

# Comparison With The Smart Check Recombinant TB Serology Assay And Direct Sputum Microscopy For Acid Fast Bacilli Among Suspected HIV Positive Patients In Northeastern Nigeria

M Kagu, A Ayilara, M Kawuwa, B Ali, G Gadzama

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## Abstract

Currently, the Sputum smear microscopy for acid fast bacilli is the corner stone of diagnosis of HIV associated active TB in Nguru, Northeastern Nigeria. This method has low sensitivity and specificity. In this study, we set out to compare the reliability of the Smart Check Recombinant TB rapid test kit with the routine direct sputum microscopy for acid- fast bacilli (AFB). Using Ziehl-Neelsen stained sputum smear microscopy for AFB as the standard, sensitivity and specificity of the Smart Check Recombinant TB rapid test kit was 96.7 % and 82.1 % respectively. These results show that the performance of the Smart Check Recombinant TB rapid test kit was adequate in comparison with direct sputum smear microscopy by sensitivity and specificity for the diagnosis of active TB in HIV infected patients when alternative is just clinical suspicion.

## INTRODUCTION

In 2003, the World Health Organization (WHO) reports that tuberculosis (TB) is the leading cause of death among people who are infected with the human immunodeficiency virus (HIV) <sup>1</sup>. Tuberculosis and HIV are a deadly duo: each speed up the progress of the other. In sub-Saharan Africa alone, approximately 31% of all new TB infections were attributable to HIV. An estimated 14 million adults in the world live with both TB and HIV; the highest number of those 14 million being reported in sub-Saharan Africa <sup>2, 3</sup>. In Nigeria several reports have shown high prevalence of HIV-infection among TB infected patients <sup>4,5,6,7,8</sup>. Traditional methods of diagnosis of TB include; tuberculin skin test, sputum smear microscopy, sputum culture and chest x-rays. Tuberculin skin test is of limited diagnostic value in HIV associated TB <sup>9,10,11</sup>. Sputum smear microscopy for acid fast bacilli is the corner stone of diagnosis of pulmonary TB in most developing countries. However, in countries with a high prevalence of both TB and HIV infection, the detection rate of acid-fast bacilli by sputum smear microscopy is low. This may be partly because of the paucibacillary nature of pulmonary TB in HIV infected patients <sup>12</sup> and also due to lack of high quality microscopy services and shortage of skilled staff in our laboratories. Sputum culture for acid-fast

bacilli using solid egg-based media (Lowenstein-Jensen medium) is the gold standard and much more sensitive than the routine sputum smear microscopy<sup>13</sup>. However, it is not readily available in most of our laboratories. Similarly, chest radiographic findings in HIV associated TB is non-specific <sup>14</sup>. Some newer test such as DNA probes are also available but have a tendency for a high degree of false positive in high prevalence areas. These tests are also expensive and not practical for developing countries. New serological tests such as the Smart Check Recombinant TB rapid test are among the simplest and fastest means of detecting active mycobacterium tuberculosis infection in HIV infected patients. In this study, we set out to compare the reliability of the Smart Check Recombinant TB rapid test kit with the routine direct sputum microscopy for acid- fast bacilli (AFB).

## MATERIALS AND METHODS

This was a prospective study carried out at the Federal Medical Centre Nguru, Yobe State. Nguru, the headquarters of Nguru Local Government Area of Yobe State, northeastern Nigeria is situated in the extreme northern part of the state. It is an arid zone situated in the Sahel Savannah surrounded by wetlands- the Hadejia-Nguru wetlands. The

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mean annual temperature is 32°C to 42°C while the annual rainfall is below 100cm lasting for a period of three months from July to September. The main occupations of the people are subsistence farming and fishing and lack basic amenities like piped-borne water, electricity and proper waste disposal facilities. The Hospital is a Federal Medical Center established 8 years ago and serves the population and the surrounding villages, some of which take about four hours by hand- peddle canoe and one hour to reach by motorized boats. This area is endemic for pulmonary TB with a rising prevalence of HIV infection amongst its population.

A total of 218 confirmed HIV positive patients with suspected pulmonary tuberculosis were evaluated during the period August 2005 to February 2006. None of the patients included were on either anti-retroviral drugs or anti-tuberculosis drugs at the time of sample collection. After proper counseling and dully obtaining consent, three consecutive early morning sputum samples were collected in leak proof containers from each patient; the samples were then subjected to Ziehl-Neelsen staining method using hot Technique according to World Health Organization standard<sup>15</sup>. Duplicate stained slides were examined by a trained medical microbiologist and two laboratory scientists.

The Smart Check Recombinant TB Rapid Device (Serum or WB), (catalog #: 06044004BM, GLOBALEMED, LLC, 1101 King St., Suite 370, Alexandria, Va. 22314-2944, URL: www.globalmed.com) kit was used for the serological diagnosis of pulmonary tuberculosis. This kit is the newer generation lateral flow immunochromatographic type assay. The test employs the use of an antibody binding protein conjugated to a colloidal gold particle and a unique conation of TB antigens immobilized on the membrane. Once the sample is added (serum was used in our study) to the test cassette along with the diluents, the mixture passes through the antibody binding/gold complex, which then binds the immunoglobulin in the sample. As this complex passes over the immobilized recombinant antigens on the membrane, if any antibodies to tuberculosis are present the recombinant antigens capture them in turn. This produces a pink/purple band in the B zone of the test card. The remaining complex continues to migrate to a control area in the test card and produces a pink/purple band in C area. This control band indicates that the test has been performed properly. Manufacturer's instructions were strictly adhered to.

SPSS Software version 11.0 for windows was used for all statistical analysis. For sensitivity and specificity, the test

kits were compared with the Ziehl-Neelsen stained direct sputum smear microscopy results. Sensitivity was calculated as the proportion of positive test results obtained among samples containing TB bacilli by microscopy; specificity was calculated as the proportion of negative test results obtained among samples whose sputum smear were negative. Positive predictive values (PPVs) and negative predictive values (NPVs) were calculated as the proportion of true positive results among all positives reactors and as the proportion of true negative results among all negative reactors, respectively.

## RESULTS

A total of 218 confirmed HIV positive patients with suspected pulmonary TB were evaluated. Their median age was 30 years (range 4-90 years). There were 140 (64.2%) males and 78 (35.8%) females. Of 218 patients evaluated, 158 (72.5%) patients were diagnosed as cases of active TB by Smart Check Recombinant TB serology and 151 patients (69.3%) by direct sputum smear microscopy. Tables I and II shows the cross tabulation of TB serology and sputum AFB microscopy as well as the sensitivity, specificity, positive predictive value and negative predictive value respectively.

### Figure 1

Table 1: Direct sputum smear microscopy and Smart Check Recombinant TB serology for the diagnosis of HIV associated active pulmonary TB.

TB SEROLOGY	DIRECT SPUTUM AFB MICROSCOPY		
	Positive	Negative	Total
positive	146	12	158
Negative	5	55	60
Total	151	67	218

### Figure 2

Table 2: Sensitivity and specificity of the Smart Check Recombinant TB serology assay for detecting HIV associated active pulmonary TB

	Microscopy
Sensitivity	96.7%
Specificity	82.1%
Positive predictive value	92.4%
Negative predictive value	91.7%

## DISCUSSION

The Smart Check Recombinant TB rapid test kit is a useful diagnostic tool for the rapid diagnosis of active tuberculosis

in HIV infected patients with suspected TB in this environment. This rapid test kit is among the simplest and fastest means of identifying active mycobacterium tuberculosis in HIV infected patients. The major goals of developing such tests was that these should be handled with ease and accuracy by relatively unskilled staff in developing countries where high quality microscopy services and skilled staff for direct sputum smear examination and/or sputum culture detection are lacking.<sup>16</sup> The reported sensitivity of AFB microscopy vary considerably from more than 70 % to as low as 30 % to 40 %, <sup>17,18,19,20</sup> depending on a number of factors relating to how the test is implemented. Sputum digestion with sodium hypochlorite and concentration by centrifugation which can improved the sensitivity of AFB microscopy is not employed in most of our laboratories due to lack of high quality microscopy services and shortage of skilled staff. The Smart Check Recombinant TB rapid test kit can be used by relatively inexperienced person to diagnosed active TB in HIV infected patients even in rural areas where microscopic facilities are not available.

In conclusion, the performance of Smart Check Recombinant TB rapid test kit was adequate in comparison with Ziehl-Neelsen stained direct sputum smear microscopy by sensitivity and specificity.

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**Author Information**

**M.B. Kagu, FMCpath, Cert Immunology**

Lecturer and Consultant Haematologist, University of Maiduguri Teaching Hospital

**A. O. Ayilara, FIMLS**

Medical Laboratory Scientist, Federal Medical Centre

**M.B. Kawuwa, FWACS**

Lecturer and Consultant Obs/Gynaecologist, University of Maiduguri Teaching Hospital

**B. Z. Ali, AIMLS**

Medical Laboratory Scientist, Federal Medical Centre

**G. B. Gadzama, FMCpath**

Lecturer and Consultant Medical Microbiologist, University of Maiduguri Teaching Hospital