EDITORIAL

Antiretroviral Therapy Program in Ethiopia Benefits From Virology Treatment Monitoring

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Introduction of combination ART was instrumental to mitigate the burden of HIV pandemic in Ethiopia and other resource limited settings. Combination ART archives sustained HIV viral suppression and contributes to reductions in mortality, progression to AIDS, opportunistic infections (OIs), and hospitalization (1). Viral suppression is also associated with decreased HIV transmission to uninfected persons. In Ethiopia, improved coverage of free antiretroviral therapy (ART) program helped to enroll hundreds of thousands of ART needy people living with HIV; an overall ART coverage reached 73% (2-3).

Failure of antiretroviral treatment and toxicity are feared complication of long-term ART users. Noncompliance to medical instruction and poor adherence fosters emergence of drug resistant mutant. An observational cohort study from HIV clinic in South Africa which enrolled 19,645 patients (29,935 person-years) showed that 9.9% of first line ART (4.5/100 person-years) failed at median 16 (IQR: 12–23) months following ART initiation. Five years following ART treatment, the failure rate was 16.9% and 7.8% when using a confirmatory threshold of 400 and 10,000 copies/ml, respectively. The same study reported a 10.1% overall rate of switch to second-line by five years on ART (4). The emergence of primary and secondary HIV drug resistance is on the rise due to accumulation of mutant HIV strains and weak error proof reading capability of the virus. A systematic review of studies on prevalence of HIV-1 drug resistance in treatment-naïve individuals in resource-limited settings since roll out of ART programs, showed the highest estimated rate of increase at 29% per year (95% CI 15 to 45; p=0.0001) in East Africa; an estimated prevalence of HIV-1 drug resistance at eight years after ART program is 7.4% (5). Moreover, there is an increase incidence of resistance to non-nucleoside reverse transcriptase inhibitors in East Africa (36% per year; p<0·0001) and Southern Africa (23% per year; p=0·0049). Among the subset of studies reporting treatment failure with HIV-specific resistance mutation data (27 studies with 734 patients), the most common mutations were the M184V mutation, found in 65% of patients, and the K103N mutation, found in 52% of patients (5-6).

The clinical and epidemiological implications of drug toxicity and treatment failure from HIV drug resistance are huge. In addition to mortality and morbidity, the increased transmission of HIV resistant virus to intimate sex partners and increased health care cost will be enormous. At individual patient level, failed ART regimen or HIV drug resistance limits treatment options,complicates succession of therapy and puts the patient at increased risk for drug toxicity from second-line regiments who may need close vigilance and laboratory monitoring. In addition, limited availability of laboratory services such as drug toxicity screening, HIV virology and drug resistance testing monitoring may contribute to delay in diagnosis of treatment failure in resource limited setting where virology monitoring is not a component of routine ART monitoring (6-8).

The World Health Organization (WHO) recommends viral load determination, if feasible, to improve the identification of treatment failure. Due to financial and logistical constraints in resource limited settings, however, access to this expensive and technically demanding test is limited. Therefore, as a substitute, WHO-recommended clinical criteria and CD4 cell counts are commonly used by clinicians to diagnose ART

failure and guide treatment switch (9). In the absence of viral load monitoring, unnecessary regimen switches are common, resulting in increased treatment costs and loss of future options for treatment succession. Also, late detection of treatment failure results in high frequencies of accumulated mutations conferring broad cross-resistance to NRTIs, which may impair the success of the program. Therefore, it is vital to understand factors that determine success of ART and treatment follow up for such evidence informs program monitoring, quality and safety of HIV prevention, treatment and care services in Ethiopia. In this special edition of the EJHS, the authors present readers insightful articles on antiretroviral therapy program in Ethiopia with emphasis on antiretroviral therapy monitoring and lessons learnt from the ACM cohort of HIV positive individuals enrolled to ART program in seven university hospitals at higher education institutions across Ethiopia. It is very much hoped that esteemed readers will read through the articles in this edition. It is also believed that the evidences and lessons learnt from these articles will encourage further research, incite scientific debate on treatment monitoring and inform national guidelines on HIV/ART program monitoring.

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This special issue focuses on the primary aids of the advanced clinical monitoring of ART in Ethiopia as stipulated on the mother protocol – (a) evaluation of treatment effectiveness, (b) assessment of monitoring protocols, (c) assessment of adverse effects of treatment, (d) assessment of adherence, and, (e) insight into potential causes of early mortality. It has 6 papers that deals on the establishment of the multi-site clinical cohort, exploratory analysis of time from HIV diagnosis to ART Start, factors associated with mortality of TB/HIV co-infected patients, magnitude of ART related toxicity, predictors of hospitalization of pediatric patients on ART and survival of adults on ART. The papers give insight into the ART program which cannot be found from the routine programmatic reports. We hope you will enjoy reading the papers.

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