Indian J Med Res 126, September 2007, pp 171-173

Editorial

Rapid oral fluid-based point-of-care HIV testing: applicability in developing countries

In India, specific high risk sub-populations (*i.e.* sex workers, clients of sex workers, men who have sex with men and intravenous drug users) and their interactions with susceptible populations (*i.e.* spouses and partners) have created a complex heterogeneous HIV epidemic[1]. An estimated 5.7 million individuals were reported to be living with HIV in India, although this estimate excludes individuals living with undiagnosed HIV infection[2,3]. According to new estimates, 2.5 million people in India are living with HIV[4]. Many factors may reduce the acceptability and uptake of voluntary HIV counselling and testing, and result in undiagnosed HIV. These include stigma and discrimination by the community, health professionals and the society at large[2], poor awareness about availability of testing and anti-retroviral treatment (ART) services, lack of information on benefits of early detection and treatment. Efforts to control the HIV epidemic in India can be undermined by ongoing HIV transmission by undiagnosed individuals. Although HIV prevalence in some southern States is reported to be on a decline, to further control the epidemic and to curtail its spread, it is essential to enhance HIV testing, and reduce the number of undiagnosed individuals[1].

To detect undiagnosed HIV, in a rapid, accurate, time and cost-effective manner, high quality rapid point-of-care HIV tests are useful tools. A vast majority of rapid point-of-care HIV tests in India are blood based (*i.e.* they require whole blood, plasma, serum, or finger stick blood), while a few utilize alternative body fluids such as oral fluid, saliva and urine[5,6]. Oral rapid point-of-care HIV tests score over blood-based HIV tests in their quality, rapidity, convenience, ease of sample collection, and feasibility of use in traditional and non-traditional settings[7].

In India, widely used blood-based rapid HIV tests are based on older technology such as dot-blot, often require laboratory technicians, and take longer time (*i.e.* 30 min-2 h) to deliver results[7]. In emergency settings (*e.g.* emergency wards and labour rooms), this may be a disadvantage. In non-traditional outreach and rural settings, laboratory technicians are not always available, and clients are unlikely to return for receipt of test results when results are not available immediately. In such settings, rapid oral fluid point-of-care HIV testing may be an ideal solution.

Why are tests referred to as oral fluid tests? Oral fluid-based HIV tests sample oral mucosal transduate (OMT), an interstitial fluid from the capillaries of the gingival gum margin[8,9]. OMT is a salivary component, with a high concentration of IgG antibodies[10]. Currently, two oral rapid point-of-care HIV tests are available in many countries worldwide, and are currently undergoing approval in India. OraQuick® ADVANCE HIV 1/2 (Orasure Technologies Inc, PA, USA) is a US Food and Drug Administration (FDA) approved test[10]. Calypte® AWARE HIV 1/2 (Calypte Biomedical Corportation, OR, USA) is another rapid oral fluid test, but is not currently FDA approved.

What data exist on the performance of oral fluid-based HIV tests in India? Recently, a study done in a rural hospital in Sevagram, Maharashtra, found the oral fluid-based newer OraQuick® Rapid HIV1/2 test to be highly accurate[7]. When compared to a reference standard of dual ELISA and Western Blot, the estimated sensitivity and specificity was 100 per cent among 450 patients with suspected HIV[7]. In comparison to blood-based rapid tests and conventional testing (*i.e.* ELISA and Western Blot), the oral fluid-based test was the most preferred test by the study participants[7]. In previous years, two other fairly large studies of oral fluid testing in pregnant women were conducted in urban settings[11,12]. In both studies, pregnant women in antenatal clinics and labour rooms were tested with a battery of rapid

HIV tests including OraQuick® Rapid HIV saliva brush test. In the first study, 1244 pregnant women in labour were tested with an earlier version of the OraQuick test and a lower diagnostic accuracy (sensitivity 75%, specificity 100%) was reported, probably due to the use of a weak reference standard (*i.e.* ELISA)[11]. In the second study, of 1322 eligible women, 582 consenting pregnant women in labour and delivery rooms were tested with many rapid tests including OraQuick® Rapid HIV saliva brush test and 9 found HIV positive (1.6%) were counselled successfully[12]. These studies have demonstrated that oral fluid-based HIV tests can work well in both urban and rural settings. In other settings worldwide, these tests have been well accepted by clients and have reported high diagnostic performance[13-15].

What concerns are to be kept in mind in the conduct of these tests? Although the diagnostic accuracy of oral fluid-based tests is high, their accuracy and clinical utility depend on disease prevalence, clinical presentations of populations, and type of populations tested[6,8]. Thus, false-positive, false-negative and non-reactive results can occur with oral-fluid testing, as with any rapid HIV testing. When isolated instances of false positives or false negatives occur, diagnostic performance is often called into question, and might result in good tests falling out of favour. For example, reports of false-positive OraQuick oral tests created a lot of concern and uncertainty in the United States a few years ago[16]. To minimize test error, and obtain consistent, high quality results, quality control and quality assurance procedures must be strictly followed[17]. These procedures involve running external serum controls after opening each test kit lot, maintaining temperature logs in the testing room, discarding poorly performing batches of kits and maintaining quality assurance at all times even in outreach settings[17]. Further, certain medical conditions (*i.e.* lupus, syphilis, hepatitis, IgM and IgG gammopathy) and interfering substances (*i.e.* heparin) can produce non reactive results[9]. These conditions should be kept in mind while interpreting test results[6]. Like any rapid point-of-care test, oral fluid tests cannot, however, diagnose acute HIV infection. Thus, re-testing high risk populations at three to six months intervals, can detect sero-conversions[18]. Further, like all rapid tests, oral point-of-care HIV test results must be considered as preliminary and require confirmation with reference standard tests such as ELISA, Western Blot or immuno-fluorescence assays[10,18].

What are the barriers and challenges in the widespread implementation of oral fluid rapid tests in India? In India, stigma is a major deterrent to effective uptake of voluntary rapid testing[3]. Therefore, testing programmes must provide client-centered, post-test counselling sessions in a private setting where privacy and confidentiality is priority. Also, it is known that rural patients do not prefer to give blood specimens, due to cultural reasons. Oral fluid specimens, therefore, may be more culturally acceptable and feasible. This, in turn, can help expedite early detection, and establish linkages to ART that may transform to substantial cost savings in the long run.

In what settings are oral rapid tests useful? In occupational exposure settings, oral tests can help greatly to expedite diagnosis, thus reducing anxiety and help with early use of ART in those exposed[19]. Use of oral fluid tests in labour and delivery settings can expedite delivery of interventions for reducing perinatal HIV transmission[11,13,20]. Use of oral fluid-based rapid HIV tests in community based surveys can help estimate the true HIV burden in India. Future studies on evaluating the impact of these tests on (*i*) rapid delivery of interventions to reduce perinatal HIV transmission in labour rooms, and (*ii*) behaviour modification of high risk clients in outreach settings require investigation[13]. In developed country settings, the use of oral fluid tests for home-based HIV self testing is being actively pursued. The role for home-based self HIV testing in developing countries such as India, is uncertain.

Several countries in Sub-Saharan Africa and Asia have approved the use of oral fluid based point-of-care HIV tests (Quoc Pham, Director Asia, Orasure Technologies, Inc, PA, USA, Personal Communication). The time is ripe for their use in India to scale up HIV screening and testing programmes. Their simplicity, versatility and feasibility enable their implementation in various settings (*e.g.* voluntary counselling and testing centres, private practitioners, outreach and emergency settings). Incorporation of oral HIV tests could form part of a multi-pronged prevention strategy in transforming the trajectory of the HIV epidemic in India.

Conflict of Interest

Dr Pant Pai has no conflict of interest with Orasure Technologies, Inc, PA, USA.

Acknowledgment

Dr Pant Pai is supported by a fellowship from the Canadian HIV Trials Network (CTN).

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