Polypharmacy is associated with neuronal injury in People with HIV (PWH)

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In older PWH, both **polypharmacy and recurrent falls associate with elevated levels of NfL and sCD14** after adjusting for comorbidities.



Background

Polypharmacy, or the use of five or more non-ART prescription medications, promote neurologic disorders and geriatric syndromes.

It is unknown if this is mediated by neuronal damage incurred by multiple medications, by inflammation, or by high comorbidity burden necessitating the use of multiple medications.

To better understand how polypharmacy influences neurologic disorder in people with HIV (PWH) we compared polypharmacy and biomarkers of neuronal injury and inflammation. To assess the clinical significance of this neuronal injury, these inflammatory biomarkers were analysed against gait speed and recurrent falls.

Methods

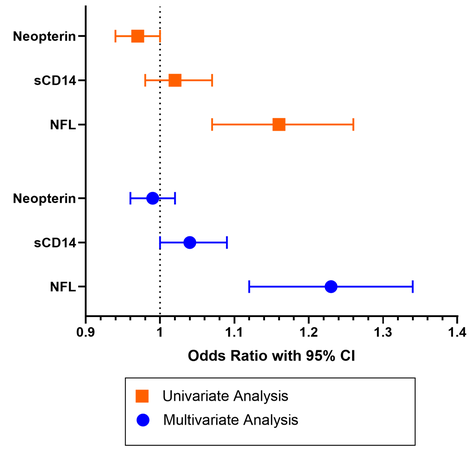
Data and specimens from 600 PWH of the longitudinal Advancing Clinical Therapeutics Globally (ACTG) A5322 (HAILO) study were included. Inclusion criteria were plasma HIV RNA below 200 cps/mL at study entry. Polypharmacy was defined as five or more non-ART prescription medications.

Neurofilament light chain (NfL) levels were quantified using a Quanterix single-molecule array assay (SIMOA) in duplicate. Neopterin was quantified by ELISA and soluble CD14 (sCD14) was assessed using a bead-based assay (Eve Tech).

Multivariable logistic regression analysis was utilized to assess the relationship between polypharmacy and NfL, sCD14, and neopterin (biomarkers of monocyte/microglial cell activation). This analysis was also used to analyse biomarkers and gait speed/recurrent falls. All biomarkers were analyzed as continuous variables.

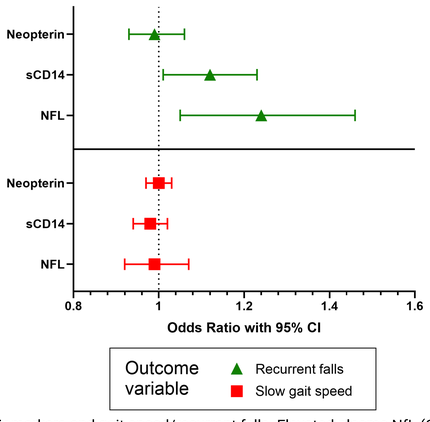
Results

Increased odds of polypharmacy with elevated plasma NfL and sCD14 in a multivariate analysis



In a univariate analysis, polypharmacy had an association with elevated plasma NfL (OR 1.23 [1.12, 1.34]) and sCD14 (OR 1.04 [1, 1.09]), but not neopterin. In multivariable analysis, after adjusting for age, sex, and comorbidity burden, polypharmacy had an association with elevated plasma NfL (OR 1.16 [1.07, 1.26]).

Increased odds of recurrent falls with elevated plasma NfL and sCD14 in a multivariate analysis.

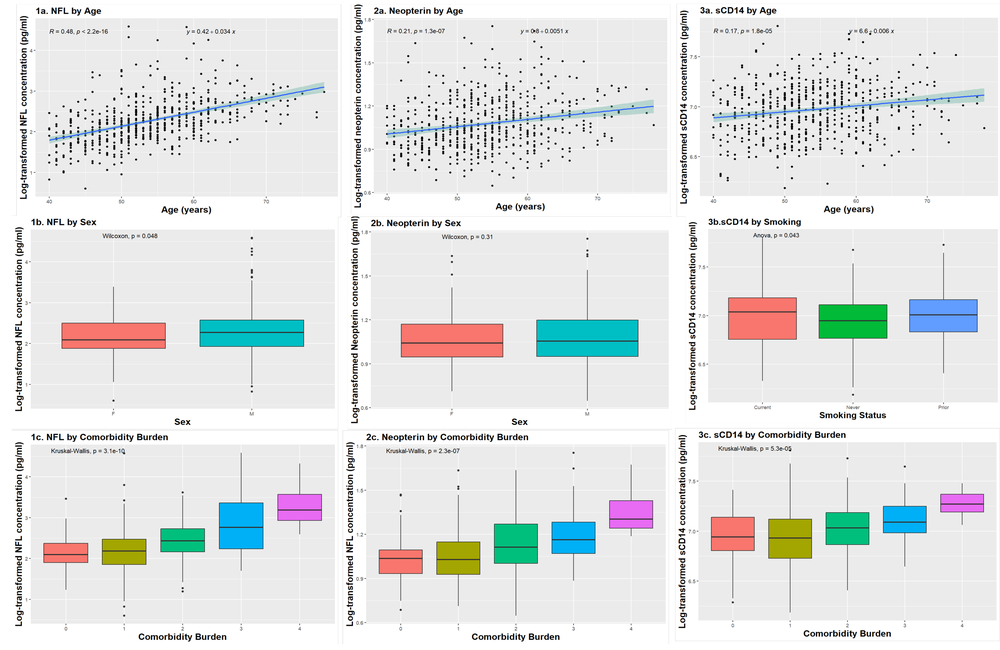


Multivariate analysis of biomarkers and gait speed/recurrent falls. Elevated plasma NfL (OR 1.26 [1.03, 1.54]) and plasma sCD14 (OR 1.13 [1.02, 1.25] were associated with recurrent falls (more than one fall in 6 months), but not with slow gait speed.

Clinical Characteristics of HAILO Participants

	Non-Polypharmacy (n= 368)	Polypharmacy (n= 232)	p-value
	Median value		
CD4 nadir at entry	198 cells/mm (72, 307)	191 cells/mm (46, 297)	.28
CD4/CD8 ratio	0.8629	0.8801	.46
Years on ART	8 (4, 12)	11 (7, 13)	**<.001**
	Number of participants		
Cardiovascular Disease	18 (5%)	33 (14%)	**.007**
T2 Diabetes Mellitus	45 (12%)	69 (30%)	**<.001**
Liver Disease	3 (0.8%)	6 (3%)	.12
Kidney Disease	38 (10%)	47 (20%)	**.007**
Peripheral Neuropathy	276 (75%)	198 (85%)	**.002**

Mediating Variables of Plasma Inflammation among Participants



Higher NfL was associated with increasing age, male sex, and comorbidity burden. Analyzed comorbidities were CVD, T2 diabetes mellitus, liver disease, kidney disease, and peripheral neuropathy. High neopterin was associated with age and comorbidity burden. Sex was included as a mediator in the analysis of neopterin due to previous literature supporting its interaction with plasma inflammation. Elevated sCD14 is associated with age, smoking status, and comorbidity burden.

Conclusion

In older PWH, both polypharmacy and recurrent falls associate with elevated levels of NfL and sCD14 after accounting for comorbidities that could influence the outcomes. These results support other data that polypharmacy contributes to neurologic disorders in older PWH. Medication management may improve brain health and geriatric syndromes in PWH.

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