Delay in commencing treatment for MDR TB at a specialised TB treatment centre in KwaZulu-Natal

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Background. According to the National Department of Health (NDoH) guidelines, patients diagnosed with multidrug-resistant tuberculosis (MDR TB) must be referred to a specialised treatment centre for initiation of effective therapy. MDR TB is difficult to diagnose and the centralised referral model is beset with challenges that contribute to treatment delays, increased patient morbidity and mortality, and MDR TB nosocomial transmission. Culture and drug sensitivity testing (DST) takes 8 weeks or longer to obtain results while line probe assays (LPAs) can give a result in hours. LPAs and the GeneXpert MTB/Rif (GX) are ground-breaking discoveries for TB diagnosis. However, they are not easily accessible or available to those needing it, so culture and sensitivity testing remains the gold standard for diagnosis.

Aim. This study aimed to assess the delay in the initiation of MDR TB treatment and profile the patients being referred to a specialised drug-resistant treatment centre in KwaZulu-Natal.

Methods

The study hospital is a centralised treatment and referral centre for MDR TB in KwaZulu-Natal. The referral prerequisite is confirmation of MDR TB by culture and DST. Although LPAs are used, this has not been integrated into the NDoH treatment guidelines, and therefore a culture and DST is still the gold standard for diagnosis.5,6 Patients referred with results using tests other than culture and DST are assessed, and treatment is only initiated with confirmed results.3 Patients are admitted if they do not have a local clinic to receive their injections, are very ill or do not have social support to enable outpatient treatment. For outpatient treatment, a step-down facility or a local clinic close to home is required to supervise treatment. Both inpatient and outpatient facilities have long waiting lists of patients awaiting treatment.

We included all patients referred to the hospital in 2010 with a DST result confirming MDR pulmonary TB that qualified for treatment. Patients who presented with extrapulmonary MDR TB, mono- or polyresistant TB (not to isoniazid and rifampicin) and who did not present with results, were excluded. On average during 2010, 100 patients per month were initiated on treatment. A sample size of 200, representing 20% of the study population, was chosen. All the charts of patients initiated on treatment in 2 random months were analysed. Data from patient records and the hospital database were gathered on a data collation sheet and entered on a Microsoft Excel spreadsheet and analysed using the SPSS programme.

Descriptive analysis involved mean, standard deviation and range in normally distributed quantitative variables. As this was a descriptive study, no hypothesis was tested. The time interval (in weeks) between the collection of the sputum sample for culture and DST and the start of treatment was calculated. A delay was defined as the interval between sending sputum for DST testing and initiation of effective treatment exceeding 8 weeks; an acceptable range is between 6 and 8 weeks.5,6

Ethical approval was obtained from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal and the Research Ethics Committee of the hospital where the study was conducted.

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Results
In total, 1 158 patients were referred to the study hospital in 2010; 207 patient charts were reviewed of which 21 were excluded because they did not meet the inclusion criteria. Most patients were black, aged between 19 and 50 years, with an almost equal representation of men and women. Patients were mostly unemployed and symptomatic for TB with at least one previous TB episode. MDR TB contact history was poorly documented (Table 1). Of the patients, 69% were HIV-positive, on antiretroviral therapy (ART) (75%) with CD4 counts <250 (59%); 74 (40%) were managed as inpatients, 101 (54%) as outpatients, and 11 (6%) were placed on the surveillance programme. This programme applies to patients referred with confirmatory DST results but who were not considered to have active MDR TB disease. Patients from the eThekwini municipality comprised 47%, while 63% were from neighbouring districts; 111 (59.7%) were on standard TB regimens at the time of referral, while 75 (40.3%) were not on treatment. The mean delay from the date of collection of the sputum sample for culture and DST to initiation of treatment was 12.36 weeks (range 3 - 30 weeks) (Table 2).

Discussion
We aimed to investigate the time from the collection of sputum samples for DST to the initiation of effective therapy. A similar study in Cape Town showed an average of 5 - 6 weeks’ delay in initiation of treatment for patients with MDR TB. However, in our study 131 (75%) of patients experienced delays of up to 22 weeks, and only 44 (25%) patients were started on treatment without a significant delay. This is of concern, since almost 90% of all patients seen were coughing. Delaying treatment for patients who are actively coughing perpetuates the spread of MDR TB. It was previously believed that resistant strains of TB were not virulent enough for high transmission rates and that infection control was therefore not important. However, human-to-human spread of MDR TB is more common than anticipated, and the disease spreads while patients await diagnosis and initiation of treatment. In the Western Cape, 90% of all tested drug-resistant TB cases were smear-positive, suggesting that person-to-person spread of MDR TB is a significant risk. Patients who are on ineffective drug regimens fuel TB drug resistance. South Africa has limited data on reasons for delays associated with the initiation of treatment for MDR TB, and more research is needed. Studies on drug-sensitive TB suggest that healthcare workers, systems and patient factors all contribute to delayed initiation of treatment.

| Table 2. Time from the date of collection of sputum to start of treatment |
|---------------------------------|-----------------|-----------------|-----------------|
| Cumulative weeks*               | No. of months   | N=175           |                 |
|                                 | delay (at 4-week intervals) |                 |                 |
| 0 - 8                           | 0               | 44              | 25              |
| 9 - 12                          | 1               | 54              | 31              |
| 13 - 16                         | 2               | 42              | 24              |
| 17 - 20                         | 3               | 21              | 12              |
| 21 - 24                         | 4               | 7               | 4               |
| 25 - 28                         | 5               | 5               | 2.9             |
| 29 - 30                         | >5              | 2               | 1.1             |

Table: Time from the date of collection of sputum to start of treatment

*Time interval between the collection date of sputum sample for DST and start date of treatment in weeks.
†This average expected time interval from collection of the sputum sample for culture and DST and receiving a result is 6 - 8 weeks. For the purposes of this study, a delay is defined as a time period exceeding 8 weeks.

As part of the solution, the NDoH has suggested a decentralised model of MDR TB management; this may help to reduce the number of days between diagnosis and treatment initiation by increasing the number of treatment centres for referral, which will in turn reduce the transmission of disease. To meet this need, nurse-initiated treatment programmes, which are currently successful for HIV management throughout the world, are being strongly considered by the NDoH to integrate MDR TB and HIV management in communities.

The World Health Organization (WHO) endorsed the use of LPAs for detecting TB and MDR TB, which decreases time to diagnosis from weeks to a day, and which requires highly trained technical staff. The GeneXpert MTB/Rif (GX) molecular test assay provides TB case detection and rifampicin-resistance testing with results being available from raw sputum in about 2 hours and does not require highly trained personnel. Availability of this test will enable the rapid detection of MDR TB for point-of-care management of patients who can be referred for treatment timeously. In 2009, the NDoH set a target to roll out 20 new secondary laboratory services by the end of 2010 to achieve rapid diagnosis of MDR TB. However, only 11 laboratories were established by the end of 2010. In March 2011, the NDoH approved 25 sites in South Africa’s high-burden districts for GX to be installed; however, by the end of 2011, only 1 site had been fully capacitated. Lack of capacity at all sites for rapidly diagnosing
MDR TB is compounded by the current policy of only treating MDR TB based on DST, regardless of the results from the GX. This policy completely negates the advantages of using the GX to diagnose MDR TB. Although documentation was poor, 22 patients (11.8%) gave a history of a known MDR TB contact. There were 31 patients (16%) with primary MDR TB (i.e. no previous TB history), with an incidence of 55% in women and 45% in men. The high number of primary MDR TB patients in the sample is of concern, as it is much higher than the 1.8% of the MDR TB population estimated by the NDoH. Ours is a small sample but, if representative, it warrants further investigation. Based on this finding, healthcare workers must ensure that all high-risk patients presenting with TB are screened for MDR TB as per NDoH guidelines. In particular, HIV-positive patients with symptoms of TB need screening for MDR TB, as 71% of our patients with primary MDR TB were HIV-positive, with 59% of them having a CD4 count <250. HIV-positive patients have an 8.4 times higher risk of harbouring MDR TB strains than HIV-negative patients. A small percentage of patients did not know their HIV status; a larger percentage of the HIV-positive patients did not know their CD4 count; and a significant number of HIV-positive patients were not on ART. This suggests that gaps remain in the South African HIV counselling and testing programme. All patients with MDR TB should be on ART, according to the NDoH.13

Conclusion

There is a significant time delay in the initiation of effective treatment for patients with MDR TB. Most of the patients who presented to the clinic were coughing, thereby fuelling the spread of community-transmitted MDR TB. LPAs and the GX are ground-breaking discoveries for TB diagnosis; however, they are not yet easily accessible or available to those in need of it. In view of the findings from this study, current policy on the initiation of effective treatment based on these results will need to be revised urgently. In addition, all staff should receive appropriate training if the newer technology is to reduce delays in initiation of treatment for MDR TB. The NDoH’s proposed plans for rapid diagnosis and reducing the treatment burden on centralised MDR TB management facilities are all in the early phases of implementation, and it will take many more years to achieve a favourable and significant outcome.

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References


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