

Organisation: International Hospital Kampala, Uganda

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Abstract: Uganda spend \$33 per capita each year on health. Sputum smear microscopy, to diagnose Tuberculosis, has the advantage of being low cost and simple to implement, especially in the developing world, which has the greater TB burden. The disadvantages of this simple test is that its sensitivity for the detection of all cases is low and is thought to miss up to 80% of all HIV co-infected TB cases² who have a higher mortality.

Uganda is twentieth on the WHO's list of high burden countries, with a TB incidence of 330 new cases per 100,000 population per year¹ with the current HIV prevalence in Uganda estimated at 6.5% amongst adults. The National TB reference laboratory estimates that up to 50% of patients with TB are co-infected with HIV/AIDS⁵. Uganda relies mainly on sputum smear microscopy for diagnosis of TB, with the Bactec 960 Mycobacterial Growth Indicator Tube (MGIT) culture system available for re-treatment and research cases. This investigation costs \$70 per test.

Microscopic Observed Technique (MOT) was developed in the low-resource, high TB-burden setting of Peru. It is a low-technology, low cost (\$5) liquid culture-based methodology performed directly on sputum samples.

In 2008 Dr Grania Brigden, a respiratory physician went as a VSO (Voluntary Services Overseas) volunteer to work at International Hospital Kampala. The TB laboratory had just been upgraded to a Category 2-3 biosafety level with a highly trained technician Bosco Byewako. Dr Brigden successfully applied for a grant from Target TB in UK to investigate the use of MOT to diagnose TB in HIV cases in Kampala. She started a trial of MOT compared with MGIT in 600 specimens and this work was continued by another VSO volunteer, Dr Richard Feinmann.

Having demonstrated that MOT had a sensitivity of 88% and a specificity of 98% compared with MGIT system the test was used routinely for investigating the HIV patients from the Touch Namuwongo outreach clinic.

A TB clinic was started at International Hospital and over 100 volunteers were trained to find patients with potential TB in the local community and administer treatment, using DOTS (Directly Observed Treatment).

All cases are cultured using the MOT system and then using a simple addition to MOT, drug resistance was tested for (MOD).

In keeping with VSO's vision of sharing skills, changing lives the programme is now run by Ugandan doctors, clinical officers, TB nurses and an increasing number of trained volunteers.

Methodology: Realising the lack of culture facilities in sub-saharan Africa and the excessive cost of most methods International Hospital Kampala installed a category 2-3 microbiology laboratory. MOT requires a highly trained technician to examine specimens as biosafety is an issue if TB organisms start to multiply on the liquid culture. The purpose of this project

was to investigate the effectiveness of deploying a microscopic observation technique (MOT) for clinical use in a low-resource, HIV-prevalent setting; and provided the trial gave sufficient validation, to start using this test for diagnostic purposes in a laboratory to test and treat patients referred from a community outreach programme.

The hospital then applied to VSO for volunteers and Dr Brigden was successful with a bid for funding from Target TB in the UK to fund this work using MOT.

The first part of the project involved doing a large trial of sputum culture using MOT and comparing the results with same specimens using MGIT. This is the first large trial of MOT in Africa and the first using MOT to investigate patients known to be HIV positive.

The study is a cross-sectional observational study. Samples were collected from 383 patients recruited from the Mildmay Centre and TASO Mulago in Kampala, Uganda from July 2008 to July 2009. Mildmay and TASO Mulago are diagnostic and treatment facilities for clients with HIV and currently have over 6500 active clients between them living within a 30 km radius of the centres.

Processed sputum specimens were inoculated in parallel into the MOTS and Bactec 960 MGIT culture systems and both ZN and IFM smears were performed on the resulting sediment. The detection and time to detection of *M. tuberculosis* growth was compared in these two systems with the Bactec 960 MGIT cultures acting as the gold standard for growth.

The median and range times to each end point for the different methods were calculated. The novel MOT method were compared to the MGIT gold standard approach by calculating the sensitivity, specificity, positive predictive value and negative predictive value.

Once this first part of the project was running a TB clinic was started at International Hospital in February 2009 to investigate and treat clients from Namuwongo, a very poor district of Kampala which has about 100,000 inhabitants. An outreach clinic known as "Touch Namuwongo" had been set up to manage HIV and had already collected 200 HIV positive clients when the TB clinic started.

The clinical team now consists of one physician, 2 TB nurses, 3 laboratory technicians, and 60 community based volunteers (CVW's). The CVW's have been very instrumental in community peer education exercises and provide weekly and monthly reports of their activities. We work with them during the weekly outreaches to schools, home visits and in community patient follow up. TB training is a 2 day non-residential workshop. Information covered in this workshop include issues on TB diagnosis, symptoms and signs of TB, HIV co-infection, treatment of TB and HIV, Adherence (pill counting), nutrition and general care of TB/HIV patients.

By August 2010 464 patients with symptoms of TB had been investigated.

Results: Phase 1

MOT has not been shown to be quite as sensitive as MGIT in this study; nevertheless it provided a diagnosis faster than MGIT at a substantially reduced cost. Where there are disagreements between MGIT and MOT these have been shown to be not MTB on PCR. Concentrating the sputum and keeping the TB organisms alive and then culturing is complex and requires a level 2-3 laboratory. This is necessary to reduce the biohazard of a potential huge increase in numbers of the organism some of which may be drug resistant. Health and safety is a key element of this procedure and considerable training of technicians is required.

1. Sensitivity of MOT as compared to gold standard (target 95%) = 86.4%
2. Specificity of MOT as compared to gold standard (target 80%) = 98.4%
3. Average number of days for MOT diagnosis (target <= MGIT) = 20.5 days
4. Average number of days from MGIT diagnosis (target 10dys) = 31 days
5. Marginal cost of MOT (expected \$10, target <= 25% MGIT) = \$8 for MOT, expanded test, MODS \$9
6. Marginal cost of MGIT (expected \$64) = \$75

Phase 2

Total number screened from touch Namuwongo = 464 patients

Total cases of Tuberculosis confirmed and initiated on treatment = 123 patients

Cases on treatment transferred in = 28 cases transferred in while on treatment

Cases transferred out = 9 cases transferred out

Deaths = 5 cases have died after diagnosis

Defaulters/loss to follow up = 23 defaulted, of which 6 have restarted treatment.

Drug resistance/treatment failure = 2 patients; have been referred to the National TB ward

High defaulter rates for TB treatment in Uganda are generally alarming. What we have done is to counsel patients at the beginning of therapy and provide reading material to further enhance importance of adherence to medications and appointments. We also take phone contacts and relative/friends number in order to be able to trace people. In some cases this has helped, but in others it hasn't worked well as phone numbers and addresses change

constantly and difficult to track some patients as when they feel better they move out of the slum to get jobs elsewhere. At the beginning of therapy, we attach a CVW to some patients who appear problematic, however even then they may fail to traces people.

This has been a successful community health project involving initially UK VSO volunteer doctors and funding from Target TB in UK. International Hospital is a hospital committed to improving healthcare in Uganda and the research project is to be published but the main outcome is the ongoing management of TB in Kampala by Ugandan health care workers. The research has provoked much interest and admiration from the National TB & Leprosy departments of the countries of sub-Saharan Africa.