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Virological success in early treated HIV-infected infants: evaluation after 2 years of cART in the PEDIACAM study, Cameroon

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To our knowledge there are few data concerning the effect of socio-economic and familial environment on virological outcomes of cART in HIV-infected infants. In this study, we evaluated the probability of and identified factors associated with a first confirmed virological success (CVS) in HIV-infected infants within the first two years after cART start. We included 190 infants who started cART no later than age 12 months. The main outcome variable was time from cART initiation to a first confirmed virological success (CVS), defined as having plasma HIV RNA levels of <1000 copies/mL in two successive visits (3 months) on three successive visits (6 months). Time-to-event analysis was the primary method of analysis. Cumulative incidence of the outcome was calculated. Univariate and multivariable competing-risks regressions were fitted to assess association between the outcome and the exposure variables in the presence of competing death. In our study, cumulative incidence of CVS was 38.4% (73/190), almost all of these successes occurring before one year of cART (36.8%). Virological response was better in infants recruited in the Yaoundé sites (CHE and CME) than in the Douala site (HLD) (p=0.034). The likelihood of achieving a first CVS was unrelated to clinical, immunological, virological and other baseline socio-demographic characteristics of the infants (p>0.05). Socio-demographic characteristics are not a barrier to virological success in HIV-infected infants started on combined antiretroviral therapy in a low-resource setting with free of charge care system. Further studies are needed to understand the effect of healthcare provision system of health facilities on virological success in HIV-infected infants started on cART.

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Kynurenines inhibits the ability of memory CD4 T-cells to respond to IL-2 through generation of ROS during the primary HIV-1 infection

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The first months of HIV-1 infection are crucial for the establishment of the chronic phase of the infection and the disease progression. Indeed, the early infection is crucial for establishing the reservoirs and, thus, the chronic phase. The objective of this study is to analyse the underlying mechanisms responsible for reduced response of memory T-CD4 to IL-2 cytokine in early HIV infection involving deregulated metabolism. We demonstrate a clear correlation between the inflammation markers (sCD14, IL-6) of primary HIV-1-infected subjects (PHI) and the capacity of their T-CD4 to respond poorly to IL-2. This is validated by the lower level of induced phospho-STAT5 (pSTAT5) expression when compared to uninfected controls. Our results demonstrate that this impaired response to IL-2 results in the cell's inability to properly protect themselves from the Fas-mediated cell death. Moreover, we demonstrate that the reduced response to IL-2 in memory CD4 T-cells from PHI directly involves the generation of reactive oxygen species (ROS). Interestingly, we also show that it is possible to partially restore the cytokine response in memory CD4 T-cells from PHI by treating the cells with n-acetyl cysteine (NAC), an antioxidant. We recently showed that kynurenines, derived from tryptophan metabolism, are clearly responsible for inhibiting IL-2 response through the oxidative stress. Finally, our study also reveals that the administration of early antiretroviral treatment leads to the restoration of IL-2 response in these subjects. Our study provides for the first time a link between the impaired memory T-CD4, the oxidative stress and kynurenine production during the first months of HIV-1 infection. This work is currently in submission in *Journal of Clinical Investigation.*

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