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The impact of HIV-1 subtypes on virologic and immunologic treatment outcomes at the Lagos University Teaching Hospital: A longitudinal evaluation

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Abstract

Introduction

HIV is a highly diverse virus with significant genetic variability which may confer biologic differences that could impact on treatment outcomes.

Materials and methods

We studied the association between HIV subtypes and immunologic and virologic outcomes in a longitudinal cohort of 169 patients on combination antiretroviral therapy. Participants were followed up for 5 years. Demographic data, CD4 cell count and viral loads (VL) were extracted from medical records. Whole protease gene and codon 1–300 of the reverse transcriptase gene were sequenced and analysed.

Results

Sixty-four percent of participants were females with a median age of 35 years. Twelve different subtypes were observed, the commonest being CRF 02_AG (55.0%) and subtypes G (23.1%). All subtypes showed steady rise in CD4 count and there was no difference in proportion who achieved CD4+ cell count rise of ≥100 cells/μL from baseline within 12 months' post-initiation of ART, or ≥350 cells/μL at 60 months' post-initiation. Median time to attaining a rise of ≥350 cells/μL was 24 months (6–48 months). The proportion that achieved

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undetectable VL at month 6 and 12 post-initiation of ART were comparable across subtypes. At end of 5th year, there was no statistical difference in proportion with virologic failure.

Conclusion

No association between HIV subtypes and immunologic or virologic response to therapy was observed, suggesting that current first-line ART may have similar efficacy across subtype predominating in South-West Nigeria.

Introduction

HIV-1 remains a global health problem of unparalleled magnitude, with an estimated 36.9 million people living with HIV in 2017 [1]. The pandemic is dynamic, with 1.8 million new infections each year. An estimated 3.2 million Nigerians are currently estimated to be living with HIV, making it the second largest epidemic worldwide [2].

HIV-1 is a highly diverse virus due to significant genetic variability. It is classified into four groups: M (major), group O (outlier), group N (nonmajor nonoutlier), and P [3, 4]. HIV-1 group M is the most prevalent circulating group, has nine subtypes (designated A to D, F to H, and J and K), numerous circulating recombinant forms (CRFs) and multiple unique recombinant forms (URFs) [4, 5].

The distribution of HIV-1 subtypes and recombinants across the world varies and this regional diversity may have clinical implications. CRF02_AG is the fourth most prevalent subtype globally, together with subtype G remain the dominant variants observed in West Africa [6]. In Nigeria, subtypes A, B, C, D, F2, G, J, and group O have been identified along with several CRFs in varying proportions [7–10]. The distribution of HIV-1 variants in Nigeria seems to differ based on geography, as subtype G is most prevalent in the north and CRF02_AG in the south [8, 11].

There are significant sequence differences in the structural and regulatory genes of different HIV-1 subtypes and recent research suggests that the variability among HIV groups, subtypes and CRFs carry functional biological differences [12]. Subtypes have been shown in previous studies to be associated with disease progression [10–14] and mother-to-child transmission of HIV [15]. Reports on the impact of HIV subtypes on response to antiretroviral therapy vary; majority of studies which showed that subtypes have no effect on outcomes once on antiretroviral were either cross-sectional studies or longitudinal studies of 24 months or less [16–22]. However, Scherrer et al in a cohort study (1996–2009) reported an improved virologic outcome in white patients with non-B subtype particularly subtypes A and CRF02_AG compared to subtype B [21]. Resistance rates among children has been reported to be higher for non-B subtypes than for B subtypes; however, in the same study, subtypes were not associated with virologic response at 24 and 48 weeks after initiation of treatment [19]. While De Wit et al, reported no difference in the proportion of patients with viral loads below 400 copies/mL at month 24 post-initiation of ART, they found a significant difference in the median CD4+ T cell increase at month 24 when data from subtype B and non-subtype B infected patients were compared [18]. Mortality has also been reported to be associated with subtype D compared to other subtypes, though this finding may be confounded by socio-demographic factors [23, 24].

The majority of studies examining association of HIV-1 subtype with patient outcomes have largely focused on subtype B, the commonest variant in the USA and Western Europe and one that represents less than 15% of HIV-1 infections worldwide. Few studies have