MTB lineage distribution in paediatric population - A whole genome sequencing analysis

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ABSTRACT

Introduction: Paediatric TB accounts for 8% of total TB cases in India. Among the 9 lineages of M. tuberculosis (MTB), lineage 1(L1) is most common in South India and lineage 2(L2), Lineage 3(L3) and lineage 4(L4) are spread over the Northern region. While studies on whole genome sequencing (WGS) in paediatric tuberculosis (TB) is already limited, reports on lineage distribution gains least attention. With the recent studies in adult population demonstrating the association between lineage and drug resistance, characterization of MTB isolates at lineage level is crucial in children. In this study, we aimed to look at the phenotypic and genotypic drug resistance pattern of MTB isolates and their association with lineage distribution. **Materials and Method:** A total of 14 paediatric MTB isolates obtained between the years 2017-2023, were subjected to phenotypic drug susceptibility test (DST) and WGS. The output data in FastQ was mapped to H37Rv reference genome using NIRT CAMRespred Bioinformatics tool and poor quality samples were filtered by Trimmomatic software. A phylogenetic tree was generated using RAxML tool. **Results:** Among the 14 samples, 13 were included for the analysis as one sample was excluded due to poor quality. Sequence analysis revealed around 44 mutations in 6 samples and when their association with phenotypic and genotypic drug resistance was explored, a high level of discordance was observed. While all the 6 samples were sensitive by phenotypic DST, the mutations identified in them by WGS needs further analysis to demonstrate its significance. Lineage distribution analysis identified, L1 in eight samples, L4 in three samples and L2 in two samples and around 12 mutations were seen in L4, 23 in L1 and 9 in L2. **Conclusion:** The study findings indicate that L1 is dominant among the paediatric population. This is in agreement with our earlier findings in adult population, and this paves pathway for further transmission dynamics study. However, discordance between mutations identified and phenotypic DST requires further investigation to check its role in drug resistance.