

Increased risk of virological failure to the first antiretroviral regimen in HIV-infected migrants compared to natives: data from the ICONA cohort



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Background

Migrant populations in Europe are disproportionately affected by HIV compared to natives: in fact, according to the European Center for Disease Control, in the period 2007-2011, 39% of all new cases of HIV infection were registered in foreign patients.

In Italy the proportion of non-nationals among the new HIV cases increased from 11% of all cases in 1992 to a maximum of 32% in 2006; in the last available 2012 report, migrants represent a quarter (25.7%) of all subjects newly diagnosed with HIV, with a median incidence of HIV infection of 22.3 in migrants compared to 5 per 100.000 in Italian-born subjects.

Migrants have higher rate of late presentation compared to native-born individuals, thus suggesting barriers to health service access, responsible for delayed HIV testing, linkage of care and antiretroviral therapy (ART) initiation. This risk is particularly high for illegal immigrant patients.

Data regarding the probability of response to ART in migrant patients compared to natives are still scarce and at least in part controversial. However, differences in viral characteristics (HIV-1 subtype, co-receptor tropism, rate of transmitted drug resistance), host genetic factors (such as frequency of HLA B5701 status), epidemiology of other concomitant infections and co-morbidities, and different profiles of tolerability and side effects, might determine disparities in virological response to ART in the immigrant population compared to native patients.

Objectives

Aim of the study was to evaluate possible disparities in access and/or risk of failure to the first ART regimen for migrants compared to Italian-born patients and to assess determinants of failure for migrants living with HIV.

Methods

All native and migrant naïve patients enrolled in the ICONA cohort in 2004-2014 were included.

Firstly, variables associated to ART initiation were analyzed.

In a second analysis, the primary endpoint was time to failure after at least 6 months of ART, defined as:

- virological failure (VF: first of two consecutive viral load >50 and >200 copies/ml),
- treatment discontinuation (TD) for any reason,
- treatment failure (TF: confirmed VL>200 cp/ml or TD).

A Poisson multivariable analysis was performed to control for confounders.

Results (1)

Baseline characteristics

A total of 5777 HIV-pos ART-naïve patients (1179 migrants and 4598 natives) were evaluated.

Most migrants were from Sub-Saharan Africa (35.3%) and South-Central America/Caribbean (29%).

Median duration of residency in Italy was 5 years (IQR 1-10).

Baseline characteristics significantly differed between the two groups (Table 1); in particular, lower CD4 counts and higher frequency of AIDS events were observed in migrants vs natives.

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Table 1. Characteristics of migrant and native-born HIV-positive antiretroviral naive patients enrolled in the ICONA cohort during the period 2004-2014 at time of inclusion.

	Migrants n=1179	Natives n=4598	P value
Total n=5777			
Male gender, n(%)	674 (57.2%)	3914 (85.1%)	<0.001
Age, yrs, median (IQR)	34 (28-40)	39 (32-47)	<0.001
Education, n(%)			<0.001
less than high	355 (30.1%)	1075 (17.3%)	
high	309 (26.2%)	1980 (43.1%)	
missing	515 (43.7%)	1543 (33.6%)	
Employment, n(%)			<0.001
full employed	444 (37.7)	2786 (60.5%)	
occasionally employed	99 (8.4%)	78 (1.7%)	
unemployed	353 (30.0%)	554 (14.5%)	
other/missing	229 (19.4%)	1180 (25.7%)	
Mode of HIV transmission, n(%)			<0.001
heterosexual	703 (59.6%)	1634 (35.5%)	
homosexual	312 (26.5%)	2194 (47.7%)	
IVDU	48 (4.1%)	436 (9.5%)	
other/unknown	116 (9.8%)	334 (7.3%)	
Recent drug use, n(%)			0.005
no	904 (76.7%)	3352 (72.9%)	
yes	21 (1.8%)	149 (3.2%)	
unknown	254 (21.5%)	1097 (23.9%)	
Smoke, n(%)			<0.001
no	677 (57.4%)	1757 (38.2%)	
yes	252 (21.4%)	1780 (38.7%)	
unknown	250 (21.2%)	1061 (23.1%)	
Pregnancy status, n(%)	51 (4.3%)	17 (0.4%)	<0.001
HIV subtype, n(%)			<0.001
B	203 (17.2%)	1344 (29.2%)	
Non-B	218 (18.5%)	316 (6.9%)	
unknown	758 (64.3%)	2938 (63.9%)	
First HIV RNA (per 1 log cp/mL more)	4.5 (IQR 3.7-5.2)	1.6 (IQR 3.9-5.2)	0.066
First CD4 count (per 100 cell/mm ³ more)	317 (IQR 137-509)	396 (223-577)	<0.001
First CD4, cell/mm ³			0.003
<200	324 (27.5%)	876 (19.1%)	
200-350	226 (19.2%)	732 (15.9%)	
>350	440 (37.3%)	2197 (47.8%)	
missing	189 (16.0%)	793 (17.3%)	
AIDS event pre-treatment, n(%)	140 (11.9%)	362 (7.9%)	<0.001
HCV co-infection, n(%)			<0.001
positive	71 (6.0%)	446 (9.7%)	
negative	794 (67.3%)	2882 (62.7%)	
unknown	314 (26.6%)	1270 (27.6%)	
HBV co-infection, n(%)			0.008
positive	58 (4.9%)	144 (3.1%)	
negative	785 (66.6%)	3060 (66.6%)	
unknown	336 (28.5%)	1394 (30.3%)	
CMV co-infection, n(%)			<0.001
positive	492 (41.7%)	1579 (34.3%)	
negative	45 (3.8%)	246 (5.3%)	
unknown	642 (54.4%)	2773 (60.3%)	

Results (2)

ART initiation

Migration was not associated with the probability to initiate ART by univariate analysis. However, when adjusting for CD4 count and other baseline confounders, migrants presented a lower chance to initiate ART compared to natives (OR 0.78, 95% IC 0.65-0.93, p=0.006) (Table 2).

Table 2. Variables associated with ART initiation by multivariate analysis

Multivariate Analysis	OR	95% CI	P value	
•Age (for 10 yr increase)	1.01	1.01	1.02	0,001
•Migrants vs Natives	0.78	0.65	0.93	0.006
•Mode of HIV transmission				
Heterosexual	1.00			
Homosexual	0.78	0.66	0.93	0.004
IVDU	0.64	0.48	0.84	0.001
•Baseline CD4 count /mmc				
<200	1.00			
200-350	0.68	0.49	0.94	0.019
>350	0.15	0.11	0.19	<0.001
• Baseline Log ₁₀ HIV-RNA basale				
<4	1.00			
4-4.99	1.38	1.17	1.62	<0.001
>=5	2.39	1.93	2.96	<0.001
• AIDS event pre-treatment	2.36	1.64	3.39	<0.001
• Pregnancy status	5.75	2.40	13.82	<0.001

Results (3)

Response to ART

After ART initiation, the incidence rate of VF >50 cp/ml was 15.5 per 100 person-years (95%CI 12.8-18.8) in migrants and 8.9 in natives (95%CI 7.9-9.9), the incidence rate of TF was 44.7 per 100 person-years (95%CI 40.3-49.7) in migrants and 33.2 in natives (95%CI 40.3-49.7), respectively.

Multivariable analysis confirmed that migrants had a significantly higher risk of VF, both >50 cp/ml (OR 1.50, 95%CI 1.17-1.193, p=0.001) and >200 cp/ml (OR 1.59, 95%CI 1.23-2.05, p<0.001), and of TF (OR 1.15, 95%CI 1.00-1.32, p=0.045), while no difference was observed in TD risk (Figure 1)

Figure 1. Cumulative probability of virological failure (1a) and treatment failure (1b) (Kaplan Meier method)

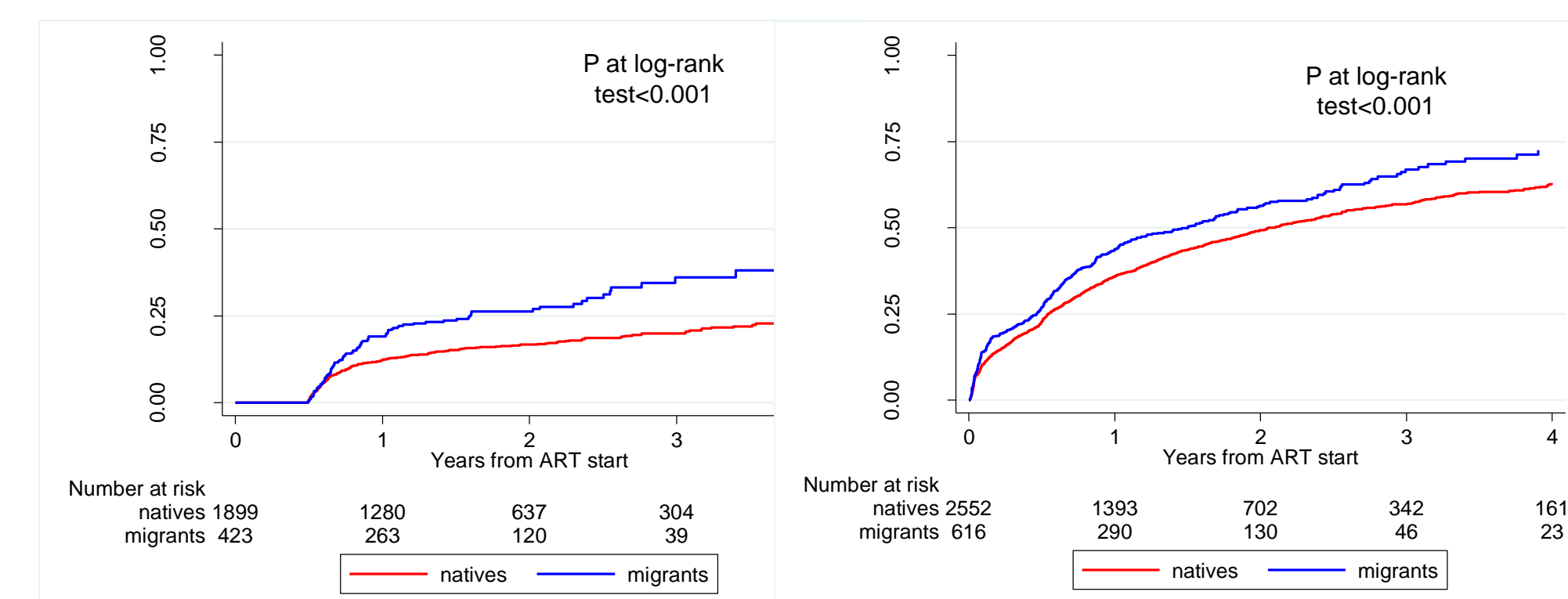


Table 3. Variables associated with VF>50 cp/ml by multivariate analysis

Multivariate Analysis	OR	95% CI	P value	
•Age (for 10 yr increase)	1.01	1.01	1.02	0,001
•Migrants vs Natives	0.78	0.65	0.93	0.006
•Mode of HIV transmission				
Heterosexual	1.00			
Homosexual	0.78	0.66	0.93	0.004
IVDU	0.64	0.48	0.84	0.001
•Baseline CD4 count /mmc				
<200	1.00			
200-350	0.68	0.49	0.94	0.019
>350	0.15	0.11	0.19	<0.001
• Baseline Log ₁₀ HIV-RNA basale				
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>=5	2.39	1.93	2.96	<0.001
• AIDS event pre-treatment	2.36	1.64	3.39	<0.001
• Pregnancy status	5.75	2.40	13.82	<0.001

Results (4)

Determinants of failure in migrant patients

Among migrants, variables associated with a higher VF risk were age (for 10 yr increase, OR 0.96, 95% CI 0.93-0.98, p=0.002), unemployment (OR 1.96, 95% CI 1.20-3.20, p=0.007) and use of a boosted PI based-regimen (OR 2.04, 95% CI 1.25-3.34, p=0.005 vs NNRTI-based).

Conclusions

Despite the use of more potent and safer antiretroviral drugs in the last ten years, and even in a setting of universal access to ART, migrants living with HIV still present barriers to ART initiation and increased risk of virological failure compared to natives.

This information can help clinicians to adopt strategies for improving the management of this patient population.

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