Background: To determine the proportion of Extensively drug resistant (XDR) strains among multidrug resistant (MDR) tuberculosis positive cultures with uncommon resistance pattern in Line Probe Assay (LPA) in Delhi region. Also, an attempt was made to carry out band pattern analysis obtained in LPA strips for determining resistance associated with uncommon mutations in Rifampicin and Isoniazid. DNA sequencing was outsourced for confirmation of uncommon mutations.

Material/methods: Sputum samples collected from MDR-TB suspects submitted to Intermediate Reference Laboratory (IRL) at New Delhi Tuberculosis Centre in Delhi. For confirmation of MDR-TB, LPA was performed using MTBDRplus kit (Hain Life Sciences, GmbH) as per manufacturer’s instructions. Among these pre-identified MDR samples with uncommon mutations, Phenotypic drug susceptibility (MGIT-SLDST) test for two of the second line drugs (e.g., Kanamycin and Ofloxacin) was carried out for confirmation of XDR-TB strains.

Results: A total of 3558 MDR-TB suspects were screened by LPA, resulting in 500 MDR-TB and mono-Rif resistant cases. Out of these 500 MDR-TB cases, cases with uncommon mutations were 100 which were included in this study. The most common mutation detected by LPA in the rpoB gene was Ser516Leu (29.0%). Novel mutations reported in this study include mutation from CAG (Gin) to CAT (His) at codon 517, AGC (Ser)-AGG (Arg) at codon 512, ACA (Thr) to GCA (Ala) at codon 526, TTG (Leu)-CTG (Leu) at codon 524. Hetero-resistance was observed in 43.6% cases.
Mutations on the basis of missing Wild type band and any of the Mutation probes were 56.4%. XDR TB among these MDR-TB cases were 2%. Mono-resistant to Ofloxacin (fluoroquinolone) were 12%, mono-resistant to Kanamycin (second line anti TB injectable) were 0 %.

**Conclusions:** High frequencies of uncommon mutations in rpoB gene by LPA were observed, highlighting possibility of those in-silico detected mutations that may not impart phenotypic resistance further. There is the need to put in place strategies to identify Pre-XDR TB patients among these MDR-TB patients and ensured for treatment initiation at the earliest and forestall the progression to XDRTB.