934 CYSTATIN C: A MARKER FOR INFLAMMATION AND RENAL FUNCTION AMONG HIV-INFECTED CHILDREN AND ADOLESCENTS

[1] A. Deyà-Martinez, [1]C. Fortuny, [2] P. Soler-Palacín, [4]O. Neth, [3]E. Sánchez, [2]A. Martín-Nalda, [4]L. Falcon-Neyra, [1]A. Vila, [1]A. Valls, [1]A. Noguera-Julian
[1]Hospital Sant Joan de Déu, Universitat de Barcelona; [2]Hospital Vall d'Hebron; [3]Universitat Ramon Llull, Barcelona, [4]Hospital Virgen del Rocío (Spain)

Clàudia Fortuny
Pg. Sant Joan de Déu 2
08950 Esplugues (Spain)
cfortuny@hsjdbcn.org
Phone: +34932804000
Fax: +34932033959

ABSTRACT

Background. *Renal disease is a leading cause of morbidity in HIV-infected adults in the HAART era. Cystatin C has been proposed as a more sensitive marker of renal function, but it may be affected by ongoing inflammation. We aimed to study Cystatin C levels in a cohort of HIV-infected pediatric patients at 3 Spanish centers.*

Methods. *Multicenter cross-sectional observational study. Renal function was assessed by means of first morning urine protein/creatinine and albumin/creatinine ratios and creatinine-estimated glomerular filtration rates (GFR), together with the following inflammation markers: Cystatin C, reactive C protein, beta-2-microglobulin and 25(OH)-vitamin D levels. A control group of healthy children and adolescents was used.*

Results. *Eighty-three patients (51 females, mean age 12.7 years) and 44 controls were included. Among the former, mean CD4 cell count was 860/mm³, 29 (35%) patients had a previous AIDS diagnosis, 73 (88%) were on HAART and HIV viremia was undetectable in 61 (73%). No differences in Cystatin C levels were observed between the two groups.*

In HIV-infected patients, Cystatin C levels correlated with GFR (r=-0.27; p=0.013), age at first HAART (r=-0.21; p=0.05), and beta-2-microglobulin (r=0.56; p<0.001). In multivariate analysis, lower GFR (p=0.014) and higher beta-2-microglobulin levels (p=0.001) remained as independent risk factors for higher Cystatin C values.

Conclusions. *Cystatin C values were associated with GFR and beta-2-microglobulin. Cystatin C may be useful as a marker of renal function in HIV-infected pediatric patients, independently of ongoing inflammation or viremia.*

Introduction

- Renal disease has become an important cause of morbidity in HIV-infected children in the HAART era.
- Cystatin C has been proposed as a more sensitive marker of renal function.
- Some studies conducted in HIV-infected adults suggest that Cystatin C is an inflammation marker. This could represent a bias when using Cystatin C in the evaluation of renal function in uncontrolled patients.
- Data on Cystatin C in HIV-infected pediatric patients are scarce.

Study objectives

- To determine Cystatin C levels in a cohort of HIV-infected children and adolescents and a group of healthy controls to evaluate how Cystatin C correlates with epidemiologic and renal function variables.
- To associated Cystatin C with HIV infection variables, and renal function and inflammation markers in the HIV-infected cohort.

Patients and Methods

Multicenter cross-sectional study

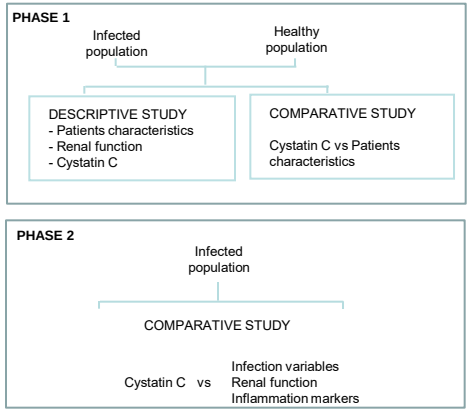
Inclusion criteria:
- HIV-infected children and adolescents aged up to 18 years.

Exclusion criteria:
- Previous renal disease.
- Previous thyroid disease or corticoid therapy.

Epidemiologic and medical history data were collected from medical charts.

Laboratory methods
- Blood sample was used to determine CD4+ cells count, HIV-RNA viremia, creatinine, reactive C protein, beta-2-microglobuline and Cystatin C.
- A urine sample to determine albumin/creatinine ratio and protein/creatinine ratio was collected too.
- Glomerular filtration rate was estimated from creatinine levels using Schwartz formula in patients aged up to 11y. and according to Cockroft-Gault formula in patients > 12y.

- **Study design**



Results

- **Main characteristics of infected and healthy patients**

Patient characteristics	HIV-infected patients N=83	Controls N=44	p
Female gender; n (%)	51 (61.4)	24 (54.5)	0.452
Black ethnicity; n (%)	11 (13.4)	2 (4.5)	0.125
Age (years); median (IQR)	13.4 (10.1-16.4)	11.5 (7.3-14.5)	**0.015**
BMI, Z-score; median (IQR)	-0.2 (-0.8 to 0.3)	0.04 (-0.5 to 1.2)	**0.03**
Renal function variables			
Abnormal albumin/creatinine ratio	7 (10.8)	5 (11.3)	0.787
Abnormal protein/creatinine ratio	13 (20.3)	4 (9.1)	0.207
GFR; median (IQR)	137 (124-150)	125 (118-145)	**0.036**
GFR < 90 mL/min/1.73m²	2 (2.4)	0 (0)	0.296
Cystatin C, mg/L; mean (SD)	0.87 (0.15)	0.88 (0.12)	0.881

- **Descriptive analysis of HIV infected cohort**

Patient characteristics	HIV-infected patients N=83
Age at HIV infection diagnosis (years); median (IQR)	0.7 (0.2-2.6)
AIDS diagnosis; n (%)	29 (34.9)
Hepatitis B virus co-infection; n (%)	1 (1.2)
Hepatitis C virus co-infection; n (%)	1 (1.2)
Inflammatory variables	
Cystatin C, mg/L; mean (SD)	0.87 (0.15)
Abnormal beta-2-macroglobulin; n (%)	9 (10.8)
Abnormal vitamin D; n (%)	59 (71.1)
CRP, mg/L; median (IQR)	1.1 (0.6-2.4)

Patient characteristics	HIV-infected patients N=83
Details on previous ARV therapies	
Prior tenofovir use; n (%)	22 (26.5)
Prior indinavir use; n (%)	2 (2.4)
At assessment:	
Naïve; n (%)	5 (6.0)
Tenofovir use; n (%)	28 (36.4)
HAART regimen including a PI; n (%)	49 (63.6)
CD4 cells/mm³; median (IQR)	860 (610-1200)
Undetectable HIV viremia; n (%)	61 (73.5)

Comparative analysis: cystatin C vs HIV infection variables

- None of the patients in either groups presented abnormal levels of Cystatin C
- Among HIV-infected patients, higher Cystatin C levels were observed in:
  Naïve (0.95 vs 0.87; p= 0.019)
  HAART regimen based in IP (0.88 vs 0.82; P=0.06)

Comparative analysis: cystatin C vs renal function

- A negative correlation with glomerular filtration was observed (r= -0.27; p=0.013)
- No relation between Cystatin C and albuminuria or proteinuria was observed.

Comparative analysis: cystatin C vs inflammation activity

- A strong positive correlation between beta-2-microglobuline and Cystatin C was observed (r=0.56; p< 0.001)
- No other relations were observed.

Mutivariate analysis

	Beta coefficient	95% CI	p
HAART regimen including a PI	0.032	-0.032 to 0.097	0.317
Age at first HAART (years)	0.002	-0.009 to 0.009	0.995
Undetectable HIV viremia	-0.012	-0.089 to 0.065	0.752
Estimated glomerular filtration rate	-0.001	-0.002 to 0.000	0.027
Beta-2-microglobulin values	0.105	0.044 to 0.165	0.001

In the multivariate analisys, Cystatin C remained significantly associated with An beta-2-microglobulin levels and GFR values.

Conclusions

- Neither infected children nor healthy controls presented abnormal levels of Cystatin C.
- In our cohort of well controlled HIV infected children, Cystatin C remained as a good renal marker independently of ongoing inflammation.