A Clinical Prediction Rule for the Diagnosis of Tuberculosis in Seriously Ill HIV-infected Adults

Rulan Griesel1, Annemie Stewart1, Helen van der Plas2, Welile Sikhondezi1, Molebogeng Rangaka3, Mark Nicol4, Gary Maartens1, Marc Mendelson2

1 Division of Clinical Pharmacology, Department of Medicine, University of Cape Town 2 Division of Infectious Diseases and HIV Medicine, Department of Medicine, University of Cape Town 3 Department of Infection & Population Health, University College London 4 Department of Microbiology, University of Cape Town

Introduction
Undiagnosed tuberculosis remains a major cause of death among hospitalised HIV-infected patients.1 The World Health Organization (WHO) algorithm for the diagnosis of tuberculosis in seriously ill HIV-infected patients presenting with danger signs (any one of respiratory rate >30/min; heart rate >120/min; temperature >39°C; unable to walk unaided) and cough for ≥14 days, recommends chest radiography and sputum smear results to start empiric antituberculosis therapy.2 Studies in high burden countries have shown that pulmonary tuberculosis commonly has an acute presentation (cough history <14 days) among HIV-infected patients.3,4 Tuberculosis symptoms (fever, night sweats, and weight loss) were omitted from the WHO algorithm and its development preceded the availability of the rapid Xpert MTB/RIF assay. We aimed to develop a clinical prediction rule (CPR) for the diagnosis of tuberculosis in seriously ill HIV-infected adults, by determining an evidence base for the duration of cough, the WHO danger signs, the role of tuberculosis symptoms, chest radiography, and simple laboratory tests (haemoglobin and white cell count). In addition we determined the diagnostic performance of Xpert MTB/RIF.

Methods
We conducted a cross-sectional diagnostic research study at 2 secondary level hospitals in Cape Town, South Africa, with a six-day follow-up period post-discharge.

Inclusion criteria: HIV-infected patients presenting with any cough duration and WHO danger signs, age ≥18 years and able to produce spontaneous/induced sputum.

Exclusion criteria: Patients who were unable to present to the hospital (transported), had a history of tuberculosis, 7 previous enrolment, 30 recently completed, 50 recently defaulted, 149 (31%) of the participants were auramine smear positive and 230 (48%) were Xpert MTB/RIF positive. Among the participants with culture-positive tuberculosis, 223 (54%) as possible tuberculosis, and 42 (10%) as unlikely tuberculosis.

Antituberculosis therapy was commenced in 309 (64%) participants, 256 (53%) of whom had culture-positive tuberculosis. 149 (31%) of the participants were auramine smear positive and 230 (48%) were Xpert MTB/RIF positive. Among the culture-positive tuberculosis patients, 73 (29%) had a cough duration <14 days.

Table 1 Baseline characteristics of 484 participants with WHO danger signs and cough

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Baseline characteristics</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Died in hospital</td>
<td>Median (IQR)</td>
<td>4 (1 to 6)</td>
<td></td>
</tr>
<tr>
<td>Discharged alive</td>
<td>Median (IQR)</td>
<td>11 (7 to 15)</td>
<td></td>
</tr>
<tr>
<td>Transfer to tertiary hospital</td>
<td>Median (IQR)</td>
<td>2 (1 to 4)</td>
<td></td>
</tr>
<tr>
<td>Days in hospital</td>
<td>Median (IQR)</td>
<td>7 (3 to 12)</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>Median (IQR)</td>
<td>2 (1 to 4)</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions
Our CPR could facilitate rapid initiation of empiric antituberculosis therapy among seriously ill HIV-infected patients presenting with a history of cough. Haemoglobin, WCC and chest radiography were the most important variables influencing the predictive ability of our CPR. A cut-off value used for the diagnosis of tuberculosis will depend on available resources, duration of patient illness and observer expertise. The classic tuberculosis symptoms had a low value in diagnosing tuberculosis among hospitalised seriously ill HIV-infected patients, which was unexpected given the strong evidence that these symptoms are helpful in outpatient studies. However, the WHO danger sign of inability to walk unaided was predictive of tuberculosis. Even though a cough duration of ≥14 days was predictive of tuberculosis in our cohort, there was a high prevalence of culture-positive tuberculosis participants with a cough duration <14 days, emphasising that tuberculosis often presents acutely. Xpert MTB/RIF performed well in our study population and where possible should be incorporated in the diagnostic work-up of tuberculosis.

References