

2 TB AND HIV

a Investigation of a cluster of DR-TB cases in Mpumalanga Province

In October 2015, the NICD Centre for TB (CTB) received a notification that a clinic in Mpumalanga had experienced a 6-fold increase in the number of drug-resistant TB (DR-TB) cases in September 2015 compared with previous months, with 15 cases being reported in total. Outbreak Response Unit (ORU) and CTB conducted a desk-top review prior to a field visit to ascertain the reason for the increase. The objectives of the desk-top review were to describe patients identified with DR-TB; to understand background rates of DR-TB in the area; to understand genetic relatedness of TB through evaluation of line-probe assay results, and to make recommendations related to further investigation.

Of 15 patients, 7 (47%) were male, with mean age 46 years (8-72 yrs). Time of diagnosis of DR-TB is presented in Figure 2. The geographical locations of the patients' place of residence as per the laboratory information system were plotted on GIS software. All patients were located within a 35 km radius of each other, but none lived in the same village. Of the 15 patients, 14 had confirmed DR-TB. Of the 14 with confirmed DR-TB, all but one patient was diagnosed with line probe assay without an Xpert MTB/RIF (GXP) test done on sputum as the first-line diagnostic test. Review of line probe assay results revealed at least 6 different genetic mutation patterns amongst 15 patients (Figure 3). Review of all Xpert MTB/RIF results, and culture/line probe assay for the district revealed no year-on-year increase in the number of DR-TB cases identified in the district or sub-district as a whole.

Following this review, ORU and CTB interpreted that there was no evidence of an outbreak based on

available molecular and epidemiological evidence. Rather, the evidence suggested multiple co-transmission events of unrelated strains of DR-TB. The desk-top review methodology is limited in scope as complete genome sequences or other molecular typing methodologies are not used. Furthermore, interview with patients is not possible. ORU and CTB made the following recommendations: 1) A site visit to the district and clinic be undertaken to establish diagnostic recording and reporting procedures; 2) interviews with patients be done to evaluate potential epidemiological linkages and health seeking behaviour; 3) Further molecular investigations be done on patient isolates.

This preliminary investigation has highlighted the need for proactive monitoring of TB burden at the lower levels of health delivery for early signals of change (such as an unusual increase in the number of cases). It also shows that routine data can provide a rich and powerful source of information. The use of line probe assay proved a valuable aid to defining potential genetic relatedness. In this instance, the line probe assay together with sputum culture detected cases of drug resistance that were missed by the GXP. This confirms the importance of inclusion of culture and line probe assay in the TB diagnostic the algorithm. Further investigation will be undertaken to conclude the investigation in partnership with the provincial teams.

Source: Centre for Tuberculosis and Division of Public Health Surveillance and Response, NICD-NHLS.

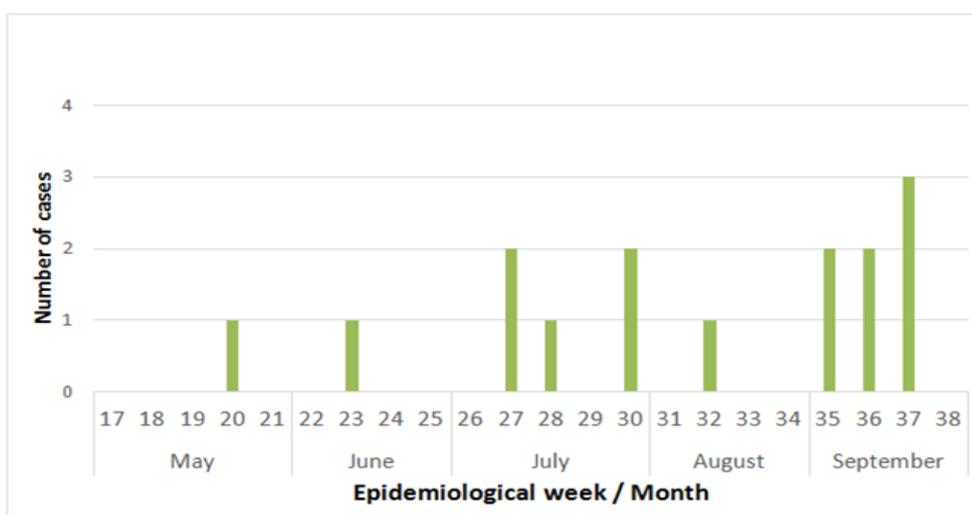


Figure 2. Epidemiological curve showing the number of cases of drug-resistant TB diagnosed at a primary health clinic in Mpumalanga, each epidemiological week from May to September 2015.

Patient #	Rifampicin	Rif mutation description	Isoniazid	INH mutation description
1	Resistant	rpoBWTmut3	Resistant	inhA WT absent
5	Resistant	NA	Resistant	NA
8	Resistant	rpoBWTmut2A	Resistant	katGmut1
10	Resistant	rpoBWTmut2A	Resistant	katGmut1
11	Resistant	rpoBWTmut3	Resistant	katGmut1
13	Resistant	rpoBWTmut3	Resistant	katGmut1
2	Resistant	NA	Sensitive	NA
3	Resistant	rpoBWTmut3	Sensitive	none
4	Resistant	NA	Sensitive	none
6	Resistant	rpoBWTmut2A	Sensitive	none
12	Resistant	rpoBWTmut3	UN (inhA absent, katG WT)	None
9	Resistant	rpoBWTmut1	UN (inhA absent)	katGmut1
15	Sensitive	none	Resistant	katGmut1
14	NA	NA	NA	NA
7	NA	NA	NA	NA

Figure 3. Results of line-probe assay (MTBDRplus, Hains Lifescience) amongst 15 patients with DR-TB diagnosed by a clinic in Mpumalanga, May-September 2015. Red colour indicates confirmed multi-drug-resistant TB (MDR-TB); orange indicates rifampicin mono-resistant TB; blue indicates probable MDR-TB but genotype uncertain; purple indicates isoniazid mono-resistant TB. NA=not available; UN=test uninterpretable.