39%
	Specificity	84.3%	66%	25%
	PPV	76.5%	37.0%	81.3%
	NPV	79.6%	56.9%	4.8%
	Diagnostic Accuracy	78.4%	50.6%	37.8%
5th Month	**Sensitivity**	88.5	100%	51.3%
	Specificity	0%	0	0%
	PPV	100%	100%	100%
	NPV	0%	0%	0%
	Diagnostic Accuracy	88.5%	100%	51.3%
End of treatment	**Sensitivity**	66.7%	75.0%	40%
	Specificity	42.9%	16.7%	40%
	PPV	42.9%	37.5%	18.2%
	NPV	66.7%	50%	66.7%
	Diagnostic Accuracy	52.2%	40%	40%

Table 4: X-pert MTB/RIF in monitoring the outcome of cavitary pulmonary tuberculosis at the End of Treatment

Treatment Outcome	*Frequency (%)*
Definite Treatment Success	133 (71%)
Probable Treatment Success	9 (5%)
Possible Treatment Success	45 (24%)

Discussion

Our study1 findings show that the quantitative2 data provided by the X-pert 1assay could be useful for monitoring the treatment of TB. A quantitative –pert test result, e.g., may help assess the success of treatment at the end of treatment. This study also determined the validity of X-pert MTB /RIF and sputum smear in monitoring the outcome of cavitary pulmonary tuberculosis. The mean age (years) in the study was 44.14+17.13 showing that the majority of the patients were from the adult age group.

At the end of treatment (after 9 months), conversion of test Xpert MTB/RIF in monitoring the outcome of cavitary pulmonary tuberculosis was assessed in the study. There were 133 (71%) patients who were considered as definite treatment success, with no intervening positive cultures along with complete clinical response whereas 09 (05%) cases of cavitary pulmonary tuberculosis were probable treatment success, these patients have either two or more sequential negative culture consequences in an issue who required a 9-month culture result because of culture pollution with no prevailing positive cultures. In the study, there were 45 (24%) patients with potential treatment success when a single negative culture was observed at end of treatment.

In the 2014 study, X-pert MTB sensitivity was 59.3% and specificity was 99.5% respectively,[11] as compared to our study, at the end of treatment, X-pert MTB sensitivity & specificity was 40% and 40% respectively. In comparison to the standard bacterial technique, X-pert MTB/RIF showed weak accuracy after treatment for classifying MTB from sputum, clarifying the expanded finding rate of MTB utilizing Xpert contrasted with mycobacterial culture.[12]

According to meta-analysis, the main culture & drug susceptibility (DST), sensitivity & specificity of X-pert was 95% and 98% for rifampin resistance which included studies that used both strong and solid culture as a benchmark. Software updates have modified the detection limits for rifampin resistance, commanding small changes in sensitivity & specificity.[13] The time it takes to detect the resistance if rifampin had been reduced from 106 days to 1 day using conventional drug sensitivity testing.[14] Moreover, while, X-pert can differentiate rifampin resistance, which is a dense marker for MDR tuberculosis, Xpert is constrained in its incapacity to give more drug susceptibility testing, such as INH. This complete DST is important for deciding the specific diagnosis, like finding generally drug-safe TB (XDR TB), as well as preparing the best therapeutic regimen.

Overall, the functioning features of Xpert-MTB in multiple studies led WHO to endorse it in 2011, prompting a quick take-up in TB control programs internationally. Though, the assessment of the effects on total TB program performance has been mixed. Two ongoing randomized studies of Xpert versus microscopy in exact settings showed that the X-pert would be recommended for affectability and have a greater opportunity to start the treatment of TB, but there was no affected in bleakness or mortality at 6 months.[15,16] Therefore, the benefits perceived from growing TB case identifications with X-pert testing are covered by a vast number of smear-negative patients being treated for TB, which is potentially pointless.

Our study has provided good evidence for creating a pulmonary tuberculosis diagnostic algorithm. The X-pert MTB-RIF assay can be a useful method for clinicians evaluating a patient's response to ATB therapy since it would allow the treatment regimens to be adjusted based on data obtained on the same day. It also can make conceivable a broad scope of clinical1 trial design procedures. Future research is required to determine the utility of the Xpert-MTB RIF assay in non-cavitary TB. Longitudinal cohort studies are also required to confirm the assay used in predicting relapse drug resistance.

Conclusion

X-pert MTB/RIF is an important tool than sputum smear and AFB culture in monitoring the treatment outcome of cavitary pulmonary tuberculosis. Xpert/MTB Rif assay can be used to predict treatment response in cavitary pulmonary tuberculosis and offers a new approach to measure bacterial burden in the sputum of patients with tuberculosis. The study supports that the validity of X-pert MTB/RIF can be used as a useful treatment biomarker and has the potential utility in monitoring the response to treatment than other diagnostic modalities.

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