Poster Number: H-2310

METABOLIC PROFILE AND CARDIOVASCULAR RISK FACTORS IN LATIN AMERICAN HIV-INFECTED PATIENTS RECEIVING HAART

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ABSTRACT

Background: Metabolic abnormalities (MA) and increased cardiovascular risk (CR) are well known complications of HAART. The prevalence of these conditions is not well known in Latin America, however the incorporation of preventive measures to reduce CR are very important and desirable in regional and national guidelines.

Methods: A longitudinal study evaluating MA and associated treatment practices to reduce CR has been conducted in seven Latin American countries (RAPID II study). Adult HIV patients with at least six months of HAART were enrolled. Baseline data are presented in this analysis.

Results: A total of 4010 patients were enrolled. Mean age (SD) was 41.9 (10) years; median time on HAART (IQR) was 25 months (10-51), 44% received protease inhibitors. Median CD4 cell count was 417 (266-621) cells/mm^3, and mean viral load (SD) was 2.4 (1.0) log$_{10}$ copies/ml. The prevalence of dyslipidemia and metabolic syndrome was 80.2%, and 22.8%, respectively. Both were homogeneously distributed across countries. The overall prevalence of type 2 diabetes mellitus was 3.3%, lower than that of the general population in Latin America, but was not evenly distributed. The mean overall 10-year CR (SD), as measured by the Framingham risk factor score (FRF) was intermediate at 10.4 (24.7), and was also not uniformly distributed, with 10.2% of patients belonging to the highest risk category. Longer exposure to HAART correlated with dyslipidemia, metabolic syndrome, diabetes mellitus and 10-year CR. In contrast to females, males had more dyslipidemia, high blood pressure, smoking habit, higher FRF, but lower prevalence of metabolic syndrome, abnormal waist circumference and obesity.

Conclusions: Dyslipidemia and CR are prominent and higher in males compared to females in this cohort of HAART treated patients. Careful attention to the management of lipid disorders is needed to reduce CR in these settings.

INTRODUCTION

- Beneficial effects of HAART are currently being offset by its long-term complications of therapy
- Dyslipidemia, changes in body composition, insulin resistance and glucose intolerance, mineral bone disease and lactic acidosis are recognized long-term complications of HAART
- Current evidence suggests that patients on HAART are at increased risk of developing cardiovascular disease (CVD)
- Scaling-up HAART programs have been implemented in almost all Latin American countries
- A similar trend in metabolic complications and increased CVD risk is also expected in the region, but no information is available on these issues
- Baseline data from the RAPID II study is analyzed to evaluate the prevalence of metabolic derangements and CVD risk among Latin American HIV-infected patients on HAART

METHODS

- **STUDY DESIGN:** The RAPID II study (Registry and Prospective Analysis of Patients Infected with HIV and Dyslipidemia) is a cohort web-based designed to prospectively collect information on metabolic parameters and treatment modalities among Latin American HIV-infected patients on HAART
- **SETTING:** Health-care centers from seven Latin American countries; Argentina, Brazil, Chile, Colombia, Ecuador, Peru and Venezuela
- **SELECTION OF SUBJECTS:**
  - **INCLUSION CRITERIA:**
    - Adult patients of both gender receiving ambulatory care
    - Confirmed HIV infection
    - HAART for at least one month prior to enrollment
    - A lipid profile assessed within one-month of enrollment
  - **EXCLUSION CRITERIA:**
    - Informed consent not granted
    - Enrollment in a clinical trial within one month before enrollment
- **PROCEDURES:**
  - Interview at enrollment to obtain:
    - Demographic data
    - Time living with HIV, time on HAART, previous use of ARVs
    - History of cardiovascular risk factors: high blood pressure, diabetes mellitus, dyslipidemia, metabolic syndrome, prior treatment for these conditions, smoking habit, exercising and diet, history of CVD, and family history of CVD
  - Complete physical examination, body mass index and waist circumference determinations
  - Laboratory evaluations: fasting glucose, total cholesterol, HDL-cholesterol, LDL-cholesterol, tryglicerides, liver enzymes, creatinine phosphokinase, CD4 cell count and viral load determination at enrollment, and every six months thereafter for a total follow-up of two years
- **EVALUATION OF OUTCOMES:**
  - Main outcomes are the baseline evaluation of metabolic parameters and CVD risk, and subsequent evaluation of cardiovascular events and lipid lowering behaviors of treating physicians during a 2-year follow-up period
  - Metabolic syndrome was defined following ATP-III criteria
  - CVD risk was estimated using the Framingham risk score algorithm
- We report here baseline, pre-lipid-lowering intervention data only

RESULTS

- A total of 4010 patients were recruited from November 2006 to September 2007; Argentina (1015 pts), Brazil (1001 pts), Venezuela (807 pts), Colombia (474 pts), Peru (417 pts), Ecuador (252 pts) and Chile (44 pts).
- Distribution of patients by age, gender and country is shown in Figures 1 and 2.
- Demographic, anthropometric and serum biochemical parameters are shown in Table 1.
- HIV related characteristics are shown in Table 2. NNRTI based HAART predominated.
- The metabolic profile is shown in Table 3. Dyslipidemia was highly prevalent and driven by hipertrygliceridemia (55.8%) and low-HDL (49.5%) serum levels.
- Time on HAART correlated with dyslipidemia (35.1 vs. 31.6 months, p=0.0034), type 2 diabetes mellitus (48.4 vs. 33.9, p<0.001) and metabolic syndrome (39.4 vs. 33.1, p<0.001).
- The 10-year CVD risk as measured by the Framingham risk score was intermediate at 10.4%, but increased with exposure to HAART; 0.09 increase per month of HAART, p<0.001
- Gender differences in metabolic parameters and CVD risk were observed, Table 4.
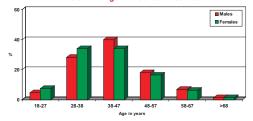
FIGURE 1. Age and Gender Distribution
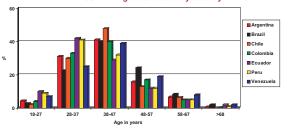

FIGURE 2. Age Distribution by Country

TABLE 2. HIV Related Characteristics*

Characteristic	Argentina (n=1015)	Brazil (n=1001)	Chile (n=44)	Colombia (n=474)	Ecuador (n=252)	Peru (n=417)	Venezuela (n=807)	Overall (n=4010)
Time on HAART, months[‡]	23 (9-49)	40 (16-77)	24.5 (9-43)	23 (9-40)	19 (9-35)	18 (7-27)	27 (10-55)	25 (10-51)
NNRTI-based HAART, %[§]	61.9	51.8	81.8	58.9	70.6	71.7	38.2	56.0
PI-based HAART, %[§]	36.2	51.4	20.0	38.0	30.6	31.9	61.5	44.0
Cd4 cell count, cells/mm[‡]	447 (280-661)	474 (329-677)	362 (220-537)	390 (272-589)	363 (262-544)	255 (177,376)	452 (285-661)	417 (266-621)
Viral load, log$_{10}$ copies/ml	2.1 (1.0)	2.3 (0.9)	2.2 (0.9)	2.2 (0.9)	2.7 (0.8)	2.8 (0.9)	2.4 (1.1)	2.4 (1.0)

* Values are mean (SD) unless noted otherwise
[‡] Median (IQR)
[§] NNRTI: non-nucleoside reverse transcriptase inhibitor, PI: protease inhibitor

TABLE 3. Metabolic Profile and Cardiovascular Risk Factors*

Characteristic	Argentina (n=1015)	Brazil (n=1001)	Chile (n=44)	Colombia (n=474)	Ecuador (n=252)	Peru (n=417)	Venezuela (n=807)	Overall (n=4010)
Older age	23.2	33.1	22.7	26.6	17.5	18.0	30.2	26.6
Smoking habit	34.1	22.1	50.0	18.9	10.3	15.6	18.2	22.8
High blood pressure	39.2	39.2	25.0	15.6	25.0	14.6	32.7	31.5
Abnormal waist circumference	7.1	7.5	4.6	2.1	6.4	3.6	7.4	6.2
Dyslipidemia	78.5	79.3	90.9	82.1	84.5	67.9	86.9	80.2
Type 2 diabetes	2.7	6.1	6.8	0.8	2.0	1.7	3.4	3.3
Lack of exercise	46.8	57.9	59.1	63.9	61.1	28.5	60.2	53.4
Obesity	8.2	9.1	2.3	3.4	8.7	6.5	9.5	7.9
Metabolic syndrome	23.0	21.5	20.0	11.7	19.0	44.8	14.9	22.8
Framingham risk score[†]	9.8 (23.5)	14.2 (30)	13.8 (28.3)	5.6 (13.5)	5.8 (17.7)	6.1 (18.3)	12.6 (27.5)	10.4 (24.7)
High risk patients	9.5	14.2	15.9	5.5	5.6	6.5	12.1	10.2

* Values are %
[†] Mean (SD)

TABLE 1. Demographic, Anthropometric and Serum Biochemical Parameters*

Characteristic	Argentina (n=1015)	Brazil (n=1001)	Chile (n=44)	Colombia (n=474)	Ecuador (n=252)	Peru (n=417)	Venezuela (n=807)	Overall (n=4010)
Age, y	41.6 (9.3)	44 (9.8)	40.6 (9.1)	40.8 (9.4)	39 (10.5)	39.1 (9.9)	42.6 (10.7)	41.9 (10)
Male gender, %	70.4	65.4	90.9	86.7	77.8	70.7	80.9	73.9
Body mass index, kg/m^2	24.8 (3.7)	24.8 (3.9)	24.8 (2.7)	23.4 (3.1)	24.4 (3.7)	24.7 (3.6)	25 (3.9)	24.6 (3.8)
Waist circumference, cm	87.9 (11.1)	88.9 (11.2)	85.3 (9.8)	84.6 (8.5)	86.1 (12.9)	86.5 (9.8)	88.6 (10.7)	87.6 (10.8)
Systolic blood pressure, mmHg	119.9 (15.4)	121.6 (15.3)	112.7 (18.4)	114.9 (9.7)	116.1 (16.1)	110.7 (12.3)	119.1 (13.3)	118.3 (14.6)
Glucose, mg/dl	92.8 (26.9)	97.1 (25.1)	83.4 (26.2)	91.9 (14.1)	95.6 (21.1)	80.9 (18.0)	92.1 (18.8)	92.4 (22.9)
Triglycerides, mg/dl	201.2 (201.6)	192.7 (153.3)	202.7 (129.4)	243.1 (165.3)	233.3 (229.2)	251.7 (191.8)	174.5 (192.9)	214.6 (188.4)
Total cholesterol, mg/dl	196.2 (46.9)	194.7 (44.2)	195.6 (57.1)	206.6 (49.7)	200.6 (66.0)	191.8 (57.9)	192.9 (52.7)	196.2 (50.7)
HDL-cholesterol, mg/dl	45.6 (15.0)	45.9 (14.1)	39.7 (12.2)	45.9 (13.7)	44.5 (13.1)	45.1 (5.3)	40.7 (13.0)	44.6 (13.5)
LDL-cholesterol, mg/dl	113.5 (46.5)	108.9 (41.7)	110.1 (48.5)	114.1 (42.9)	114.9 (44.0)	104.8 (39.4)	106.3 (46.3)	110.1 (44.1)
ALT, IU/l	29.5 (32.0)	29.3 (19.7)	22.2 (9.3)	32.9 (27.5)	34.2 (22.7)	26.7 (18.6)	28.9 (20.6)	29.5 (24.5)

* Values are mean (SD) unless noted otherwise

TABLE 4. Gender Comparison of Metabolic and Cardiovascular Disease Risk*

Characteristic	Male patients (n=2963)	Female patients (n=1047)	P Value
Mean age (SD), years	42.2 (9.9)	40.8 (10.3)	<0.001
Abnormal waist circumference	9.7	36.7	<0.001
Obesity	6.6	11.8	<0.001
Current smoking	25.0	16.7	<0.001
Lack of exercise	51.7	58.5	<0.001
High blood pressure	34.3	23.5	<0.001
Dyslipidemia	81.3	77.3	<0.001
Metabolic syndrome	19.4	22.7	0.020
Type 2 diabetes	3.7	3.3	0.631
Mean Framingham risk score (SD)	11.4 (24.7)	7.5 (24.6)	<0.001
High risk category for cardiovascular disease	11.1	6.8	<0.001

* Values are % unless noted otherwise

CONCLUSIONS

- Dyslipidemia is highly prevalent compared to that reported from developed countries (80.2% vs. 45%), and it is associated with duration of exposure to HAART.[1-2]

- The prevalence of type 2 diabetes mellitus is lower than that of the general population in Latin America (3.3% vs. 4-8%).[3]

- The overall prevalence of metabolic syndrome is comparable to that reported from developed countries (22.8% vs. 14-25%).[4,5]

- The 10-year CVD risk is intermediate but higher than that reported from the USA, Italy, Norway and Spain (10.4% vs. 6-7.4%)[6-8]

- Male patients have higher CVD risk than females

- Interventions to reduce the CVD risk in the region should focus on treating dyslipidemia and other modifiable risk factors, and change of HAART regimens when needed

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ACKNOWLEDGEMENTS