

IgE serum level: A prognostic marker for AIDS in HIV-infected adults?

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During the course of HIV infection, increased atopic manifestations, including drug hypersensitivity, are reported. These manifestations may be explained by a dysregulated IgE production, reflecting a polyclonal B-cell activation. In cross-sectional¹ and case-control² studies, it has been suggested that IgE serum level might be a marker of HIV progression in adults. The objective of our study was therefore to determine whether baseline IgE serum level in HIV-infected adults is a prognostic marker of the progression to AIDS or death.

A prospective cohort of 113 HIV-1-infected adults was set up from 1992 to 1994 to study allergic-type reactions.³ Inclusion criteria were HIV-1 infection and consent to the study. On entry, as patients were asked about personal and familial histories of allergic events, clinical stage was recorded (1993 CDC classification), and a measurement of IgE (Pharmacia FEIA method) and CD4⁺ cell count (by flow cytometry) was performed. At the time of the study, plasma HIV-1 RNA level was not routinely performed. For IgE, a result lower than 150 KUI/L was considered as a normal value according to the threshold routinely used for non-HIV-infected patients.

Probability of death or progression to AIDS was estimated with the Kaplan-Meier method. A Cox model was used to estimate the independent effect of IgE on progression of HIV disease after adjustment for gender, age, clinical stage, CD4⁺ and CD8⁺ cell counts, hemoglobin level, prophylactic treatment of *Pneumocystis carinii* pneumonia, and antiretroviral therapy.

Among the 113 patients included, median age was 33 years (range, 22 to 70 years), and 76 patients (69.9%) were male. According to HIV transmission categories, 35 patients (31.0%) were either homosexual or bisexual, 35 (31.0%) were injecting drug users, 21 (18.6%) were heterosexual, 5 (4.4%) were either homosexual or bisexual

and injecting drug users, 5 (4.4%) were blood recipients, and 12 (10.6%) were undetermined. Forty-one (36.3%) patients were classified in CDC category A, 43 (38.0%) in category B, and 29 (25.7%) in category C. Median CD4⁺ and CD8⁺ cell counts were, respectively, 167/mm³ (range, 0 to 1328/mm³) and 707/mm³ (range, 34 to 3737/mm³). Median IgE was 43 KUI/L (range, 0 to 7720 KUI/L), and IgE concentration was higher than 150 KUI/L in 6 (21%) patients with AIDS (*n* = 29) and in 19 (23%) patients without AIDS (*n* = 84). IgE serum level was not associated with survival, even after adjustment for confounding factors. The median follow-up was 541 days (range, 1 to 1373 days). The 1-year mortality rate was 17.2% (95%CI = 11.4-27.5). Among patients without AIDS, the cumulative AIDS rate at 1 year was 10.8% (95%CI = 5.8-19.7). It was 6.2% (95%CI = 2.4-15.6) in patients with IgE levels of 150 KUI/L or less (*n* = 65) and 26.3% (95%CI = 11.9-52.1) in patients with IgE greater than 150 KUI/L (*n* = 19) (*P* = .007) (Fig. 1). In the multivariate analysis, IgE level was significantly associated with progression to AIDS when adjusted for age and CD4⁺ cell count. Adjusted relative hazard for IgE greater than 150 KUI/L compared with IgE of 150 KUI/L or less was 3.4 (95%CI = 1.2-9.3) (*P* < .02). Considering IgE as a continuous variable, each increase of 75 KUI/L was associated with a faster progression to AIDS (relative hazard = 1.06 [95%CI = 1.02-1.10], *P* = 10⁻³).

In our study a high serum level of IgE was significantly associated with a faster progression to AIDS. Vigano et al⁴ had already shown such a relationship between total IgE level and progression of disease in HIV-infected children. In a case-control study of 315 adult patients, Israël-Biet et al² reported that mean IgE serum level was significantly higher in patients with CD4⁺ cell count below 300/mm³ than in patients with higher CD4⁺ cell count. Lucey et al¹ reported also such a relationship in a cross-sectional study of 622 HIV-infected patients. Mean IgE serum level was significantly higher in patients with a CD4⁺ cell count lower than 200/mm³ than in others. Our results are consistent with these 2 previous studies. Moreover, the prospective design of our work confirms the prognostic value of IgE serum level on the progression to a clinical endpoint (ie, AIDS) and not only its relationship with the value of a surrogate marker.

To explain such a relationship between IgE serum level and progression to AIDS, Vigano et al⁴ suggested that the abnormal IgE synthesis might be explained by the switch from a T_{H1} to a T_{H2} cytokine profile during the course of HIV infection, which modifies IL production. IgE production could be stimulated by an increase in IL-4 production.⁵

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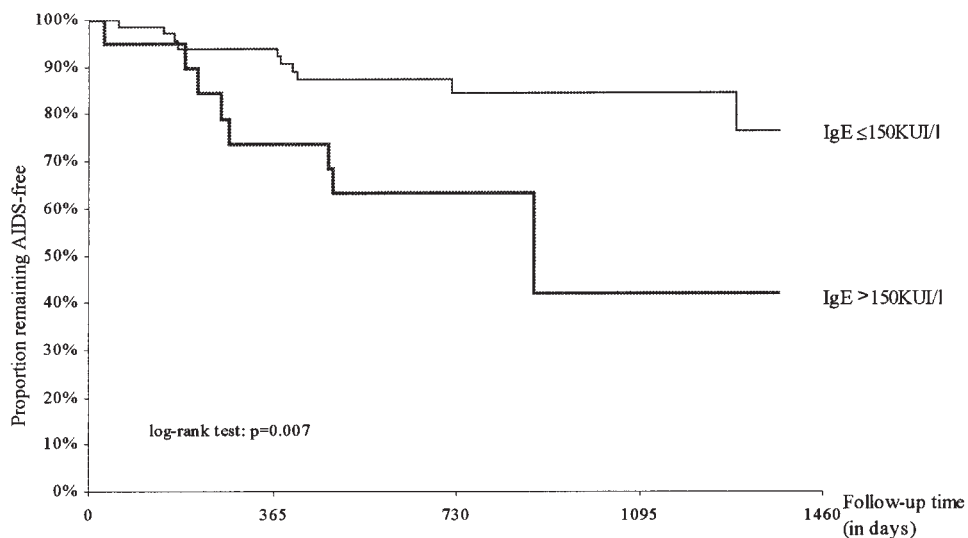


FIG. 1. Progression to AIDS according to baseline IgE serum level in 84 patients without AIDS.

Our inability to show a significant association between IgE and mortality might be explained by a short follow-up, which allowed us to show only an association with an earlier event.

In summary, IgE serum level measurement may be mentioned as an additional prognostic marker for the progression of disease in HIV-infected adults. Whether this relationship is maintained when adjusted for HIV-1 RNA level remains to be established.

REFERENCES

1. Lucey DR, Zajac RA, Melcher GP, Butzin CA, Boswell RN. Serum IgE levels in 622 persons with human immunodeficiency virus infection: IgE elevation with marked depletion of CD4+ T-cells. *AIDS Res Hum Retroviruses* 1990;6:427-9.
2. Israël-Biet D, Labrousse F, Tourani JM, Sors H, Andrieu JM, Even P. Elevation of IgE in HIV-infected subjects: a marker of poor prognosis. *J Allergy Clin Immunol* 1992;89:68-75.
3. Rancinan C, Morlat P, Chêne G, Saillour F, Guez S, Lacoste D, et al. Prevalence of allergic-type reactions during HIV infection course: a cross-sectional study of 115 patients. *Rev Med Interne* 1997;18:691-4.
4. Vigano A, Principi N, Crupi L, Oronato J, Gian Vincenzo Z, Salvaggio A. Elevation of IgE in HIV-infected children and its correlation with the progression of disease. *J Allergy Clin Immunol* 1995;95:627-35.
5. Gascan H, Gauchat JF, de Wall Malefyt R, Schneider P, Yssel H, de Vries JE. Regulation of human IgE synthesis. *Clin Exp Allergy* 1991;21(suppl 1):162-6.