SUPPLEMENT ARTICLE

Surveillance of Transmitted Drug-Resistant HIV Among Young Pregnant Women in Ouagadougou, Burkina Faso

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Burkina Faso began rapid antiretroviral therapy (ART) scale-up in 2003 and by December 2009, 26 448 individuals were on treatment. With rapid scale-up of ART, some degree of human immunodeficiency virus transmitted drug resistance (TDR) is inevitable. Following World Health Organization methods, between June 2008 and July 2009, Burkina Faso assessed TDR in primigravid pregnant women aged <25 years attending antenatal care clinics in Ouagadougou, Burkina Faso. TDR was classified as moderate (5%–15%) for both nucleoside reverse-transcriptase inhibitors and nonnucleoside reverse-transcriptase inhibitors. The observed moderate TDR in Ouagadougou is a cause for concern and calls for closer monitoring of Burkina Faso's ART program.

Burkina Faso is a landlocked country in West Africa with 274 200 square kilometers and an estimated population of 15 224 780. The country is divided into 13 regions, 45 provinces, and 350 departments. Burkina Faso has one of the world's lowest gross domestic products per capita and faces a generalized human immunodeficiency virus (HIV) epidemic. In 2009 there were an estimated 130 000 individuals (63 429 women) infected with HIV [1]. In the capital city Ouagadougou, HIV prevalence among pregnant women is 4% [3.0% – 5.3%], and the prevalence in women aged 15–24 years is 2.4% [1.4%–4.0%]. By December 2009, the national antiretroviral therapy (ART) program estimates that 26 448 individuals were receiving ART [2].

Successful ART scale-up in Burkina Faso has been possible because of the use of a standardized public health approach to HIV care and treatment. Since 2010, ART has been provided free of charge in the public sector, and patients are predominantly prescribed standardized first-line ART regimens and monitored following World Health Organization (WHO) clinical staging guidelines and CD4 cell count. The first-line ART regimen and 3 alternate first-line regimens consist of 2 nucleoside reverse-transcriptase inhibitors (NRTI) combined with a non-NRTI (NNRTI). Protease inhibitor–based regimens are generally reserved for second-line regimens. Despite Burkina Faso's unprecedented rapid ART scale-up, coverage of those patients in need is estimated at 52%, suggesting a large and ongoing unmet treatment need.

Given the current economic situation, limited human resources, and existing infrastructure within the country, individual HIV drug resistance (HIVDR) testing is neither routinely available nor recommended. However, as ART is scaled up in Burkina Faso, the emergence and transmission of HIVDR remains a fundamental concern. Beginning in 2008, following WHO recommendations, Burkina Faso implemented a comprehensive national HIVDR prevention and assessment strategy that includes

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assessment of HIVDR early warning indicators and surveys of transmitted and acquired HIVDR [3–5]. This comprehensive national strategy will provide Burkina Faso's ART program with standardized information evaluating HIVDR in the country and how well the program is functioning to minimize its emergence and transmission.

This report documents Burkina Faso's pilot of the WHO transmitted HIVDR (transmitted drug resistance [TDR]) survey. The presence of HIVDR before ART initiation is an important predictor of virological response to antiretroviral regimens [6, 7]. Therefore, the existence of significant population level TDR may undermine the success of the national ART scale-up initiative. WHO TDR surveys provide important programmatic information regarding the likely efficacy of future first-line ART and current pre-and postexposure prophylactic regimens and will indirectly provide evidence of how well current HIV prevention programs function in preventing new infections. Ouagadougou, the capital of Burkina Faso, was chosen for this pilot because it is a large urban area where ART had been available since 1999.

The WHO TDR survey method supports classification of TDR as low (<5%), moderate (5%–15%), or high (>15%) in a specific population in a specific geographic region using ≤47 specimens. The TDR mutations are determined using the WHO TDR mutations list available through the Stanford HIVDR Calibrated Population Resistance tool [8, 9].

METHODS

Burkina Faso adapted its TDR survey from the WHO generic protocol. Between May 2008 and June 2009, specimens for HIVDR testing were obtained from consecutively diagnosed HIV-positive women attending 11 antenatal care sites in Ouagadougou. Specimens consecutively identified as positive were eligible for HIVDR testing if they were from primigravidae (and therefore not previously exposed to antiretrovirals for prevention of mother-to-child transmission), aged <25 years (and therefore more likely to be recently infected with HIV) and with no previous history of HIV infection. Remnant diagnostic plasma specimens from women meeting TDR survey inclusion criteria were transported within 72 hours to the University Hospital Center–Yalgado Ouedraogo (CHU Yalgado), frozen at −20°C, and then shipped on dry ice to the Institut de Recherche pour le Developpement, a WHO-accredited HIVDR testing laboratory in Montpellier, France.

HIV reverse-transcriptase and protease were amplified by means of previously published methods [10]. TDR mutations were identified using the 2009 WHO TDR mutations list [6], and TDR was classified following WHO TDR guidance [2]. HIV subtypes and circulating recombinant forms (CRFs) were determined by phylogenetic tree and recombination analysis [11].

RESULTS

In total, 52 HIV-positive specimens meeting eligibility criteria were obtained between June 2008 and July 2009. Among the first 47 specimens, 3 had detected HIVDR: the first specimen had the NRTI mutations M184I and G190A, the second had the NNRTI mutation Y181C, and the third had both NRTI (K70R, M184I, T2115I/T, K219E) and NNRTI mutations (K103N, Y181C). To exclude erroneous inclusion of ART-exposed women, eligibility criteria were double-checked for specimens with HIVDR. The observed HIV subtype distribution was CRF 06_CPX (34%), CRF 02_AG (10.6%), G (6.38%), and A1 (2.1%). Following WHO truncated sequential sampling guidance [2], TDR was classified as moderate (5%–15%) for both NRTIs and NNRTIs.

DISCUSSION

ART scale-up began rapidly in Burkina Faso in 2003. Some degree of HIVDR is inevitable even when appropriate regimens are prescribed and optimal adherence to treatment is supported. Routine surveillance of TDR provides important public health information regarding the efficacy of current pre- and postexposure prophylaxis and may predict the population-level efficacy of first-line regimens when recently infected populations require ART.

Burkina Faso is one of the first countries in sub-Saharan Africa to report moderate TDR using the WHO TDR survey method. Notably, a previous TDR survey conducted in 2005 following WHO guidance in Bobo Dioulasso, the second largest city in Burkina Faso, classified TDR as <5% for all drug classes [11], and much of the published literature suggests low rates of TDR in sub-Saharan Africa [13–18]. The findings of moderate (5%–15%) TDR for NRTIs and NNRTIs in young primigravidae with no previous antiretroviral exposure merit concern and warrant further investigation. Rigorous quality assurance of both laboratory and epidemiological data were performed to ensure that each specimen came from a woman meeting eligibility criteria. This was of particular importance, given that the third specimen had multiple NRTI and 2 NNRTI mutations, which raised concern for possible acquired HIVDR.

Results of TDR surveys cannot be interpreted adequately in isolation and require a programmatic context for interpretation; therefore, the Burkina Faso ART program is implementing early warning indicators, such as rates of lost to follow-up, retention rates on first-line ART at 12 months, on-time pill pick-up, and drug supply continuity at ART clinics. The routine monitoring of these indicators will provide important clinic and program

information about factors contributing to emergence of HIVDR in populations receiving ART in Ouagadougou and throughout the country. Additionally, the result of this TDR survey reinforces the need to strengthen prevention and adherence support interventions for those receiving ART.

To further investigate the relationship between clinic and site factors that may be leading to emergence of HIVDR, Burkina Faso has implemented WHO surveys of acquired HIVDR in 2 ART clinics and plans to repeat the TDR survey in the same population in Ouagadougou and expand it to other areas of the country in the near future.

CONCLUSIONS

In conclusion, although the findings of moderate TDR are of concern, they should be treated with caution. Present findings are insufficient to change current ART guidelines in Burkina Faso but do signal the importance of routine robust programmatic monitoring of factors know to be associated with the emergence of HIVDR at all treatment sites and the need for ongoing routine surveillance of transmitted and acquired HIVDR.

Notes

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