Use of the GeneXpert tuberculosis system for HIV viral load testing in India

The Xpert MTB/RIF assay (Cepheid; Sunnyvale, CA, USA) on the GeneXpert molecular system, which was endorsed by WHO in 2010, is the biggest advance in tuberculosis diagnosis and the most scaled-up new tuberculosis technology. Between 2010 and 2016, more than 6500 GeneXpert machines and 23 million Xpert assay cartridges were procured in the public sector in 130 of the 145 countries eligible for concessional pricing.1 India alone has acquired more than 750 GeneXpert systems in the public sector and more than 100 systems in the private sector. However, GeneXpert systems are often underused because of high cost, restrictive algorithms, inadequate decentralisation, exclusion of the private sector from concessional pricing, and weak implementation of policies.2

One potential solution is to expand access to tuberculosis testing, while simultaneously using the GeneXpert platform to test for other diseases of global health importance. Given the high co-prevalence of tuberculosis and HIV in many settings, and the need for greater integration of tuberculosis and HIV services, it makes sense to use the GeneXpert technology for HIV viral load testing.

The new global 90-90-90 targets for HIV/AIDS require scaled-up HIV-1 viral load testing,3 which is the preferred approach to assess treatment efficacy and confirm suspected treatment failure.4 The use of viral load testing to assess treatment failure can reduce delays in switching to second-line drugs and limit unnecessary switching, thus reducing accumulation of drug-resistance mutations and improving clinical outcomes.5 High viral loads can also indicate non-adherence and identify patients who could benefit from adherence support.

Although viral load testing is critical for antiretroviral therapy roll-out, access to such testing remains a problem in many countries.6,7 Current assays require sophisticated facilities, expensive equipment, and skilled technicians, making them impractical for widespread use in resource-constrained settings.3 As such, patients in low-income and middle-income countries are mostly managed by CD4 cell counts and clinical staging. In India, serious concerns have been expressed over the scarcity of adequate access to HIV viral load testing; according to one estimate, more than 800000 tests are needed annually, whereas only about 7000 are being done.7

In this context, the Xpert HIV-1 Viral Load (Cepheid) cartridge was launched in 2014, as a potential point-of-care, rapid viral load assay. However, before the Xpert HIV-1 Viral Load cartridge can be clinically used in India, validation is essential. In March, 2017, Xpert HIV-1 Viral Load cartridges were approved by the Indian regulatory agency, but there are no published data on test performance in India. We validated a research use only version of this new HIV-1 viral load assay in India, in a hospital setting where GeneXpert was already used for tuberculosis testing.

We recruited 246 known HIV-1-positive adults receiving care at Kasturba Medical College, Attavar Hospital in Mangalore, India, between July, 2016, and September, 2016, irrespective of antiretroviral therapy status. 146 (60%) were male and 172 (70%) were receiving antiretroviral therapy. The median age of participants was 41 years. We assessed the correlation between the viral loads obtained from Xpert and from a current reference standard—the COBAS TaqMan HIV-1 assay (Roche Molecular Diagnostics, CA, USA). This assay was performed in an accredited, centralised, national chain laboratory. Ethics approval was obtained and all participants provided written informed consent. Clinical decisions were made using the TaqMan assay.

Of the 246 blood samples collected, 21 (9%) were precluded from testing because of insufficient blood volume or breaks in the cold chain. These events were unlikely to be related to the viral loads of the patients. Of the 225 (91%) patient samples remaining, 22 tests generated Xpert error results and 17 tests were invalid, resulting in an Xpert error and invalid rate of 17%. 10 samples were retested and their results were included in subsequent analyses. Ultimately, 196 samples had valid Xpert results. Of these, 89 (45%) patients had viral load values above the lower limit of detection for Xpert

Figure: Comparison of the Xpert viral load assay with the reference standard
(A) Pearson correlation plot of GeneXpert and COBAS TaqMan viral loads. Pearson’s r coefficient indicates the strength of the linear relationship between two variables, where values close to 1 indicate stronger linear relationships. (B) Bland-Altman scatter plot. Bias was defined as the COBAS TaqMan log_{10} copies/mL of viral load minus the Xpert log_{10} copies/mL of viral load. The solid red line indicates the mean bias and the dashed red lines show the limits of statistically acceptable bias defined as the mean bias ±1·96 SD of bias.
and the reference. The turnaround time from specimen collection to receipt of results was less than 1 day for Xpert assays, compared with 7–10 days for TaqMan assays (including sample transportation time).

We compared the Xpert viral load results with the reference standard and the Pearson correlation coefficient was 0.96 (95% CI 0.94–0.97; figure). Bland-Altman analysis showed close quantification of the samples with a mean bias of 0.133 (95% CI 0.073–0.192), and 96.6% of viral load pairs fell within the threshold of statistical acceptability. Our results are consistent with similar validation studies in other countries. 8–16

After a detailed investigation by the company, the high invalid and error rate was primarily attributed to a suboptimal cartridge lot. We also identified supply chain issues, such as broken cartridges during shipping and a defect that caused plasma sample leakage within the cartridge.

In summary, our data show that the results of the Xpert HIV-1 Viral Load assay correlated highly with the current reference standard and therefore could be considered for wider use in India by using the large installed base of GeneXpert systems in the tuberculosis programme. However, the supply chain and quality issues we identified will need to be adequately investigated and addressed. In addition, subsidised pricing, similar to that of the Xpert tuberculosis cartridge, will be essential for scaled-up use in India.

We declare no competing interests. This project was supported by a Dr TMA Pai Endowment Chair in Translational Epidemiology & Implementation Research held by MP at Manipal University, India. MN received a Cavazzoni Family Undergraduate Research held by MP at Manipal University, India. We are grateful to Cepheid India for their engagement and support, and for addressing the supply chain issues identified during the project.