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D-dimer and anti-coagulation activity markers in children and adolescents with HIV infection

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Purpose of the study

The SMART trial showed an increased risk of clinical events not-AIDS related in a large cohort of HIV-infected adults after antiretroviral treatment (ARV) interruption. Many of these events (cardiovascular, liver and kidney diseases) are associated with inflammation, immune activation and impaired fibrinolysis. A recent analysis showed that the increase of D-dimer, a marker of thrombosis, together with the elevation of other inflammatory markers, are related to the suspension of ARV and the consequent increase of HIV viral load; moreover, it showed an huge association between D-dimer levels and the risk of death [1].

HIV-infected children and adolescents, typically with perinatal transmission of the infection, have a long story of viral replication and could develop the same non-AIDS related alterations demonstrated in adults (metabolic syndrome or carotid intima medial thickness) associated with cardiovascular events. The aim of our study was to investigate in an HIV-infected pediatric population the prevalence and risk factors for the alterations of coagulation activation markers.

Methods

We performed a cross-sectional study among the cohort followed at Bambin Gesù Children's Hospital of Rome: between December 2007 and June 2008 we assessed for each patient D-dimer levels together with other coagulation and inflammation markers (antithrombin, protein C anticoagulant, protein S anticoagulant, C-reactive protein), and their relation with HIV-RNA load, CD4 count, clinical CDC classification, and current antiretroviral treatment. Patients with HBV or HCV co-infection were excluded.

Summary of results

Eighty-eight patients (59.1% females; 86.4% on cART) ranging from 3 to 25 years (mean age 13.6 years) were studied.

Table 1 shows the main results obtained. D-dimer results were significantly elevated in patients with HIV viral load >1000 cp/mL. The reduction of anticoagulant activity of C protein, S protein and antithrombin, similarly showed a strong relation with viral replication.

Conclusion

The higher anticoagulant activity present in symptomatic patients (CDC classification B and C) could be explained by the treatment, and its related viral suppression, more frequent in these subjects. No relation has been observed regarding C reactive protein levels. These preliminary data seem to confirm the same observation done in adult cohorts, but further studies are necessary to correlate such alterations with clinical events and to investigate the protective role of therapy in this particular population.

Table 1:

	Total	D-dimer (ng/mL) mean ± SD	p*	Protein C activity % ± SD	p*	Protein S activity % ± SD	p*	Antithrombin activity % ± SD	p*	C-reactive Protein (mg/dL) mean ± SD	p*
CDC classification N/A	27 (30,7%)	256 ± 169	>0.05	89,9 ± 20,4	**0,02**	74,4 ± 21,9	N.S.	107,2 ± 9,2	**0,002**	0,21 ± 0,37	>0.05.
classification B/C	61 (69,7%)	240 ± 170		103,1 ± 24,1		68,4 ± 20,1		116,1 ± 13,6		0,25 ± 0,35	
CD4% >25	68 (77,3%)	229 ± 136	>0.05.	100,5 ± 23.2	>0.05	74.1 ± 19.5	**0,001**	114,6 ± 13,2	**0,024**	0,23 ± 0,33	>0,05
<25	20 (22,7%)	297 ± 249		94.3 ± 25,4		57.2 ± 20,0		108,9 ± 11,5		0,27 ± 0,41	
HIV-RNA <1000	63 (71.6%)	206 ± 100	**0.024**	101,9 ± 26,0	**0,007**	75,3 ± 18,2	**0.0003**	115,5 ± 13,6	**0,005**	0,23 0,30	>0.05
(cp/mL) >1000	25 (28,4%)	341 ± 253		92,0 ± 14,7		57,6 ± 21,7		107,5 ± 9,2		0,27 0,47	

* Mann-Whitney Test

References

1. **Elevated levels of interleukin-6 and D-dimer are associated with an increased risk of death in patients with HIV. Lewis Kuller and SMART Study Group.** *CROI* 2008. Abstract 139