

Background

❖ Tuberculosis (TB) remains the significant cause of morbidity and mortality in the world.¹

❖ Current treatment regimens consist of 6-months of standard treatment, with approximately 85% of cure rate.¹ However. treatment default is common and leads to higher treatment failure, recurrence, mortality and emergence of drug resistance.²

❖ Early phase trials use 2-month culture conversion as a surrogate timepoint to assess the treatment success. However, this timepoint has not had consistently predicted the adverse TB treatment outcomes.³

❖ Several clinical trials have been (are) aiming to optimize treatment duration to as short as 3-months or less⁴ while maintaining treatment efficacy

❖ However, several pitfalls exist for the current 2-month surrogate endpoint as it takes a minimum of 6-8 weeks to confirm the results, which will be well beyond a shortened regimen of 3 months.

❖ Hence, it is critical to identify earlier timepoints that can predict adverse TB treatments.

❖ In this study we sought to assess if the best timepoint of culture conversion that predicted TB treatment failure could be earlier than the eight week timepoint in a tertiary care public hospital in India.

Design/Methods

Study Design: Longitudinal prospective cohort study of patients with pulmonary TB with and without Diabetes Mellitus.

Study Sites: Byramjee-Jeejeebhoy Government Medical College-Sassoon General Hospitals (BJGMC-SGH) clinical research site and Dr. DY Patil Medical College (DYPMC) in Pune, India.

Laboratory Procedures- All participants underwent testing with two sputum samples-(spot and early morning). Gene Xpert (Xpert® MTB/RIF assay), microscopy (ZN method) and cultures by MGIT (liquid culture) as well as LJ (solid culture) were performed at baseline on each of the samples. One SIRE test was done per participant at baseline. All enrollees underwent sputum smear, MGIT and LJ culture every two weeks after TB treatment initiation through 8 weeks and then monthly until month 6. SIRE was repeated if the culture was positive after week 20/ recurrence/ failure visits.

Statistical Analysis- A Univariable and multivariable logistic regression was performed to assess whether 2, 4 or 6-week culture conversion predicted TB treatment failure.

Outcome- Earliest timepoint that predicts TB treatment outcome.

Results

❖ Of the 718 participants with culture positive TB at baseline, 652 (91%) were cured/completed treatment.

❖ Overall, median age was 32 (IQR, 24-45). 472 (66%) were Males; 202 (28%) had Diabetes

❖ 66 (9%) failed treatment.

❖ After adjusting for age, gender, body mass index, diabetes, tobacco and alcohol use, culture conversion at 6 weeks (adjusted odds ratio (aOR, 2.07; 95% CI: 1.10 – 3.91,C statistic- 0.67), 8 weeks (aOR, 1.81; 95% CI: 0.94 – 3.48) and 12 weeks (aOR, 4.44; 95% CI: 1.88 – 10.45) and 16 weeks (aOR, 8.0; 95% CI: 3.52 – 18.16) predicted TB treatment failure.

❖ **Table: Univariable and Multivariable Analysis**

Time	Univariable Analysis			Multivariable Analysis		
	OR (95% CI)	p-value	C-statistic	OR (95% CI)	p-value	C-statistic
Week 2 N = 698	1.57 (0.83 – 2.99)	0.16	0.54	1.57 (0.82 – 3.01)	0.17	0.67
Week 4 N = 578	1.35 (0.76 – 2.40)	0.31	0.54	1.25 (0.70 – 2.25)	0.45	0.62
Week 6 N = 564	2.14 (1.16 – 3.96)	0.02	0.59	2.07 (1.10 – 3.91)	0.02	0.67
Week 8 N = 561	2.06 (1.10 – 3.86)	0.02	0.56	1.81 (0.94 – 3.48)	0.07	0.67
Week 12 N = 517	5.02 (2.24 – 11.24)	p < 0.001	0.59	4.44 (1.88 – 10.45)	0.001	0.66
Week 16 N = 587	7.86 (3.64 – 16.98)	p < 0.001	0.61	8.0 (3.52 – 18.16)	p < 0.001	0.72

Conclusions

❖ The earliest culture conversion that predicted failure was at 6 weeks and potentially can be used as an earlier surrogate endpoint than the current standard of 8 weeks.

❖ Unsurprisingly, the odds of treatment failure increased with later TB culture conversion, however earlier culture results did not.

❖ Future studies should confirm our findings.

References

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