# Prevalence, incidence and correlates of autoimmune diseases in people with HIV

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## BACKGROUND

The combination of immune dysfunction in people with HIV (PWH) and the development of inflammatory-autoimmune diseases (IADs) are apparently paradoxical yet very intriguing. Prevalence data on IADs in the ART era are diverging. Multiple systemic immune-inflammation scores have emerged as novel predictive markers of IADs. We. aimed to study the prevalence and incidence of IADs, determinants of IADs and role of inflammation markets on IADs onset,

## METHODS

We led a retrospective study on PWH followed in 1997-2023 in the ICONA cohort. We investigated the prevalence at enrolment and in follow-up and incidence of IADs. Adjusted Cox regression model (including age, calendar ART period, sex, CD4) was used to explore baseline determinants of time to IADs from ART start.

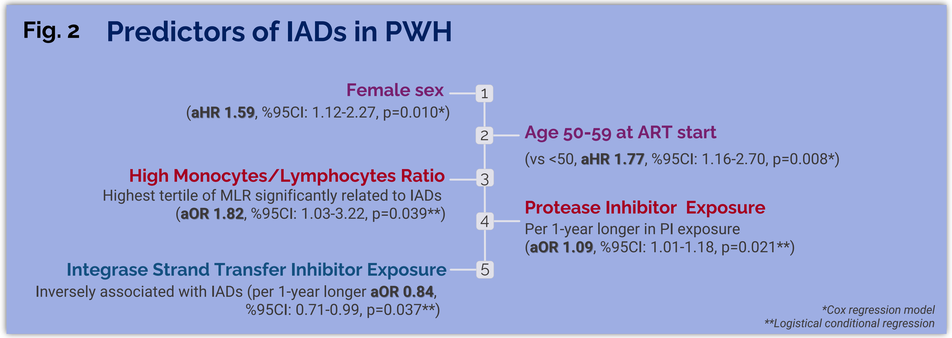
We used a nested case-control study comparing PWH with new diagnosis of IADs post-ART with up to 5 age-, sex- and ART duration-matched controls to investigate the roles on IADs onset of indirect markers of inflammation (divided by tertiles of distribution), current CD4, CD4/CD8, HIV-RNA and cumulative exposure to ART classes by adjusted conditional logistic models.

**Table . 1 Spectrum of IADs* observed in PWH**

| Condition | Percentage (%) |
|---|---|
| Psoriasis | 37.77 |
| Ulcerative colitis | 16.09 |
| Thyroiditis | 14.38 |
| Crohn's disease | 6.65 |
| Celiac disease | 4.51 |
| Vasculitis | 3.22 |
| Basedow's disease (Graves' disease) | 2.36 |
| Rheumatoid arthritis | 2.15 |
| Autoimmune hepatitis | 1.72 |
| Autoimmune thrombocytopenia | 1.50 |
| Multiple sclerosis | 1.50 |

*prevalence >1%*

**Fig. 2 Predictors of IADs in PWH**




## RESULTS

A total of 466 IADs were diagnosed in 449/20.495 PWH (2.2%,multiple IADs in 15 individuals). At enrolment, the median age in PWH with IAD was 40 years and 31.0% were female. The median CD4 count was 329 cells/μL [IQR: 109–548], 35.6% had CD4 levels<200 cells/μL, and the median CD4/CD8 ratio was 0.2 [IQR: 0.1-0.6]. The 24.4% of PWH with IAD presented an AIDS-defining condition at enrolment. The median HIV RNA level in this group was 41,051 copies/mL [IQR: 9,660–204,198].

Most PWH showed the IAD at enrolment (60%). Among observed IADs, psoriasis was the most reported disorder (38%), followed by autoimmune thyroiditis (16%), ulcerative colitis (14%) and Crohn's disease (7%) (Table 1). During follow-up, the prevalence of IADs among PWH increased from 1.4% in 1997-2002 to 2.5% in 2017-2023 (p<.001). A total of 143 new IADs occurred post-ART start with an incidence rate of 1.21/1000 PYFU [95%CI:1.02-1.43] and an estimated cumulative probability after 25 years of 2.6% (Fig.1).

In the adjusted Cox model, females (aHR 1.59, 95%CI:1.12- 2.27) and PWH aged 50-59 years at ART start (vs<50, aHR 1.77, 95%CI:1.16-2.70) had a higher risk of IAD (Fig.2).

In the adjusted nested case-control analysis, concentrations in the highest tertile of monocyte/lymphocyte ratio (MLR, aOR 1.82, %95CI: 1.03-3.22) and exposure to PI class (per 1-year more, aOR 1.09, %95CI: 1.01-1.18,) were significantly related to IADs, whereas INSTI was inversely associated (per 1-year more, aOR 0.84, %95CI: 0.71-0.99); low current CD4 count and CD4/CD8 ratio were marginally associated (Table 2, Fig. 2).

**Fig. 1 Cumulative probability of IAD on ART**

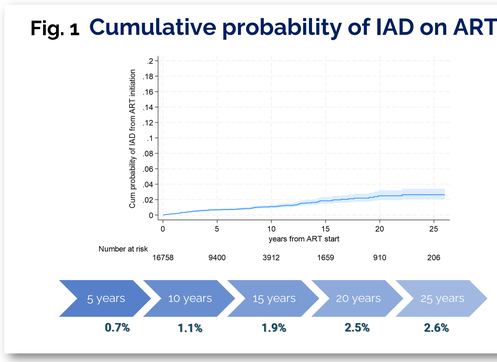



**Table 2. Predictive factors of new onset IADs by conditional logistic regression.**

| | AOR | 95%CI | p |
|---|---|---|---|
| **Pan Immune Inflammation Value[1]** | | | |
| T2 (vs T1) | 1.09 | 0.63-1.9 | 0.757 |
| T3 (vs T1) | 1.56 | 0.91-2.65 | 0.104 |
| **Systemic Immune-inflammation Index[1]** | | | |
| T2 (vs T1) | 0.78 | 0.45-1.34 | 0.364 |
| T3 (vs T1) | 1.25 | 0.75-2.06 | 0.391 |
| **Systemic Inflammatory Response Index[1]** | | | |
| T2 (vs T1) | 0.79 | 0.43-1.42 | 0.427 |
| T3 (vs T1) | 1.62 | 0.96-2.74 | 0.071 |
| **Neutrophils/lymphocytes ratio[1]** | | | |
| T2 (vs T1) | 0.95 | 0.55-1.61 | 0.839 |
| T3 (vs T1) | 1.59 | 0.96-2.63 | 0.069 |
| **Platelets/lymphocytes ratio[1]** | | | |
| T2 (vs T1) | 1.15 | 0.69-1.94 | 0.588 |
| T3 (vs T1) | 1.33 | 0.77-2.3 | 0.302 |
| **Monocytes/lymphocytes ratio[1]** | | | |
| T2 (vs T1) | 1.05 | 0.59-1.87 | 0.867 |
| T3 (vs T1) | 1.82 | 1.03-3.22 | 0.039 |
| **Neutrophils/monocytes ratio[1]** | | | |
| T2 (vs T1) | 1.1 | 0.64-1.91 | 0.728 |
| T3 (vs T1) | 0.91 | 0.51-1.61 | 0.744 |
| **CD4 <350 cells/mmc (vs >350)[2]** | 1.67 | 0.94-2.95 | 0.078 |
| **HIV-RNA >200 cps/ml (vs<=200)[3]** | 1.12 | 0.54-2.32 | 0.761 |
| **CD4/CD8, <1.00 (vs >=1.00)[4]** | 1.57 | 0.92-2.66 | 0.095 |
| **Cum. exposure PI, per 1-year more[5]** | 1.09 | 1.01-1.18 | 0.021 |
| **Cum. exposure INSTI, per 1-year more[5]** | 0.84 | 0.71-0.99 | 0.037 |
| **Cum. exposure NNRTI, per 1-year more[5]** | 0.96 | 0.9-1.03 | 0.250 |
| **Calendar year ART start, per 1-year more[6]** | 0.97 | 0.94-1 | 0.034 |

*Adjusted for: 1 current CD4, current HIV-RNA, calendar year ART, HIV-RNA ART start; 2 current CD4 and HIV-RNA, calendar year ART, HIV-RNA ART; 3 current HIV-RNA, CD4 ART, calendar year ART; 4 current HIV-RNA, CD4/CD8 ART, calendar year ART; 5 current CD4 and HIV-RNA, CD4 and HIV-RNA ART start, calendar year ART; 6 CD4 and HIV-RNA ART; Formulas: Pan Immune Inflammation Value: (neutrophils*platelets*monocytes)/lymphocytes; Systemic immune-inflammation index): (platelets*neutrophils)/lymphocytes; Systemic inflammatory response index): (neutrophils*monocytes)/lymphocytes; Abbreviation: T1 first tertile, T2 second tertile; T3 third tertile*

## CONCLUSIONS

IADs are a relatively rare comorbidity in PWH yet increasing in recent years. Females and PWH aged 50-59 have a higher risk of IADs, as occurring in general population.

High current MLR and -marginally- low current CD4 and CD4/CD8, as indicative of residual inflammation and immune dysregulation, are associated with IAD after ART.

The impact of different ART classes on IADs onset might be related to complex interplays between drug potency and toxicity and the persistent immune activation triggered by chronic HIV infection.

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