Descriptive Baseline Characteristics, Treatment Outcomes and Biorepository of Pediatric TB Cases in CTRIUMPh-RePORT India Prospective Cohort

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INTRODUCTION

- India has the world's largest absolute burden of pediatric TB.
- Establishing pediatric TB cohorts is critical for novel diagnostics and discovery of factors and biomarkers associated with clinical presentation and treatment outcomes.
- The CTRIUMPh study at BJMC, Pune and NIRT, Chennai, is a prospective, observational cohort enrolling adult and paediatric TB cases and establishing a biorepository.
- We aimed to describe baseline characteristics, treatment outcomes, and biorepository specimens available for children < 14 years of age with newly diagnosed drug sensitive TB.

METHODS

- Participants >6 months of age with pediatric TB were enrolled in the CTRIUMPh study between August 2014 and December 2016.
- Clinical characteristics and TB treatment outcomes were summarized using descriptive statistics. Graham et al, CID 2015 definition for confirmed and unconfirmed TB was used. In addition, unconfirmed TB was further categorized into probable and possible using WHO/RNTCP definitions.
- The number of laboratory specimens in the biorepository at baseline and follow up visits were extracted from the Laboratory Data Management System (LDMS).

RESULTS

- 97 participants with pediatric TB were enrolled. The baseline characteristics of cohort are presented in Table 1.
- 64/97 (66%) had pulmonary TB (PTB) including 6 participants who had both PTB and extrapulmonary TB (EPTB).
- TB diagnostics showed 9.3%, 12.4%, and 13.4% of sputum AFB smear, Xpert MTB/Rif, and culture positives, respectively.
- TB was microbiologically confirmed in 14/64 (22%) of PTB and histopathologically confirmed in 12/39 (31%) of EPTB cases.
- The unconfirmed PTB (n=50) comprised of 40 probable TB (80%) and 10 possible TB cases (20%).
- There were 5/79 (6%) treatment failures, 5/74 (7%) recurrence/relapses, and no deaths were observed.
- The biorepository specimens at various study time-points are tabulated for PTB and EPTB in Table 2 and Table 3 respectively.

Table 1: Baseline Characteristics of the Pediatric TB Cohort

Characteristics	n/N (%)
Median Age	8 years (Range: 1-13, IQR: 6-11)
Gender:	
Males	48/97 (49%)
Females	49/97 (50%)
Moderate to Severe malnutrition	26/97 (27%)
Presence of BCG Scar	72/97 (75%)
HIV coinfected	5/97 (5%)
Known contact with active TB case	58/97 (60%)
Median duration of illness (days)	21 (IQR: 15-30)
Type of TB	
PTB	58/97 (60%)
EPTB	33/97 (34%)
Both	6/97 (6%)
Site of EPTB (n= 39)	
Lymph node	15/39 (39%)
Abdominal	16/39 (41%)
Pleura	2/39 (5%)
Meninges	2/39 (5%)
Bone/Joints	2/39 (5%)
Spine	1/39 (2.5%)
Skin	1/39 (2.5%)

Table 2: Biorepository Specimens at Baseline and Follow-up Visits for Pulmonary TB Participants (N= 64; Confirmed PTB = 14/64)

Specimen	Entry	Wk2	Wk4	Wk8	M5	M6	EOT	M12	M18	M24	R/ F	Total
Gastric Aspirate	4	1	1	2								**8**
Hair	55		56		46	43				2	6	**208**
MTB Isolates	6	5	2	2								**15**
PAXgene mRNA	52		57	58		38	2	28		7	7	**249**
PBMC	58		61	57		42	2	28		7	7	**262**
Plasma	58		61	58		42	2	28		7	7	**263**
Plasma PK	1		57		46							**104**
QGIT	21		26	22		13		4				**86**
Sputum/ Deposit	58	57	57	54	48	43	1		14		7	**339**
Stored DNA					49		1					**50**
Urine	59		61	56		42	2	27		6	7	**260**
Total	372	63	439	309	189	263	10	115	14	29	41	**1844**

Table 3: Biorepository Specimens at Baseline and Follow-up Visits for Extra-Pulmonary TB Participants (N= 33; Confirmed EPTB = 12/39)

Specimen	Entry	Wk 2	Wk 4	Wk 8	M5	M6	EOT	M12	M18	M24	R/F	Total
Gastric Aspirate	2											**2**
Hair	34		33		31	25				2	3	**128**
MTB Isolates	1											**1**
PAXgene mRNA	28		28	37		23	1	18		8	3	**146**
PBMC	37		36	37		30	1	18		8	3	**170**
Plasma	38		36	37		30	1	18		8	3	**171**
Plasma PK			32		29							**61**
QGIT	16		16	17		12		3				**64**
Sputum/ Deposit	36	36	35	32	31	29	1		14		3	**218**
Stored DNA					32							**32**
Urine	37		38	37		28	1	18		7	3	**169**
Total	229	36	254	197	123	177	5	75	14	33	18	**1162**

**Wk= Week, M= Month, EOT= End of Treatment visit, R/F- TB Recurrence/Failure visit, PK= Pharmacokinetics*

*** Tables depict number of participants for whom samples were collected at each time point and there are multiple aliquots available in the repository for some of the specimens.*

CONCLUSIONS

- We have established a well characterized Indian clinical cohort of pediatric PTB and EPTB with associated biorepository and this provides a unique opportunity for undertaking pediatric biomarker studies of diagnosis, clinical presentation, and treatment outcome.
- We have begun assessing the transcriptomic, miRNA and metabolic signatures changes during treatment with the eventual goal of determining predictors of TB treatment outcomes.
- We also plan to assess which of the published bio-signatures for adults' best differentiate between confirmed TB cases and negative controls in children.

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